Marriott Frenchman’s Reef
St. Thomas, U.S.V.I.

Technological Innovations: Benefits, Costs, and Impact on Training and Practice

President: Elin R. Sigurdson, MD, PhD; Fox Chase Cancer Center
Program Chair: Sue S. Yom, MD, PhD; University of California, San Francisco

www.americanradiumsociety.org/ars-96th-annual-meeting/
Technological Innovations: Benefits, Costs, and Impact on Training and Practice

Proceedings of the 96th Annual Meeting of the American Radium Society

APRIL 26–APRIL 29, 2014
MARriott FRENCHMAN’S REEF
ST. THOMAS, USVI

PROCEDINGS
LEARNING OBJECTIVES

At the conclusion of this event, attendees will be able to:

1) Describe the interaction of large-scale clinically oriented cancer databases and biorepositories and their projected future impact on day-to-day clinical practice.

2) Direct care for patients with concerns of the skull base in a multispecialty environment.

3) Direct care for patients with rectal and anal cancers and help determine the role of individualized therapies for each patient.

4) Identify barriers to patient-oriented decision making in cancer care.

5) Recognize best practices in cost containment and quality assurance from around the world and when/how such technologies are best applied.
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ROOM ASSIGNMENTS

Exhibit Hall and Poster Session Harbour I
General Sessions Harbour II & III
Hospitality Suite Beacon Lounge
Meet the Professor Luncheons Island Rooms I & II
Tumor Board Luncheons Harbour IV
Presidential Categorical Session Harbour II & III
Registration Grand Harbour Foyer
Speaker Ready Room West Indies Board Room
Welcome Reception Harbour I
Social Event Main Pool

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New Membership Application

APPLICATION FOR MEMBERSHIP

APPLICATION DATE: ____________________

PLEASE ACCEPT MY APPLICATION FOR THE FOLLOWING MEMBERSHIP CATEGORY (CHECK ONE):

- **ACTIVE** – Active membership may be held by physicians and allied scientists:
  - **Physicians** Graduates of recognized medical colleges; adequate formal training and ongoing practice in those branches of medicine and surgery that are closely allied in the management of cancer; must be certified by a medical or surgical board that governs their area of specialty or have equal qualifications acceptable to the Membership and Credentials Committee. If there is an oncology board in their specialty, they must be certified by that subspecialty board or provide evidence of oncologic qualifications; must have published in peer-reviewed journals or have made a single contribution to science, in keeping with the criteria of the Membership and Credentials Committee.
  - **Allied scientists** shall be graduates of recognized graduate schools and have qualifications acceptable to the Executive Committee of this Society. They shall have adequate formal training, ongoing professional experience, and clinical or academic contributions in the oncologic sciences. They must have published in peer-reviewed journals or have made a single contribution to science, in keeping with the criteria of the Membership and Credentials Committee. Membership Dues: $190 paid at time of application; upon acceptance will be applied to first year’s dues. Thereafter $275 per year.

- **CANDIDATE** – Candidate membership may be held by physicians and allied scientists. These members will be non-voting members:
  - **Physicians** shall be graduates of a recognized medical college and be enrolled in an oncology training program (surgical, radiation, medical, gynecologic.)
  - **Allied scientists** shall have corresponding qualifications; eligible for Active membership upon completion of training and board certification as described for active membership. Their membership status shall exist until the candidate is selected for Active membership or until no more than two years have passed since board certification. Candidate membership shall be terminated three years from the completion of their training program, unless they have paid the dues as an Active member. No annual dues.

- **MEDICAL STUDENT**—Medical Student membership may be held by medical students interested in pursuing a career in an oncology specialty training program (surgical, radiation, medical or gynecologic) and currently enrolled in an Accredited medical school acceptable to the American Radium Society.

APPLICANT’S FULL NAME:

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<tr>
<th>(LAST/FAMILY NAME)</th>
<th>(FIRST/GIVEN NAME)</th>
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<tbody>
<tr>
<td>MD</td>
<td>DO</td>
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Date of Birth (month/day/year): __________________ Gender: M F Country of Birth ______________________

PROFESSIONAL ADDRESS:

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<td>(Department/Division Name)</td>
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<td>(Professional Street Address <strong>including</strong>: suite#; floor#; mail-stop#; building name; room# as applicable)</td>
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Please list all degrees earned below, including honorary degrees and fellowships:

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Dear Colleagues,

Welcome to the American Radium Society’s 96th Annual Meeting! The theme of this year’s ARS meeting, *Technological Innovations: Benefits, Costs, and Impact on Training and Practice*, highlights how technological advances in science are changing the face of care for patients with cancer. Although the meeting this year has been shortened by one day, in response to suggestions from past attendees, our meeting is still packed with presentations on original data that can affect treatment decisions for our patients, and some exciting innovations that will advance the future of our specialties.

The caliber of science that we received in the abstract submissions this year was outstanding, and we had a record number of applicant submissions. This has led to an outstanding set of scientific sessions and posters being presented at the meeting. We look forward to sharing valuable information in all the presentations, including the five Essay Awards and ten presentations associated with the Travel Grants awarded to Young Oncologist recipients.

Dr. Sue S. Yom, of the University of California, San Francisco and Chair of the Scientific Program Committee, deserves much praise, having recruited an extraordinary group of lecturers and panelists for the program this year. The committee has worked on initiatives to improve your experience, including, but not limited to, clustering the program by areas of interest, increasing the number of practical case discussions, and adding optional afternoon special topics sessions, including a Career Development Seminar and a Brachytherapy Course. This year’s expert-led debates will focus on increasing aspects of technology in two common cancers: the role of advanced surgery in the management of high-risk prostate cancer and the utility of magnetic resonance imaging for early-stage breast cancer management. Not to be missed is the opportunity to attend one of two luncheon options—*Meet the Professor* and *Tumor Boards*—each focused on different specialty areas. We again offer Self-Assessment Modules for qualification...
toward the American Board of Radiology’s Maintenance of Certification program; this year there will be many more offerings, so make sure to check the program and maximize your learning credits!

In addition, I am excited to extend a special welcome to our distinguished speakers, Dr. Murray Brennan of Memorial Sloan-Kettering Cancer Center, who will give the Janeway Lecture, and our Keynote Speakers, Dr. Carolyn Compton of Arizona State University and Dr. Peter Ubel of Duke University. I am honored to join these experts in sharing important scientific knowledge through this year’s special Presidential Categorical Course, What’s New in the Treatment of Rectal and Anal Cancer. Dr. Lisa Kachnic, Dr. Joshua Meyer, and Dr. Nancy You will provide an update on the exciting changes in the management of rectal and anal cancer.

Our deepest gratitude goes to our industry supporters for providing educational grants, including Varian Medical Systems, Hitachi, Ltd., Genomic Health, Mevion Medical Systems, Elekta, Inc., IBA, and all of the other companies that have traveled to St. Thomas to exhibit. Finally, all involved with the meeting owe our sincerest gratitude to the ARS staff for their work in organizing this superb conference.

The ARS meeting is the oldest multidisciplinary cancer conference in the world and has a tradition of scientific excellence, collegiality, and a strong multidisciplinary scientific program. This year promises much more of the same. We hope you enjoy the academic and social programs, and encourage you and your family to take advantage of the beautiful Marriott Frenchman’s Reef Hotel and Resort and enjoy the island breeze and carnival.

Sincerely,

Elin R. Sigurdson, MD, PhD
Fox Chase Medical Center
ARS President, 2013–2014
### Past Presidents of the American Radium Society

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<th>Year</th>
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<td>W.H.B. Aikins, MD*</td>
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<td>2013</td>
<td>Thomas Buchholz, MD*</td>
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* Deceased
## Committees of the ARS

### Executive Committee
- **Elin R. Sigurdson, MD, PhD**, President (2013-2014)
- **Kenneth Rosenzweig, MD**, President-Elect (2013-2014)
- **Quynh-Thu Le, MD**, Treasurer (2012-2014)
- **Steven Frank, MD**, Industry Relations Chair (2013-2014)
- **Kenneth Roberts, MD**, Member-at-Large (2012-2014)
- **Sue S. Yom, MD, PhD**, 2014 Scientific Program Committee Chair (2013-2014)
- **Thomas Buchholz, MD**, Immediate Past President (2013-2014)

### Constitution and By-Laws Committee
- **Lynn Wilson, MD** (Chair) (2011-2014)
- **Thomas Buchholz, MD** (Ex officio)
- **Kenneth Russell, MD** (2012-2015)
- **Mark Henderson, MD** (2010-2013)

### Educational Resources Committee
- **Mary Katherine Hayes, MD** (Chair) (2011-2014)
- **Ben Movsas, MD** (2011-2013)
- **Jim Wallace, MD** (2012-2015)
- **Arnold Paulino, MD** (2010-2013)

### Industry Relations/Development Committee
- **Steven Frank, MD** (Chair) (2013-2014)
- **Tom Buchholz, MD** (Ex officio) (2011-2015)
- **Chung Chung, MD** (2010-2014)
- **Alan Pollack, MD, PhD** (2012-2016)

### Janeeway Lecture Committee
- **John A. Ridge, MD, PhD** (Chair) (2011-2014)
- **Tom Buchholz, MD** (Ex officio) (2012-2015)
- **J. Frank Wilson, MD** (2012-2015)

### Membership and Credentials Committee
- **Kenneth Rosenzweig, MD** (Chair) (2011-2013)
- **Tom Buchholz, MD** (Ex officio) (2012-2015)
- **Mack Roach, MD** (2012-2015)
- **Martin Colman, MD** (2010-2013)
- **Erich Sturgis, MD** (2012-2015)
- **Quynh Le, MD** (2011-2014)
- **Meena Moran, MD** (2011-2014)
- **David Rohde, MD** (2010-2013)
- **Arnold Paulino, MD** (2012-2015)

### Nominating Committee
- **Jay Cooper, MD** (2012-2015)
- **Erich Sturgis, MD** (2010-2013)

### Resident and Attending Educational Committee
- **Jeffrey Michalski, MD** (Chair) (2012-2015)
- **Tom Buchholz, MD** (Ex officio) (2011-2014)
- **Shiao Woo, MD** (2010-2013)

### Website and Public Relations Committee
- **Jonathan J. Beitler, MD** (Chair) (2011-2014)
- **David Wazer, MD** (2012-2015)
- **John Ward, MD** (2010-2013)
- **Cynthia Ballenger, MD** (2011-2014)

### Scientific Program Committee
- **Sue S. Yom, MD, PhD** (Chair) – San Francisco, CA
- **Matthew Abramowitz, MD** – Miami, FL
- **Beth Beadle, MD** – Houston, TX
- **Thomas A. Buchholz, MD** – Houston, TX
- **James D. Cox, MD** – Houston, TX
- **Ted DeWeese, MD** – Baltimore, MD
- **Tom Galloway, MD** – Philadelphia, PA
- **Mary Katherine Hayes, MD** – New York, NY
- **Mark Henderson, MD** – Indianapolis, IN
- **Joe Herman, MD** – Baltimore, MD
- **Peter A.S. Johnstone, MD** – Indianapolis, IN
- **Andre Konski, MD** – Detroit, MI
- **Ben Movsas, MD** – Detroit, MI
- **Alan Pollack, MD, PhD** – Miami, FL
- **John A. Ridge, MD, PhD** – Philadelphia, PA
- **Kenneth Roberts, MD** – New Haven, CT
- **Kenneth Rosenzweig, MD** – New York, NY
- **Elin R. Sigurdson, MD, PhD** – Philadelphia, PA

### Representative to the Board of Chancellors of the American College of Radiology
- **Peter A.S. Johnstone, MD** (2011-2014)

### American College of Radiology Councilor
- **Andre Konski, MD** (2010-2013)

### American College of Radiology Assistant Councilor
- **Jonathan Beitler, MD** (2010-2013)

### Representative to the Commission on Cancer
- **John A. Ridge, MD, PhD** (2012-2015)

### Representative to the National Council on Radiation Protection & Measurements
- **Ritsuko Komaki, MD** (2013-2016)

### Trustees of the American Board of Radiology
- **Bruce Haffty, MD** (2009-2013)
- **Lynn Wilson, MD** (2011-2015)
- **Kaled Alektiar, MD** (2013-2017)
MURRAY F. BRENNAN, MD
Dr. Murray Brennan is an oncology surgeon with special expertise in the treatment of soft tissue sarcomas, endocrine tumors, and pancreatic and stomach cancers. He was Chairman of the Department of Surgery at Memorial Sloan-Kettering Cancer Center from 1985 until June 2006 and is currently Vice President for International Programs and Director of the Bobst International Center. Dr. Brennan has lectured throughout the world and has authored or coauthored more than 1,000 scientific papers and book chapters, as well as two books on soft tissue sarcoma. He has served as Director of the American Board of Surgery, Chairman of the American College of Surgeons Commission on Cancer, President of the American College of Surgeons, and President of the American Surgical Association. He has been awarded Honorary Fellowships in the Royal Colleges of Surgeons in Ireland, Edinburgh, England, Australasia, and the Royal College of Physicians and Surgeons of Glasgow and Canada. Dr. Brennan has received Honorary Doctorates from the Universities of Edinburgh, Otago, and Goteborg, and University College London. In 1995, Dr. Brennan was honored with membership in the Institute of Medicine of the National Academy of Sciences, and in 2000, he received the American College of Surgeons’ highest award—the Distinguished Service Award.

The Janeway Medal
The heraldry of the Janeway Medal is drawn from Norse Mythology: Odin, the Allfather with power over the precious minerals of the earth, sought enlightenment for the sons of men. He traveled to Mimir’s Well where Wisdom and Wit lodged hidden. The face of the Janeway Medal shows Odin standing before the giant Mimir, warden of the well, yielding one of his eyes for a draught of the precious water. The reverse side of the medal shows Odin’s two ravens, who spent the day flying throughout the expanse of the universe: Hugin (Thought-Reflection) and Munin (Memory-Remembrance). The ravens returned each evening to perch on Odin’s shoulders and whisper in his ears the events and progress observed.

Odin’s physical privation, as a price for wisdom, is symbolic of the self-sacrifice of the heroic pioneers of radium therapy for cancer. Odin’s ravens, as shown on the Janeway Medal, have become the symbols of the American Radium Society.

Since 1933, the American Radium Society has sponsored an annual lecture in memory of Doctor Henry H. Janeway (1873-1921), a great American pioneer in the therapeutic use of radium. Originally a large bronze medal, the Janeway Medal was changed to a gold medal in 1971. A special committee of the Society chooses the lecturers on the basis of their outstanding scientific contributions. Each lecturer is presented with the handsome Janeway Medal.
1933.............................. James Ewing, MD
New York, NY
“Early Experience in Radium Therapy”

1934.............................. Francis Carter Wood, MD
New York, NY
“Recent Advances in Experimental Cancer Research”

1935.............................. George F. Pfahler, MD
Philadelphia, PA
“The Protection of the Radiologist”

1936.............................. Curtis F. Burnam, MD
Baltimore, MD
“Early Experience With Radium”

1937.............................. Douglas Quick, MD
New York, NY
“Carcinoma of the Larynx”

1938.............................. Henry Schmitz, MD
Chicago, IL
“Historical Retrospect of the Treatment of Carcinoma of the Uterus”

1939.............................. Gioacchino Failla, ScD
New York, NY
“Some Aspects of the Biological Action of Ionizing Radiation”

1940.............................. Edith H. Quimby, ScD
New York, NY
“The Specification of Dosage in Radium Therapy”

1941.............................. Edward H. Skinner, MD
Kansas City, MO
“The Philosophy and Economics of Cancer”

1942.............................. William P. Healy, MD
New York, NY
“The Role of the Gynecologist in the Field of Cancer”

1946.............................. Frederick O’Brien, MD
Boston, MA
“Radium Treatment of Cancer of the Cervix: A Historical Review”

1947.............................. Robert S. Stone, MD
San Francisco, CA
“Neutron Therapy and Specific Ionization”

1948.............................. Sir Sanford Cade
London, England
“The Achievement of Radium in the Fight Against Cancer”

1949.............................. Charles L. Martin, MD
Dallas, TX
“Low Intensity Radium Element Needles”

1950.............................. Otto Glasser, PhD
Cleveland, OH
“Evolution of Radiological Physics as Applied to Isotopes”

1951.............................. H. Dabney Kerr, MD
Iowa City, IA
“Some Thoughts on the Training of a Radiation Therapist”

1952.............................. A. Purdy Stout, MD
New York, NY
“Intraepithelial Carcinoma of the Larynx”

1953.............................. Leon O. Jacobson, MD
Chicago, IL
“Factors Concerned in Recovery From Radiation Injury”

1954.............................. Lauriston S. Taylor, ScD
Bethesda, MD
“Education in Radiation Protection”

1955.............................. Herbert M. Parker, FIP
Richland, WA
“The Radiological Sciences”

1956.............................. Lloyd E. Graver, MD
New York, NY
“Reflections on Malignant Lymphomas”

1957.............................. Simeon T. Cantril, MD
Seattle, WA
“The Contributions of Biology to Radium Therapy”

1958.............................. Leonidas R. Marinelli, MA
Lemont, IL
“Natural Radioactivity in the Human”

1959.............................. James T. Case, MD
Santa Barbara, CA
“The Early History of Radium Therapy and the American Radium Society”

1960.............................. William S. MacComb, MD
Houston, TX
“The Treatment of Head and Neck Cancer”

1961.............................. Clifford L. Ash, MD
Toronto, Ontario, Canada
“Oral Cancer: A Twenty-Five Year Study”

1962.............................. Virginia Kneeland Frantz, MD
New York, NY
“Privileges and Challenges in the Study and Treatment of Thyroid Cancer”

1963.............................. A.N. Arneson, MD
St. Louis, MO
“Long-Term Observations in Endometrial Cancer”

1964.............................. Harold W. Dargeon, MD
New York, NY
“Considerations in the Treatment of Reticuloendotheliosis”

1965.............................. T.A. Watson, MD
London, Ontario, Canada
“Cancer of the Breast”

1966.............................. Gordon P. McNeer, MD
New York, NY
“The Problem of the Local Recurrence of Malignant Melanoma”

1967.............................. R. Lee Clark, MD
Houston, TX
“Systematic Cancer: Philosophy and Modalities of Treatment”

1968.............................. W. Gerald Cosbie, MD
Toronto, Ontario, Canada
“Cancer Services – How Far Should It Go?”

1969.............................. Franz J. Buschke, MD
San Francisco, CA
“Radiotherapy – Past, Present, and Future”

1970.............................. Gilbert H. Fletcher, MD
Houston, TX
“The Cancer of the Uterine Cervix”

1971.............................. Lauren W. Ackerman, MD
St. Louis, MO
“The Pathology of Radiation Effect on Normal and Neoplastic Tissue”

1972.............................. Alfred Gelhorn, MD
Philadelphia, PA
“Cancer and Other National Problems”

1973.............................. Juan A. del Regato, MD
Colorado Springs, CO
“Total Body Irradiation in the Treatment of Chronic Lymphogranulomatous Leukemia”

1974.............................. Milford D. Schulz, MD, Boston, MA
“The Supervoltage Story”

1975.............................. George C. Lewis, Jr., MD
Philadelphia, PA
“Ovarian Cancer: Multifaceted Disease; Multifarious Therapy and Therapists”

1976.............................. Audrey Evans, MD
Philadelphia, PA
“Pediatric Cancer Treatment: A Model for Oncology”

1977.............................. Henry S. Kaplan, MD
Stanford, CA
“Fundamental Mechanisms in Combined Modality Therapy of Cancer”
Keynote Lecturers

**CAROLYN COMPTON, MD, PhD**, is an academic pathologist specializing in gastrointestinal disease, and is board-certified in both anatomic and clinical pathology. She is a Professor at Arizona State University and an Adjunct Professor of Pathology at both the University of Arizona and Johns Hopkins. At ASU, she is on the faculty of the School of Life Sciences, and at Mayo Clinic, she is a Research Affiliate in the Department of Pathology and Laboratory Medicine. She is the Chief Medical Officer of the National Biomarkers Development Alliance and a member of the Bodesign Institute and the Complex Adaptive Systems Initiative. She is a former Professor of Pathology at Harvard Medical School, Chief of Gastrointestinal Pathology at Massachusetts General Hospital, and Pathologist-in-Chief of Boston Shriners Children’s Hospital. More recently, she has served as the CEO and President of the Critical Path Institute (2012), the Director of Biorepositories and Biospecimen Research and the Innovative Molecular Analysis Technologies program at the National Cancer Institute (2005–2011), and the Strathcona Professor and Chair of the Department of Pathology at McGill University and Pathologist-in-Chief of the McGill University Health Center (2000–2005). She is the immediate past Chair of the American Joint Committee on Cancer (AJCC) and the Chair of the Precision Medicine Core of the AJCC. She has authored more than 500 scientific manuscripts, review articles, books, and chapters.

**PETER UBEL, MD**, is a physician and behavioral scientist whose research and writing explore the mixture of rational and irrational forces that affect our health, our happiness, and the way our society functions. (What fun would it be to tackle just the easy problems?) Dr. Ubel is the Madge and Dennis T. McLawhorn University Professor of Business, Public Policy, and Medicine at Duke University. His research explores controversial issues about the role of values and preferences in healthcare decision-making, from decisions at the bedside to policy decisions. He uses the tools of decision psychology and behavioral economics to explore topics such as informed consent, shared decision-making, and healthcare cost containment. His books include *Pricing Life: Why It’s Time for Health Care Rationing* (MIT Press, 2000) and *Free Market Madness: How Economics Is at Odds With Human Nature—And Why It Matters* (Harvard Business Press, 2009). His newest book, *Critical Decisions* (HarperCollins, 2012), explores the challenges of shared decision-making between doctors and patients. His blogs and other information can be found at http://www.peterubel.com/.
2014 YOUNG ONCOLOGIST ESSAY AWARDS

Program Number: S025
Presenter: Corey Spears, MD, PhD
Abstract Title: Radiation-Induced Increases in PARP1 Activity Predict for Long-Term Radiosensitization by PARP1 Inhibition in Preclinical Breast Cancer Models

Program Number: S026
Presenter: Matthew E. Johnson, MD
Abstract Title: Postmastectomy Radiation Therapy for T3N0 Breast Cancer: A SEER Analysis

Program Number: S027
Presenter: Dana L. Casey
Abstract Title: Patterns of Failure for Rhabdomyosarcoma of the Perineal and Perianal Region

Program Number: S028
Presenter: Stephanie Markovina, MD, PhD
Abstract Title: Sequential Short-Course Radiotherapy and FOLFOX Chemotherapy as Preoperative Therapy for Rectal Cancer Provide Increased DFS Compared to Historical Controls

Program Number: S029
Presenter: Jeffrey M. Vainshtein, MD
Abstract Title: Patient-Reported Voice and Speech Outcomes and Their Clinical and Dosimetric Predictors After Chemo-IMRT of Oropharyngeal Cancer: A Prospective Longitudinal Study

TRAVEL GRANTS

Program Number: S010
Presenter: Sara R. Alcorn, MD, MPH
Abstract Title: Prospective and Real-Time Data Analysis of Image-Guided Radiotherapy Across a Multinational Pediatrics Consortium: Methodology and Considerations

Program Number: S011
Presenter: M.T. Scott, MD, MBA
Abstract Title: Comparison of Toxicities and Outcomes for Conventionally and Hypofractionated Radiation Therapy for Early Glottic Carcinoma

Program Number: S016
Presenter: Dayssy A. Diaz, MD
Abstract Title: Head and Neck Second Primary Cancer Rates in the HPV Era: A SEER Analysis

Program Number: S017
Presenter: Brad J. Greenfield, MD
Abstract Title: Long-Term Outcome of Intensity-Modulated Radiation Therapy in Pediatric Craniopharyngioma

Program Number: S021
Presenter: Henry S. Park, MD, MPH
Abstract Title: Central Versus Peripheral Tumor Location: Influence on Survival, Local Control, and Toxicity Following Stereotactic Body Radiotherapy for Primary Non–Small-Cell Lung Cancer

Program Number: S031
Presenter: Nikhil G. Thaker, MD
Abstract Title: A Phantom-Based Simulator Approach to Improving the Quality of Prostate Brachytherapy Training

Program Number: S036
Presenter: Jung Julie Kang, MD, PhD
Abstract Title: The Low Alpha-Beta Ratio of Bladder Cancer: A Rationale for Hypofractionation

Program Number: S042
Presenter: Malolan S. Rajagopalan, MD
Abstract Title: Changing Practice Patterns for Breast Cancer Radiotherapy with Clinical Pathways: An Analysis of Hypofractionation in a Large, Integrated Cancer Center Network

Program Number: S044
Presenter: Terence T. Sio, MD, MS
Abstract Title: Repeated-Measures Analyses of the Common Terminology Criteria for Adverse Events (CTCAE v3.0)-based Dermatitis Toxicities in Breast Cancer Patients Receiving Radiotherapy in a Phase III Randomized Trial of Mometasone Furoate, N06C4 (Alliance)

POSTER AWARDS

Program Number: P059
Presenter: Aadel A. Chaudhuri, MD, PhD
Abstract Title: Increased Rates of Radiation Pneumonitis in Patients Receiving Stereotactic Ablative Radiotherapy for Central Versus Peripheral Lung Tumors

Program Number: P075
Presenter: Alan J. Katz, MD, JD
Abstract Title: Stereotactic Body Radiotherapy With and Without Pelvic Radiotherapy for Organ-Confined High-Risk Prostate Cancer

Program Number: P089
Presenter: Amber Orman, MD
Abstract Title: A Phase III Randomized Trial of MRI-Mapped Dose-Escalated Salvage Radiotherapy Postprostatectomy: The MAPS Trial. An Initial Dosimetric Assessment

Program Number: P099
Presenter: Lorraine Portelance, MD
Abstract Title: A Multidisciplinary Approach to the Management of Patients Diagnosed With Stage IV Anal Canal Cancer. A Multi-institutional Retrospective Study

Program Number: P103
Presenter: Nitin Ohri, MD
Abstract Title: Socioeconomic Status and Overall Survival Following Hepatocellular Carcinoma Diagnosis in an Urban Academic Cancer Center

Program Number: P115
Presenter: Charles E. Rutter, MD
Abstract Title: Breast Cancer Laterality Does Not Influence Overall Survival in a Large Modern Cohort: Implications for Radiation-Related Cardiac Mortality

Program Number: P117
Presenter: Julie A. Bradley, MD
Abstract Title: Anatomical Variations and Radiation Technique for Breast Cancer
<table>
<thead>
<tr>
<th>Year</th>
<th>Recipients</th>
</tr>
</thead>
<tbody>
<tr>
<td>2013</td>
<td>Andrew McBride, Adam Ferro, BS, Katherine Y. Fan, Eugene J. Koay, MD, PhD, Ravi B. Parikh, BA</td>
</tr>
<tr>
<td>2012</td>
<td>Daniela L. Buscariollo, BS, Peyman Kabolizadeh, MD, PhD, Waleed F. Mourad, MD, MSc, PhD, David H.A. Nguyen, MD, Ting Xu, MD, Joanna C. Yang, BA</td>
</tr>
<tr>
<td>2011</td>
<td>Sanjay Aneja, BS, Matthew R. McCurdy, MD, PhD, Henry S. Park, BS, Hiral Patel Fontanilla, MD</td>
</tr>
<tr>
<td>2010</td>
<td>Amol J. Ghia, MD, Matthew Koshy, MD, Baoqing Li, MD, PhD, Jeffrey R. Olsen, MD, Akshar N. Patel, BS, Andris J. Zauls, MD</td>
</tr>
<tr>
<td>2009</td>
<td>Leon M. Chen, BS, Camille P. Green, BS, Kilian Salerno May, MD, Thomas J. Pugh, MD, Naveen K. Sharma, DO, PhD, Kevin L. Stephans, MD</td>
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<tr>
<td>2008</td>
<td>Beth M. Beadle, MD, PhD, Mark W. McDonald, MD, Loren K. Mell, MD, James B. Yu, MD</td>
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<td>2007</td>
<td>Elizabeth A. Kidd, MD, Daniel J. Indelicato, MD, Erik P. Sulman, MD</td>
</tr>
<tr>
<td>2006</td>
<td>Daniel T. Chang, MD, Yee-Lu Tham, MD, Ann H. Klopp, MD, PhD, Anad Parthasarathy, MD</td>
</tr>
<tr>
<td>2005</td>
<td>Laura Granville, MD, Andrew Hope, MD, Bridget Koontz, MD, Michael Sinopoli, MD</td>
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<tr>
<td>2004</td>
<td>Ramesh Rengan, MD, Allen Chen, MD, Falguni Amin-Zimmerman, MD</td>
</tr>
<tr>
<td>2003</td>
<td>Anesa Ahamad, MD, Anurag Chandra, MD, Robert S. Malyapa, MD, Wendy A. Woodward, MD</td>
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<tr>
<td>2002</td>
<td>Jerry L. Barker, MD, Thomas J. Gergel, MD, Ramesh Gopal, MD</td>
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<tr>
<td>2001</td>
<td>Christopher Chen, MD, Ben Han, MD, Pamela Schlembach, MD</td>
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<tr>
<td>2000</td>
<td>Hany Elsaleh, MBBS, Angela Katz, MD, Jay Locke, MD, Erich M. Sturgis, MD</td>
</tr>
<tr>
<td>1999</td>
<td>Kenneth Blank, MD, Heather Curry, MD, Timothy Jamieson, MD</td>
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<tr>
<td>1998</td>
<td>Bruce C. Turner, MD, Jennifer B. Sherwood, MD, Oliver Bathe, MD</td>
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<tr>
<td>1997</td>
<td>Eddy C. Hsueh, MD, John P. Geisler, MD</td>
</tr>
<tr>
<td>1996</td>
<td>Dong Fu Chen, MD, HuiKuo Shu, MD</td>
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<tr>
<td>1995</td>
<td>Gary M. Proulx, MD</td>
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<td>1994</td>
<td>Peter P. Huang, MD, Michael R. MacDonald, MD, Turgut Alagoz, MD, Peter A. S. Johnstone, MD</td>
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<td>1993</td>
<td>Edward R. Sauter, MD, Sonia Brisson, MD, Noreen C. Gleson, MD, Donald J. Martinelli, MD</td>
</tr>
<tr>
<td>1992</td>
<td>Edward L. Levine, MD, Seth A. Rosenthal, MD, James R. Wong, MD, Brigette Miller, MD</td>
</tr>
<tr>
<td>1991</td>
<td>Thomas Buchholz, MD, Joseph Poen, MD, Paul Monsour, MD, Patrick DePotter, MD</td>
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<tr>
<td>1990</td>
<td>Jerrey Goldstein, MD</td>
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<td>1989</td>
<td>Jeffrey Williams, MD</td>
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<td>1988</td>
<td>Stephen C. Rush, MD</td>
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<tr>
<td>1987</td>
<td>Richard S. Godfrey, MD</td>
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<tr>
<td>1986</td>
<td>Colleen Lawton, MD, Nabil C. Arlan, MD</td>
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<tr>
<td>1985</td>
<td>Michelle Burnison, MD, John Zaleberg, MD, David C. Beyer, MD</td>
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<tr>
<td>1984</td>
<td>Michael J. Marchese, MD</td>
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<tr>
<td>1983</td>
<td>Robert A. Rostock, MD</td>
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<tr>
<td>1982</td>
<td>Judith A. Stitt, MD</td>
</tr>
<tr>
<td>1980</td>
<td>R. Dirk Noyes, MD</td>
</tr>
<tr>
<td>1979</td>
<td>Dennis F. Devereux, MD</td>
</tr>
<tr>
<td>1978</td>
<td>Joseph E. Russ, MD</td>
</tr>
</tbody>
</table>
# Program at a Glance

## SATURDAY, APRIL 26, 2014

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:00 AM – 6:00 PM</td>
<td>Registration Open</td>
</tr>
<tr>
<td>2:30 – 4:30 PM</td>
<td>Presidential Categorical Course</td>
</tr>
<tr>
<td>4:30 – 5:30 PM</td>
<td>ARS Welcome and Exhibit Hall Opening Reception</td>
</tr>
<tr>
<td>5:30 – 6:00 PM</td>
<td>Guided Poster Walk</td>
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## SUNDAY, APRIL 27, 2014

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:00 – 7:45 AM</td>
<td>Continental Breakfast, Residents Breakfast, and Exhibits/Posters</td>
</tr>
<tr>
<td>7:45 – 8:30 AM</td>
<td>Panel: Difficult Cases in Gynecology</td>
</tr>
<tr>
<td>8:30 – 9:30 AM</td>
<td><strong>Scientific Session #1:</strong> Gynecologic Cancer/Sarcoma/Health Services</td>
</tr>
<tr>
<td>9:30 – 10:30 AM</td>
<td>Janeway Lecture: Dr. Murray F. Brennan, Memorial Sloan-Kettering Cancer Center</td>
</tr>
<tr>
<td>10:30 – 10:45 AM</td>
<td>Break</td>
</tr>
<tr>
<td>10:45 – 11:45 AM</td>
<td><strong>Scientific Session #2:</strong> Head and Neck Cancer/Pediatrics/CNS Tumors</td>
</tr>
<tr>
<td>11:45 AM – 12:30 PM</td>
<td>Panel: Difficult Cases at the Skull Base</td>
</tr>
<tr>
<td>12:30 – 1:30 PM</td>
<td>Meet the Professor Luncheon: Head and Neck**</td>
</tr>
<tr>
<td>12:30 – 1:30 PM</td>
<td>Tumor Board Luncheon: Sarcoma Cases**</td>
</tr>
<tr>
<td>1:30 – 2:30 PM</td>
<td>Career Development Seminar</td>
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<tr>
<td>2:30 – 4:00 PM</td>
<td>Satellite Symposium by Elekta</td>
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<tr>
<td>6:45 – 8:45 PM</td>
<td>ARS Social Event (onsite): Island Carnival Dinner Banquet</td>
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## MONDAY, APRIL 28, 2014

<table>
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<tr>
<th>Time</th>
<th>Event</th>
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<tbody>
<tr>
<td>7:00 – 7:45 AM</td>
<td>Continental Breakfast and Exhibits/Posters</td>
</tr>
<tr>
<td>7:45 – 8:30 AM</td>
<td>Panel: Lung Cancer Review</td>
</tr>
<tr>
<td>8:30 – 9:15 AM</td>
<td><strong>Scientific Session #3:</strong> Lung Cancer/Stereotactic/Metastasis</td>
</tr>
<tr>
<td>9:15 – 10:00 AM</td>
<td><strong>Keynote Lecture:</strong> Dr. Carolyn Compton, Arizona State University</td>
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## TUESDAY, APRIL 29, 2014

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
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</thead>
<tbody>
<tr>
<td>7:00 – 7:45 AM</td>
<td>Continental Breakfast and Exhibits/Posters</td>
</tr>
<tr>
<td>7:45 – 8:15 AM</td>
<td>Business Meeting: All ARS Members welcome to attend. Only Active Members may vote.</td>
</tr>
<tr>
<td>8:15 – 9:00 AM</td>
<td>Presidential Address: Evolution in the Treatment of Rectal Cancer</td>
</tr>
<tr>
<td>9:00 – 9:30 AM</td>
<td><strong>Scientific Session #6:</strong> Gastrointestinal Cancer</td>
</tr>
<tr>
<td>9:30 – 9:45 AM</td>
<td>Break</td>
</tr>
<tr>
<td>9:45 – 10:30 AM</td>
<td>Keynote Lecture: Dr. Peter Ubel, Duke University</td>
</tr>
<tr>
<td>10:30 – 11:15 AM</td>
<td><strong>Debate:</strong> MRI for Breast Cancer Conservation</td>
</tr>
<tr>
<td>11:15 AM – 12:15 PM</td>
<td><strong>Scientific Session #7:</strong> Breast Cancer</td>
</tr>
<tr>
<td>12:30 – 1:00 PM</td>
<td>Panel: Technology/Cost/QA in Health Care Around the World</td>
</tr>
</tbody>
</table>

* Schedule is subject to change.

** Registration and payment are required for this session. Space is limited.

The American Radium Society gratefully acknowledges [Varian Medical Systems](#) for their support of the poster session in the Exhibit Hall, through an educational grant.

The American Radium Society gratefully acknowledges [Varian Medical Systems](#), [Elekta, Inc.](#), [Hitachi, Ltd.](#), [Genomic Health](#), and [Mevion Medical Systems](#) for their support of the daily refreshment breaks in the Exhibit Hall, through educational grants.
# Presidential Categorical Course

**CHAIR:** Elin R. Sigurdson, MD, PhD  
**Saturday, April 26, 2014**  
**2:30–4:30 PM**  
**Harbour II & III**

## A Focus on Rectal and Anal Cancer

<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Speaker(s)</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>2:30 PM</td>
<td>Welcome and Opening Remarks</td>
<td>Elin R. Sigurdson, MD, PhD</td>
<td>Fox Chase Cancer Center</td>
</tr>
<tr>
<td>3:00 PM</td>
<td>Rectal Cancer Radiation Studies</td>
<td>Joshua Meyer, MD</td>
<td>Fox Chase Cancer Center</td>
</tr>
<tr>
<td>3:30 PM</td>
<td>Anal Cancer Updates</td>
<td>Lisa Kachnic, MD</td>
<td>Boston Medical Center</td>
</tr>
<tr>
<td>4:00 PM</td>
<td>Modern Techniques in Surgery for Rectal Cancer</td>
<td>Nancy You, MD, FACS&lt;br&gt;UT MD Anderson Cancer Center</td>
<td></td>
</tr>
</tbody>
</table>

All presentations will be followed by a short question-and-answer period.

## Objectives

*After this course, participants will be able to:*

1. Teach the appropriate surgical and radiation management of locally advanced rectal cancer.
2. Review medical and radiation therapy management of anal cancer.
# Scientific Program

## SATURDAY, APRIL 26, 2014

<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:00 AM–6:00 PM</td>
<td>REGISTRATION OPEN</td>
</tr>
<tr>
<td>2:30–4:30 PM</td>
<td>PRESIDENTIAL CATEGORICAL COURSE: A Focus on Rectal Cancer (SAM)</td>
</tr>
<tr>
<td></td>
<td>COURSE CHAIR: Elin R. Sigurdson, MD, PhD</td>
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<tr>
<td></td>
<td>Fox Chase Cancer Center</td>
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<tr>
<td></td>
<td>PANELISTS:</td>
</tr>
<tr>
<td></td>
<td>Joshua Meyer, MD</td>
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<td></td>
<td>Fox Chase Cancer Center</td>
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<td>Lisa Kachnic, MD</td>
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<td>Boston Medical Center</td>
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<td></td>
<td>Nancy You, MD, FACS</td>
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<tr>
<td></td>
<td>UT MD Anderson Cancer Center</td>
</tr>
<tr>
<td>4:30–5:30 PM</td>
<td>ARS WELCOME/EXHIBIT HALL OPENING RECEPTION</td>
</tr>
</tbody>
</table>

The American Radium Society gratefully acknowledges Elekta, Inc., and Varian Medical Systems for their support of the ARS Welcome Reception, through educational grants.

<table>
<thead>
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<th>Time</th>
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<tbody>
<tr>
<td>5:30–6:00 PM</td>
<td>POSTER WALK GUIDES: Joseph Herman, MD, and Kenneth Rosenzweig, MD</td>
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## SUNDAY, APRIL 27, 2014

<table>
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<tr>
<th>Time</th>
<th>Event</th>
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<tbody>
<tr>
<td>7:00–7:45 AM</td>
<td>CONTINENTAL BREAKFAST, RESIDENTS BREAKFAST, AND EXHIBIT/POSTER SESSION</td>
</tr>
<tr>
<td>7:45–8:30 AM</td>
<td>PANEL: Difficult Cases in Gynecology (SAM)</td>
</tr>
<tr>
<td></td>
<td>PANEL CHAIR: Ann Klopp, MD, PhD</td>
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<td>UT MD Anderson Cancer Center</td>
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<td></td>
<td>PANELISTS:</td>
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<tr>
<td></td>
<td>Joe Hsu, MD</td>
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<tr>
<td></td>
<td>University of California, San Francisco</td>
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<tr>
<td></td>
<td>Lilie Lin, MD</td>
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<tr>
<td></td>
<td>University of Pennsylvania</td>
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<tr>
<td>8:30–9:30 AM</td>
<td>SCIENTIFIC SESSION #1: Gynecologic Cancer/Sarcoma/Health Services</td>
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<td>MODERATORS:</td>
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### (S001) Limb-Sparing Surgery and Intraoperative Radiotherapy in the Treatment of Primary, Nonmetastatic Extremity and Limb-Girdle Soft Tissue Sarcoma
CHRISTOPHER L. TINKLE, MD

### (S002) Outcomes and Prognostic Factors of Stereotactic Body Radiotherapy for Soft Tissue Sarcoma Metastases
KENNETH MERRELL, MD

### (S003) Disparities in Stage at Diagnosis and Survival in Adult Cancer Patients According to Insurance Status
GARY V. WALKER, MD, MPH

### (S004) Radiation Publications Underrepresented in High-Impact General Medical and Oncology Journals
EMMA B. HOLLIDAY, MD

### (S005) Adjuvant Radiotherapy in Stage II Endometrial Carcinoma: Is Brachytherapy Alone Sufficient for Local Control?
IMA PAYDAR, MD

### (S006) Extended-Field IMRT With Concomitant Boost for Node-Positive Cervical Cancer: Analysis of Regional Control Rate and Recurrence Pattern
SUSHIL BERIWAL, MD

### (S007) Stereotactic Radiosurgery to the Brain With Concurrent BRAF Inhibitors for Melanoma Metastases
NICHOLAS FIGURA, BS

### (S008) Use of Mobile Devices for Creation of Survivorship Care Plans
CHRISTINE E. HILL-KAYSER, MD

### (S009) Two-Year Outcomes Following Triapine Radiochemotherapy for Cervical Cancer
TRACY SHERERTZ, MD

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<th>Time</th>
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<tr>
<td>9:30–10:30 AM</td>
<td>JANEWAY LECTURE: Murray F. Brennan, MD</td>
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<td>Memorial Sloan-Kettering Cancer Center</td>
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<td></td>
<td>“The Evolution of Disease-Based Cancer Care”</td>
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<td>This lecture provides a historical description of the evolution of cancer care, from radical surgery to multidisciplinary comprehensive care.</td>
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<td>10:30–10:45 AM</td>
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<td>10:45–11:45 AM</td>
<td>SCIENTIFIC SESSION #2: Head and Neck Cancer/Pediatrics/CNS Tumors</td>
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<td>MODERATORS: Thomas Galloway, MD</td>
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<td>Fox Chase Cancer Center</td>
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<td>Beth Beadle, MD, PhD</td>
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<td>UT MD Anderson Cancer Center</td>
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The American Radium Society gratefully acknowledges an unrestricted educational grant from Elekta, Inc., in support of this Scientific Session.
(S010) Prospective and Real-Time Data Analysis of Image-Guided Radiotherapy Across a Multinational Pediatrics Consortium: Methodology and Considerations
SARA R. ALCORN, MD, MPH

(S011) Comparison of Toxicities and Outcomes for Conventionally and Hypofractionated Radiation Therapy for Early Glottic Carcinoma
M.T. SCOTT, MD, MBA

(S012) Prognostic Value of Radiographic Extracapsular Extension in Locally Advanced Non-Oropharyngeal Head and Neck Squamous Cell Cancers
JERRY T. LIU, MD

(S013) Adjuvant Radiation Therapy and Temozolomide for Anaplastic Gliomas: The Twelve-Year Washington University Experience
CHRISTINA K. SPIERS, MD

(S014) GammaKnife Stereotactic Radiosurgery in the Treatment of Brainstem Metastases
K. RAINH VOONG, MD

(S015) Temporal Lobe Radionecrosis After Skull Base Radiotherapy: Dose-Volume Predictors
MARK W. MCDONALD, MD

(S016) Head and Neck Second Primary Cancer Rates in the HPV Era: A SEER Analysis
DAYSSY A. DIAZ, MD

(S017) Long-Term Outcome of Intensity-Modulated Radiation Therapy in Pediatric Craniopharyngioma
BRAD J. GREENFIELD, MD

(S018) Early Tumor Perfusion Changes Predict Time to Progression in Patients With Recurrent Low-Grade Gliomas Treated With Everolimus Under a Phase II Clinical Trial
MICHAEL WAHL, MD

11:45 AM–12:30 PM

(PANEL) Difficult Cases at the Skull Base (SAM)
The aim of this session is to highlight diagnostic and therapeutic challenges in patients with skull base malignancies. An overview of novel surgical and radiotherapeutic approaches will be discussed.

PANEL CHAIR: Mark Henderson, MD
Oregon Health Sciences University

PANELISTS:
Michael E. Kupferman, MD
UT MD Anderson Cancer Center

Mark McDonald, MD
Indiana University School of Medicine

12:30–1:30 PM

MEET THE PROFESSOR LUNCHEON: Head and Neck**
Come discuss case studies with well-known professors, and get all questions answered.

SPEAKERS:
Peter A.S. Johnstone, MD
Indiana University School of Medicine

John A. Ridge, MD, PhD
Fox Chase Cancer Center

12:30–1:30 PM

TUMOR BOARD LUNCHEON: Sarcoma Cases**
Come discuss case studies with well-known experts in the field, and get all questions answered.

SPEAKERS:
Murray F. Brennan, MD
Memorial Sloan-Kettering Cancer Center
Kaled Alektiar, MD
Memorial Sloan-Kettering Cancer Center

**Registration and payment are required for this luncheon. Space is limited.

1:30–2:30 PM

CAREER DEVELOPMENT SEMINAR
This session will focus on professional development for graduating residents as well as practitioners in their first few years of practice. The emphasis is on evidence-based discussion of common professional and practice issues.

• Committee Participation as a Means to Professional Growth
SUE S. YOM, MD, PhD

• Acquiring and Honing Educator Skills by Teaching and Mentoring
JONATHAN BEITLER, MD

• The Importance of Recertification and Lifelong Learning in Professional Life
BRUCE HAFFTY, MD

• Work-Life Balance in Radiation Oncology Practice
KAREN COHEN, MD

SPEAKERS:
Kenneth Roberts, MD
Yale University

Sue S. Yom, MD, PhD
University of California, San Francisco

Jonathan Beitler, MD
Emory University

Bruce Haffty, MD
UMDNJ Robert Wood Johnson Medical School

Karen Cohen, MD
Texas Oncology

This session is complimentary, but registration is required.
5:30–6:45 PM  COCKTAIL RECEPTION & PANEL: How Will Health Care Reform and Payment Trends Affect Radiation Oncology? 
Sponsored by Varian Medical Systems 

PANELISTS: 
James D. Cox, MD 
UT MD Anderson Cancer Center 
Andre Konski, MD 
University of Pennsylvania 
Christopher Rose, MD, FACR 
Vantage Oncology, Inc.

6:45–8:45 PM  ARS SOCIAL EVENT (ONSITE): ISLAND CARNIVAL DINNER BANQUET— Enjoy Island fare, music, and carnival. 
ATTIRE: Island casual! 
• Dinner, drinks, and entertainment are included. 
• Attendance is complimentary with conference and guest registration. Tickets may be purchased for additional guests.

The American Radium Society gratefully acknowledges Varian Medical Systems for its support of the ARS Social Event, through an educational grant.

MONDAY, APRIL 28, 2014

7:00–7:45 AM  CONTINENTAL BREAKFAST AND EXHIBITS/POSTER SESSION

7:45–8:30 AM  PANEL: Case-Based Lung Cancer Review (SAM) 

PANEL CHAIR: Ben Movsas, MD 
Henry Ford Hospital 

PANELISTS: 
Reza Mehran, MD 
UT MD Anderson Cancer Center 
Ramesh Rengan, MD 
University of Washington 
Charles Simone, MD 
University of Pennsylvania 

The American Radium Society gratefully acknowledges an unrestricted educational grant from Varian Medical Systems in support of this Session.

8:30–9:15 AM  SCIENTIFIC SESSION #3: Lung Cancer/Stereotactic/Metastasis 

MODERATORS: Quynh Nguyen, MD 
UT MD Anderson Cancer Center 
Steve Hahn, MD 
University of Pennsylvania 

The American Radium Society gratefully acknowledges unrestricted educational grants from Hitachi, Ltd., and IBA in support of this Session.

(S019) Prospective Evaluation of Stereotactic Radiosurgery for Spinal Metastases in the Postoperative Setting 
RANDA TAO, MD

(S020) Availability of Single-Fraction Palliative Radiotherapy for Cancer Patients Receiving End-of-Life Care Within the Veterans Healthcare Administration 
DREW MOGHANAKI, MD, MPH

(S021) Central Versus Peripheral Tumor Location: Influence on Survival, Local Control, and Toxicity Following Stereotactic Body Radiotherapy for Primary Non–Small-Cell Lung Cancer 
HENRY S. PARK, MD, MPH

(S022) Influence of Preoperative Radiation Field on Postoperative Leak Rates in Esophageal Cancer Patients After Trimodality Therapy 
STEVEN H. LIN, MD, PhD

(S023) Stage I Lung SBRT Clinical Practice Patterns 
CHRISTOPHER D. CORSO, MD, PhD

(S024) Correlation of Survival to CBCT-Based Tumor Response During Chemoradiation in Patients With Stage III Non–Small-Cell Lung Cancer 
SALMA JABBOUR, MD

9:15–10:00 AM  KEYNOTE LECTURE: 
Carolyn Compton, MD, PhD 
Arizona State University 
“Technology Development, Disruptive Innovation, and the Future of Medicine” (SAM)

10:00–10:15 AM  BREAK

10:15–11:00 AM  SCIENTIFIC SESSION #4: Young Oncologist Essay Awards 
MODERATOR: Elin R. Sigurdson, MD, PhD 
Fox Chase Cancer Center

(S025) Radiation-Induced Increases in PARP1 Activity Predict for Long-Term Radiosensitization by PARP1 Inhibition in Preclinical Breast Cancer Models 
COREY SPEERS, MD, PhD

(S026) Postmastectomy Radiation Therapy for T3N0 Breast Cancer: A SEER Analysis 
MAGGIE M. JOHNSON, MD

(S027) Patterns of Failure for Rhabdomyosarcoma of the Perineal and Perianal Region 
DANA L. CASEY

(S028) Sequential Short-Course Radiotherapy and FOLFOX Chemotherapy as Preoperative Therapy for Rectal Cancer Provides Increased DFS Compared With Historical Controls 
STEPHANIE MARKOVINIC, MD, PhD

(S029) Patient-Reported Voice and Speech Outcomes and Their Clinical and Dosimetric Predictors After Chemo-IMRT of Oropharyngeal Cancer: A Prospective Longitudinal Study 
JEFFREY M. VANSHEIT, MD
11:00–11:45 AM  DEBATE:  Operating on High-Risk Prostate Cancer
MODERATORS:
Alan Pollack, MD, PhD
University of Miami
DEBATERS:
Mack Roach, MD
University of California, San Francisco
Timothy Masterson, MD
Indiana University School of Medicine

11:45 AM–12:30 PM  SCIENTIFIC SESSION #5:  Genitourinary Cancer
MODERATORS:
Matthew Abramowitz, MD
University of Miami
Seungtaek Choi, MD
UT MD Anderson Cancer Center

(S030) Utilization of Postprostatectomy Radiation Therapy at an NCI-Designated Comprehensive Cancer Center
JEFFREY M. MARTIN, MD, MS

(S031) A Phantom-Based Simulator Approach to Improving the Quality of Prostate Brachytherapy Training
NIKHIL G. THAKER, MD

(S032) Stereotactic Body Radiation Therapy for Low-, Intermediate-, and High-Risk Prostate Cancer: Disease Control and Quality of Life at Six Years
ALAN KATZ, MD, JD

(S033) Dose-Escalated Radiation Therapy With or Without Short-Course Androgen Deprivation for Intermediate-Risk Prostate Cancer
ELLIOT NAVIO, MD

(S034) Do Sociodemographic Factors Influence Outcome in Prostate Cancer Patients Treated With External Beam Radiation Therapy (EBRT)?
AVIVELLE Y. MOVAS

(S035) Peripheral and Lymphatic Radiation (RT) Doses With Treatment on RTOG 9413: Immunosuppression or Scattered Doses and Death From Second Cancers
JOSEPHINE CHEN, PhD

(S036) The Low Alpha-Beta Ratio of Bladder Cancer: A Rationale for Hypofractionation
JUNG JULIE KANG, MD, PhD

12:30–1:30 PM  TUMOR BOARD LUNCHEON:
Breast Cases**
Come discuss case studies with well-known experts in the field, and get all questions answered.

SPEAKERS:
Bruce Haffty, MD
UMDNJ Robert Wood Johnson Medical School
Patrick Borgen, MD
Maimonides Medical Center
**Registration and payment are required for this luncheon. Space is limited.

1:30–2:30 PM  BRACHYTHERAPY COURSE**
Get practical pointers and learn about emerging technological refinements in the treatment of sarcoma, prostate, and gynecologic cancers.

OBJECTIVES:
After this course, participants will be able to:
1. Understand how to use image-guided brachytherapy to treat prostate cancer.
2. Understand how image-guided brachytherapy is used in difficult implant cases.
3. Understand HDR brachytherapy dose planning and optimization.

SPEAKERS:
Joe Hsu, MD
University of California, San Francisco
Ann Klopp, MD, PhD
UT MD Anderson Cancer Center
Kaled Alektiar, MD
Memorial Sloan-Kettering Cancer Center
Mack Roach, MD
University of California, San Francisco
**Registration and payment are required for this session. Space is limited.

TUESDAY, APRIL 29, 2014

7:00–7:45 AM  CONTINENTAL BREAKFAST AND EXHIBITS/POSTER SESSION

7:45–8:15 AM  BUSINESS MEETING
All ARS Members are welcome to attend. Only Active Members may vote.

8:15–9:00 AM  PRESIDENTIAL LECTURE:
Elin R. Sigurdson, MD, PhD
Fox Chase Cancer Center
“Evolution in the Treatment of Rectal Cancer” (SAM)
9:00–9:30 AM  SCIENTIFIC SESSION #6: Gastrointestinal Cancer

MODERATORS: Charles Thomas, MD
Oregon Health Sciences University
Shlomo Koyfman, MD
Cleveland Clinic

(S037) Changes in Mass Transport as an Early Marker of Response to Cytotoxic Therapy in Human Pancreatic Adenocarcinoma
EUGENE J. KOAY, MD, PhD

(S038) Patient Tolerability and Acute Toxicity of Intensity-Modulated Radiation Therapy for Treatment of Carcinomas of the Biliary Tract
LIOR Z. BRAUNSTEIN, MD

(S039) ALDH-Expressing Cancer Stem Cells Are Associated With Inferior Survival in Patients With Resected Pancreatic Adenocarcinoma Treated With Adjuvant Chemoradiation
RACHIT KUMAR, MD

(S040) Outcomes, Costs, and Patient Satisfaction in a Pancreatic Multidisciplinary Clinic: Can Multidisciplinary Oncology Models Deliver Higher-Value Care?
SHEREEF M. ELNAHAL, MD, MBA

(S041) The Effect of High-Dose Stereotactic Body Radiation Therapy on Liver Function in the Treatment of Primary and Metastatic Liver Malignancies Utilizing the Child-Pugh Score Classification System
PAVEL T. DYK, MD

9:30–9:45 AM  BREAK

9:45–10:30 AM  KEYNOTE LECTURE:
Peter Ubel, MD
Duke University

“The Challenge Physicians Have Partnering With Patients to Make Important Medical Decisions”

10:30–11:15 AM  DEBATE: MRI for Breast Cancer Conservation

MODERATOR: Mary Katherine Hayes, MD
Weill Cornell Medical College

DEBATORS:
Gary Freedman, MD
University of Pennsylvania
Rick Bleicher, MD, FACS, FRCS
Fox Chase Cancer Center

11:15 AM–12:15 PM  SCIENTIFIC SESSION #7: Breast Cancer

MODERATORS: Meena Moran, MD
Yale University
Cynthia Ballenger, MD
Carolina Radiation Medicine

12:30–1:00 PM  PANEL: Technology/Cost/QA in Health Care Around the World (SAM)

PANEL CHAIR: Kenneth Roberts, MD
Yale University

PANELISTS:
Jiade J. Lu, MD
Shanghai Proton and Heavy Ion Center
Ben Slotman, MD
VU University Medical Center
Daniel Dosoretz, MD, FACR, FACRO
21st Century Oncology

(S042) Changing Practice Patterns for Breast Cancer Radiotherapy With Clinical Pathways: An Analysis of Hypofractionation in a Large, Integrated Cancer Center Network
MALOLAN S. RAJAGOPALAN, MD

(S043) RadiotypeDx: Validation of a Radiation Sensitivity Signature in Human Breast Cancer
CORY SPEERS, MD, PhD

(S044) Repeated Measures Analyses of the Common Terminology Criteria for Adverse Events (CTCAE v3.0)-Based Dermatitis Toxicities in Breast Cancer Patients Receiving Radiotherapy in a Phase III Randomized Trial of Mometasone Furoate, N06C4 (Alliance)
TERENCE T. SIO, MD, MS

(S045) Breast Conservation Therapy in Early-Stage Female Breast Cancer Patients Aged Less Than 40 Is Not Inferior to Mastectomy: A Surveillance, Epidemiology, and End Results Data Analysis
JASON C. YE, MD

(S046) Changes in Brachytherapy-Based APBI Patient Selection in the Period Immediately Before and After Publication of the ASTRO Consensus Statement
ZHAIN A. HUSAIN, MD

AUSTIN DOSCH, BS

(S048) Impact of Breast Cancer Subtype in Locoregional Outcomes in Stage III Locally Advanced Breast Cancer (LABC) Treated With Modern Multimodality Therapy
JONATHAN VERMA, MD, DEUKWOO KWON, PhD

* Schedule is subject to change.
** Registration and payment are required for this session. Space is limited.
96th Annual American Radium Society Meeting Satellite Symposium

Best Practices on Improving Science and Technology in the Radiation Treatment Center: An Elekta Happy Hour Symposium

The symposium is not part of the official program of the American Radium Society Annual Meeting.

SUNDAY, APRIL 27, 2014

2:30–4:00 PM
Harbour Ballroom, Marriott Frenchman’s Reef
Snacks and tropical refreshments will be served.

Using Technology to Support New Ways of Delivering Quality Care to Improve Patient Experience and Measure Outcomes
Marie-Andrée Fortin, MD
Head of Radiation Oncology, Clinical Adjunct Professor
University of Montreal, CIC Laval, Montreal, Canada

Can SBRT Be a Solution for Partial Prostate Treatment? Defining the Target Volume Through a Correlation of Histopathology and Advanced Imaging
Rodney J. Ellis, MD
Vice-Chairman, Radiation Oncology Department
University Hospitals Case Medical Center, Seidman Cancer Center, Cleveland, Ohio
The American Radium Society invites you and your colleagues to participate in the

**ARS 97th Annual Meeting**

**May 2–6, 2015**

**Grand Hyatt Kauai**

**Kauai, Hawaii**

**President:** Kenneth Rosenzweig, MD

**Program Chair:** Ben Movsas, MD

**CALL FOR ABSTRACTS** All authors who wish to present papers for the ARS 97th Annual Meeting may submit an abstract online starting in August 2014. Abstracts may be selected for either oral or poster presentations.

**Deadline for submission is November 7, 2014.**

We encourage everyone to submit an abstract, whether or not you are a member of the ARS. Visit [www.americanradiumsociety.org/abstracts](http://www.americanradiumsociety.org/abstracts) for more information and complete submission instructions.

Original contributions should be submitted for consideration; any work that has already been accepted for publication or previously presented is not eligible.

For more information, please visit [www.americanradiumsociety.org](http://www.americanradiumsociety.org) or contact the ARS office:

11300 West Olympic Blvd, suite 600 | Los Angeles, CA 90064

**Travel Grants and Essay Awards:**

Trainees who submit a completed manuscript, dealing with subjects related to clinical, translational or basic research, by November 7, 2014, are eligible for the **Young Oncologist Essay Awards**. These awards provide an honorarium of $500 plus reimbursement up to $2,000 for travel. **Young Oncologist Travel Grants** of $1,000 will also be available for outstanding abstracts that are reviewed favorably for presentation at the Annual Meeting.

**Phone:** (310) 437-0581  |  **Fax:** (310) 437-0585

**Email:** info@americanradiumsociety.org  |  **Twitter:** @RadiumSociety  |  **Facebook:** www.facebook.com/AmericanRadiumSociety
SCIENTIFIC PAPERS

(S001) Limb-Sparing Surgery and Intraoperative Radiotherapy in the Treatment of Primary, Nonmetastatic Extremity and Limb-Girdle Soft Tissue Sarcoma

Christopher L. Tinkle, MD, Richard J. O'Donnell, MD, Vivian Weinberg, PhD; Stuart Y. Tsuji, MD, Daphne Haas-Kogan, MD, Alexander R. Gottschalk, MD, PhD; Department of Radiation Oncology, University of California, San Francisco; Department of Orthopedic Surgery, University of California, San Francisco; Department of Radiation Oncology, The Queen's Medical Center

PURPOSE: To investigate the efficacy and morbidity of limb-sparing surgery with intraoperative radiotherapy (IORT) for patients with primary, nonmetastatic extremity and limb-girdle soft tissue sarcoma (STS) at high risk for recurrence.

MATERIALS AND METHODS: A retrospective analysis was performed of patients with extremity and limb-girdle STS treated with IORT following limb-sparing resection by a single orthopedic oncologist at the University of California, San Francisco, from December 1998 through November 2011. Sixty-six consecutively treated patients with primary, nonmetastatic STS were identified. Upfront oncologic resection was performed in 67% of patients, while re-resection of prior excisional biopsy was performed in 33%. Close (<2 mm) or positive margins were found in 59% of patients. Sixty-seven percent received both IORT and external beam radiation (EBRT), with a median IORT dose of 1,250 cGy (range: 1,000–1,800 cGy) and median EBRT dose of 5,970 cGy (range: 4,140–6,660 cGy). Perioperative chemotherapy was delivered to 61% of patients. The most common histologies were synovial sarcoma and undifferentiated pleomorphic sarcoma (38% and 17%, respectively), and most tumors were high-grade (Coindre grade 2–3) (88%), deep in location (79%), and American Joint Committee on Cancer (AJCC) pathologic stage II or higher (88%). The Kaplan-Meier score was used to estimate disease control and survival, subsets were compared using a log-rank statistic, and toxicity was reported according to Common Terminology Criteria for Adverse Events version 4.0 (CTCAE v4) guidelines.

RESULTS: With a median duration of follow-up from surgery and IORT of 50.9 months (range: 11.8–141.5 mo), 13 patients developed a local recurrence, with 4 subsequently undergoing amputation. The 5-year Kaplan–Meier estimates for local control were 78% (95% confidence interval [CI], 65%–87%); 94% for amputation-free survival (95% CI, 84%–98%); 72% for metastasis-free control (95% CI, 59%–82%); 64% for disease-free survival (95% CI, 50%–75%); and 81% for overall survival (95% CI, 68%–90%). Age older than 50 years and having AJCC stage III disease resulted in increased local recurrence (P = .02 and P = .06, respectively), while other factors, including margin status, tumor grade, T stage, tumor depth, re-resection, and perioperative chemotherapy, did not impact local control. Interestingly, the addition of EBRT did not appear to significantly influence local control, with a 5-year estimate of local control for patients who did not receive EBRT of 71%, compared with 82% for those who did (P = .28). This was also the case in patients treated with perioperative chemotherapy (P = .58) and grade 3 tumors (P = .56); however, a benefit with EBRT was observed for those with close/positive margins (P = .01). Grade 3 or higher acute and late toxicities were reported in 16 and 18 patients, respectively.

CONCLUSIONS: IORT in combination with oncologic resection of high-risk extremity and limb-girdle STS yields excellent rates of local control and limb salvage with acceptable morbidity. This technique offers a method of delivering focal therapy to reduce the risk associated with close/positive margins while maintaining adequate local control with relatively reduced-dose EBRT.

(S002) Outcomes and Prognostic Factors of Stereotactic Body Radiotherapy for Soft Tissue Sarcoma Metastases

Kenneth Merrell, Samuel Francis, Benjamin Mou, Christopher Hallemeier, Kenneth Olivier; Department of Radiation Oncology, Mayo Clinic; University of Utah School of Medicine

BACKGROUND: Radiobiology studies suggest that soft tissue sarcoma (STS) is a radioresistant tumor. Primary therapy for localized and oligometastatic STS is surgical resection, often in combination with radiation therapy (RT). Stereotactic body RT (SBRT) allows delivery of large conformal doses of radiation, potentially overcoming radioreistance. We reviewed our institutional outcomes of patients treated with SBRT for metastatic STS.

MATERIALS AND METHODS: A retrospective chart review was performed on 21 patients with 30 metastatic STS lesions who received SBRT at Mayo Clinic between May 2008 and June 2013. Patients were treated with 3D conformal, static-field, or volumetric arc intensity-modulated radiation therapy. The median dose (cGy) and fractionation of lung, bone, liver, and soft tissue was 5,000/5, 2,400/1, 4,250/5, and 4,000/4, respectively. Tumor response was scored using Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1). Toxicity was scored using National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events version 4.0 (CTCAE v4). Local control (LC) and overall survival (OS) were estimated using the Kaplan-Meier method.

RESULTS: Median age was 49 years (range: 30–85 yr). Median follow-up time was 24 months (range: 3–65 yr). Median tumor size was 24 mm (range: 6–145 mm). The most common histologies included pleomorphic sarcoma (n = 5, 24%), leiomyosarcoma (n = 4, 19%), and synovial cell sarcoma (n = 3, 14%), with 95% (n = 20) being high-grade sarcoma. The sites that were treated included bone (n = 11, 36.6%), lung (n = 15, 50%), liver (n = 2, 6.7%), and soft tissue (n = 2, 6.7%). LC at 12, 24, and 48 months was 94.4%, 82.6%, and 82.6%, respectively. Rates of complete response, partial response, and stable disease were 6% (n = 2), 43% (n = 13), and 47% (n = 14), respectively. There were two local failures: one after a partial response and one in a patient with progressive disease on the first follow-up scan. Univariate analysis demonstrated no association with histologic subtype, tumor size, site treated, or RT dose with regard to LC. Median survival was 24 months, with rates of OS at 12, 24, and 48 months of 74.4%, 57.9%, and 12.5%, respectively.
Acute and late toxicities were rare, with none higher than grade II. The most frequent toxicities included acute pain flare (n = 2), acute nausea (n = 3), and late cough (n = 2).

CONCLUSIONS: SBRT provides excellent local control for metastatic STS. Treatments were well tolerated, with no side effects greater than grade II. Most patients received SBRT after failing multiple lines of chemotherapy, and thus, survival was poor. This study demonstrates that SBRT is an excellent option for local therapy in metastatic STS and warrants further investigation.

(SO03) Disparities in Stage at Diagnosis and Survival in Adult Cancer Patients According to Insurance Status

Gary Y. Walker, MD, MPH, Stephen R. Grant, BS, Ashleigh Guadagnolo, MD, MPH, Matthew Kooby, MD, Usama Mahmood, MD; UT MD Anderson Cancer Center

BACKGROUND: The Patient Protection and Affordable Care Act seeks to increase the rate of participation in insurance plans for the 48 million individuals without coverage. The purpose of this study is to determine the influence of insurance status on the stage of presentation and survival among non–Medicare-age adult patients with the 10 most common causes of cancer death using the Surveillance, Epidemiology, and End Results (SEER) public use database.

METHODS: A total of 473,722 patients aged 18–64 years who were diagnosed with 1 of the top 10 causes of cancer death (breast, prostate, lung, colorectal, head and neck, non-Hodgkin lymphoma, liver, pancreatic, ovarian, esophageal) in the SEER database from 2007–2010 were analyzed. Demographic information was obtained, including age, gender, race, year of diagnosis, and marital status. Insurance status was defined as insured, Medicaid, or uninsured. Extent of disease was categorized as local (no nodal or metastatic disease), regional (nodal disease), or metastatic (any distant disease). Definitive treatment was defined as surgery (for breast, colorectal, liver, ovarian, and pancreatic cancers) or surgery and/or radiation therapy (for esophageal, head and neck, lung, and prostate cancers). A Cox proportional hazards model was used for multivariate analyses to assess the effect of patient and tumor characteristics on cause-specific death, stratified by insurance status.

RESULTS: The median follow-up was 17 months (range: 0–47 mo). A total of 371,628 (78.4%) had insurance, 55,135 (11.6%) had Medicaid, and 22,442 (4.7%) did not have insurance. On univariate analysis, the following demographic characteristics were associated with the lack of insurance: younger age, male gender, nonwhite race, being unmarried, rural residence, and residing in a county with a higher poverty level. Overall, patients with insurance were less likely to present with metastatic disease (16.9%) than those with Medicaid (29.1%) or without insurance coverage (34.7%) and more likely to present with local disease (60.8%) compared with those with Medicaid (42.2%) or without insurance coverage (40.3%) (P < .001). The unadjusted 3-year cause-specific survival among those with insurance was 83.4%, compared with 64.1% among those with Medicaid and 61.8% among those without insurance coverage (P < .0001). In a Cox regression that adjusted for age, race, gender, marital status, residence (urban vs rural), percentage of county below federal poverty level, stage (local, regional, distant), and receipt of definitive treatment, patients were more likely to die of their disease if they had Medicaid (hazard ratio [HR] = 1.53; 95% confidence interval [CI], 1.49–1.56) or did not have insurance coverage (HR = 1.52; 95% CI, 1.48–1.57) compared with those with insurance (P < .001).

CONCLUSIONS: Among patients with the top 10 causes of cancer death, those with Medicaid or without insurance were more likely to present with advanced-stage disease. This group also experienced worse survival when controlling for demographic information, stage at diagnosis, and receipt of definitive treatment. The expansion of insurance coverage would be expected to substantially impact the presentation and outcome of cancer in the US.

(SO04) Radiation Publications Underrepresented in High-Impact General Medical and Oncology Journals

Emma B. Holliday, MD, Awad A. Ahmed, Stella K. Yoo, Reshma Jagsi, MD, DPhil, Karen E. Hoffman, MD, MHSc, MPH; UT MD Anderson Cancer Center; Temple University Medical School; University of Michigan

OBJECTIVE: Cancer treatment studies are well represented in high-impact oncology as well as general medical journals. We sought to evaluate the distribution and characteristics of oncology studies by intervention (radiation, surgery, cytotoxic chemotherapy, or targeted/systemic agents) in six high-impact oncology and general medical journals.

METHODS: Research articles that were published in 2012 were identified via a commercially available online database (Scopus, Elsevier BV, NL). The journals that were included were The New England Journal of Medicine, The Lancet, The Journal of the American Medical Association, The Lancet Oncology, The Journal of Clinical Oncology, and The Journal of the National Cancer Institute. Studies were included if they evaluated a therapeutic intervention in a randomized controlled trial (RCT), prospective controlled clinical trial (PCCT), or retrospective review (RR). Intervention type, outcome measure, and number of citations per article were recorded from Scopus on September 18, 2013. Each study was scored using the Effective Public Health Practice Project (EPHPP) Quality Assessment Tool, which averages six components to provide a total numeric score from 1–3, (1 = strong, 2 = moderate, 3 = weak). Total quality rating was defined as “strong” if no individual components rated 3, “moderate” if one was rated 3, and “weak” if more than one was rated 3. Data were analyzed (SPSS version 17; Chicago, IL) using Pearson chi-square test for between-group comparisons of categorical variables and Mann-Whitney U test to compare medians for continuous variables.

RESULTS: A total of 286 studies were included: 41 investigating radiation, 15 investigating surgery, 69 investigating cytotoxic chemotherapy, and 161 investigating targeted/other systemic therapies. There were no significant differences between radiation studies and the remaining studies in terms of distribution of trial type

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(P = .177); number of citations (P = .665); EPHPP average numerical score (P = .286); or designation as strong, intermediate, or weak (P = .403). When controlling for trial type in the univariate analysis, there was still no significant difference between the groups in terms of EPHPP score (P = .109). Radiation studies had lower rates of industry funding than the rest of the studies (P < .001). Additionally, more radiation studies evaluated tumor control or treatment-related toxicity, and fewer studies evaluated response/safety as endpoints (P < .001) (Table).

**CONCLUSIONS:** Far fewer radiation oncology studies are published when compared with studies evaluating either traditional cytotoxic chemotherapy or targeted/other systemic agents, although radiation studies that are published in the high-impact oncology and medical literature appear to have comparable quality. Further attention must be paid to identify and correct potential biases in oncology publications and to ensure that radiation oncology studies are not relegated to specialty-specific journals that fail to reach a broad audience.

**S005) Adjuvant Radiotherapy in Stage II Endometrial Carcinoma: Is Brachytherapy Alone Sufficient for Local Control?**

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**OBJECTIVE:** To evaluate recurrence patterns and overall survival in patients treated with adjuvant radiation after surgical staging for stage II endometrial carcinoma. Secondary goals include identification of prognostic factors for recurrence.
Materials and Methods: The medical records of 62 patients treated with adjuvant radiotherapy at Washington University School of Medicine following surgical staging for endometrial cancer (total abdominal hysterectomy and bilateral salpingo-oophorectomy, peritoneal cytology, and lymph node dissection) were reviewed. Twenty-six were treated with a combination of external beam radiotherapy and vaginal brachytherapy (EBRT + VB), and 36 patients were treated with postoperative vaginal brachytherapy (VB) alone. Median follow-up for all patients was 48 months.

Results: Median patient age was 61 years (range: 30–87 yr). All tumors had endometrioid histology. There were 30 grade 1 tumors, 20 grade 2 tumors, and 12 grade 3 tumors. For all patients, the 5-year overall survival was 75.4%, and the 5-year recurrence-free survival was 89%. There was no statistically significant difference in overall survival ($P = .770$) or freedom from vaginal recurrence ($P = .981$), pelvic ($P = .834$), distant ($P = .307$), or any recurrence ($P = .230$) with respect to modality of treatment (EBRT + VB vs VB alone) (Figure). In the multivariate analysis, the only risk factor influencing overall survival was patient age ($P = .033$). Four patients experienced a toxicity requiring hospital admission, and all of these patients were treated with pelvic external beam plus brachytherapy.

Conclusions: Vaginal brachytherapy alone results in excellent local control for patients with stage II endometrial cancer after surgical staging. Long-term toxicities are rare and are more common in patients who are treated with pelvic external beam plus brachytherapy.

(S006) Extended-Field IMRT With Concomitant Boost for Node-Positive Cervical Cancer: Analysis of Regional Control Rate and Recurrence Pattern

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Purpose: Positron emission tomography–computed tomography (PET-CT) is commonly used for nodal staging for locally advanced cervical cancer treated with primary chemoradiation therapy. Although it has high sensitivity and specificity for pelvic nodal staging, the false negative rates for para-aortic (PA) disease is 20% to 25% in patients with PET-positive pelvic nodal disease. Unless surgical staging is done in this subset to exclude PA nodal disease, pelvis-only treatment may undertreat PA disease. We have been treating patients with positive pelvic nodes with extended-field intensity-modulated radiation therapy (IMRT) to address the PA region prophylactically with a concomitant boost to the involved nodes. The purpose of this study is to assess regional control rates and recurrence patterns with this technique.

Materials and Methods: Sixty-one patients who were diagnosed from 2003–2012 with cervical cancer of stage IB1 to IVA with PET-avid pelvic nodes that were treated with extended-field IMRT were retrospectively analyzed. The nodal location was pelvic only in 41 (67%) patients and pelvis plus the PA region in 20 (33%) patients. The median cervical tumor and nodal sizes were 5.3 cm (range: 2–10 cm) and 1.8 cm (range: 0.7–4.5 cm), respectively. The median number of positive nodes in each patient was 2 (range: 1–16), with the total number of positive nodes being 179, including all patients. All but one patient was treated with concurrent weekly cisplatin. The dose to the pelvis and PA region was 45 Gy in 25 fractions, with a concomitant boost to involved nodes to a median dose of 55 Gy in 25 fractions (range: 54–59.4 Gy). The median brachytherapy dose was 27.5 Gy in 5 fractions using either intracavitary or interstitial technique. A follow-up PET-CT was performed at 12–16 weeks to assess response.

Results: Complete clinical and radiographic response at the first follow-up for all sites was seen in 47 (77%) patients. Persistent nodal disease or progression of nodal disease at the first follow-up was seen in two patients (pelvic nodal disease in one patient and another with a new PA node with lung metastases). At a mean follow-up of 29 months (range: 3–116 mo), eight additional patients developed recurrences. The median time to recurrence was 14 months (range: 10–36 mo). The sites of persistence or recurrent disease were the cervix (10, 16.3%), regional nodes (3, 4.9%), and distant (14, 23%) (some had more than one site of relapse). The 3-year risk of local, regional, and distant recurrence and disease-free survival (DFS) was 75.8%, 93.9%, 66.7%, and 56.9% respectively. The 3-year DFS for pelvic node only–versus pelvic plus PA node-positive disease was 63.8% versus 39%, respectively. On mul-

4
tivariate analysis, only stage predicted for worse DFS. The rate of late grade 3 and above complications was 4%.

CONCLUSIONS: Extended-field IMRT in patients with PET-positive pelvic nodes was well tolerated and resulted in very low regional recurrence rates. The dose of 55 Gy in 25 fractions was effective in eradicating disease in the involved nodes without increasing the risk of late complications. Distant metastases were the predominant mode of failure in these patients, and the OUTBACK trial may define the benefit of additional chemotherapy.

(S007) Stereotactic Radiosurgery to the Brain With Concurrent BRAF Inhibitors for Melanoma Metastases

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PURPOSE AND OBJECTIVES: Linear accelerator-based stereotactic radiosurgery (SRS) is an effective treatment for selected melanoma patients with brain metastases. Recently, BRAF inhibitors have shown efficacy in stage IV melanoma. We sought to determine the effectiveness of SRS in patients with melanoma who are also being treated with BRAF inhibitors.

MATERIALS AND METHODS: An analysis of patients with metastatic melanoma treated with SRS while on BRAF inhibition was performed. All patients were treated with BRAF inhibitors within 3 months of their SRS treatment and were asked to stop the drug 1–2 days before and after SRS. MRI scans were reviewed post-SRS to evaluate local control (LC). Toxicity was recorded. Disease progression by imaging was defined by the 2009 Response Evaluation Criteria in Solid Tumors (RECIST) criteria. Survival curves were calculated according to the Kaplan-Meier (KM) method from the date of diagnosis of brain metastases and the date of SRS.

RESULTS: We identified 41 metastatic melanoma brain lesions treated in 13 patients. The median age was 49 years (range: 33–74 yr). All patients presented with extracranial metastases. Three patients (23.1%) were diagnosis specific-graded prognostic assessment (DS-GPA) class 0, three patients (23.1%) were DS-GPA class 1, and seven patients (53.8%) were DS-GPA class 2. The median planning target volume (PTV) was 0.47 cm³ (range: 0.05–4.19 cm³), and lesions were treated to a median dose of 24 Gy (range: 16–24 Gy). The median lesion diameter was 8 mm (range: 3–21 mm). One patient received whole-brain radiation therapy (WBRT) prior to SRS. Two patients underwent two courses of SRS, and another two patients were treated with three courses of SRS while on BRAF inhibitors. The median follow-up was 9 months (range: 2.5–26.8 mo). Four of the 41 (9.8%) lesions showed progression by MRI at a median of 19.1 months following SRS (range: 11.8–20.1 mo); this occurred in three patients, all of whom underwent surgical resection. The pathology examination confirmed radiation necrosis in one lesion and tumor progression in three lesions. After SRS, there was no evidence of intracranial hemorrhage, scalp reactions, or other radiation-related acute toxicity. KM local control estimates at 6 and 12 months were 100% and 90.9%, respectively, for treated lesions. Ten (71.4%) patients were noted to have distant failure in the brain, with four of these patients showing disease progression systemically. Of the patients with distant brain failure, two patients received WBRT, and six patients received additional SRS. Median overall survival (OS) was 19.2 months (range: 5.5–27.2 mo) and 18 months (range: 5.1–26.1 mo) from the date of diagnosis of brain metastases and the date of SRS, respectively. The KM OS estimates at 6 and 12 months were 84.6% and 76.9%, respectively, from the time of SRS treatment. OS according to DS-GPA class at 12 months was 90.0% and 33.3% for classes 1–2 and 0, respectively (P = .02).

CONCLUSIONS: SRS to cranial melanoma metastases appears to be both safe and effective for patients treated concurrently with systemic BRAF inhibitors. In our series, we report acceptable local control and no evidence of increased toxicity.

(S008) Use of Mobile Devices for Creation of Survivorship Care Plans

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INTRODUCTION: Cancer survivors may experience myriad late effects, and the Institute of Medicine recommends that survivorship care plans be provided to all. This study explores the willingness of health care providers (HCPs) and survivors to utilize mobile devices (MDs) for this purpose.

METHODS: We launched and made an internet tool publically available for the creation of survivorship care plans in 2007. Available at www.livestrongcareplan.com and through the OncoLink website, it provides customized guidelines for survivorship care and is free for use by survivors and HCPs worldwide. With the ninth iteration of the care plan tool, launched in May 2012, the tool became available in a mobile use format. The tool is free and accessible via Apple iPhone and iPad.

RESULTS: Since the launch of the internet-based tool in 2007, it has been used to create 34,669 care plans. Overall, HCPs have created about 40% of them. The demographics of survivors for whom care plans have been created have remained relatively stable (75% women, 81% Caucasian, median age 51 years, with breast cancer being the most common diagnosis). From May 2012 to October 2013, 11,946 total plans were created, 645 (5%) of which were created using MDs. Of the MD-created plans, the majority (97%) was created by survivors or their friends and families, with only 3% being created by HCPs. Of the users of the MD plan, 74% was female and 86% was Caucasian, with a median age at diagnosis of 48 years and a median current age of 52 years. The most common diagnosis for which MD plans were completed was breast cancer (42%), followed by lymphoma (5%), colon cancer (4%), and lung cancer (4%). Of all MD users, 11% reported having received some type of survivorship information, and 15% reported having received a written treatment summary; 4% had previously created...
or received a LIVESTRONG Care Plan. The median time for completion of the patient version of the MD plan was 8:07 minutes and 6:27 minutes for the HCP version. The experience with using the MD tool was evaluated as good-excellent by 92% of users.

CONCLUSIONS: For users with access, MDs appear to be feasible tools for care plan creation. Based on preliminary data, this represents a novel way to disseminate useful information to cancer survivors, particularly those who may have MD access but not computer access. Future plans will include efforts to inform HCPs about the existence of the MD plan, which may be useful in clinical settings when tablet devices are available.

(S009) Two-Year Outcomes Following Triapine Radiochemotherapy for Cervical Cancer

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PURPOSE: Phase I and phase II trials were conducted between 2006 and 2011 to investigate the use of triapine radiochemotherapy in the treatment of cervical cancer. Triapine (3-aminopyridine-2-carboxaldehyde thiosemicarbazone) is a strong inhibitor of ribonucleotide reductase, the rate-limiting enzyme that supplies deoxynucleotides for DNA synthesis. As such, it is thought to potentiate the antitumor effects of chemotherapy and radiotherapy. Here, we present the 1- and 2-year survival outcomes from patients with stage IB2–IVB cervical cancer treated with triapine radiochemotherapy.

MATERIALS AND METHODS: Thirty-two women with clinical stage IB2–IIB cervical cancer were treated in phase I and phase II trials at a single institution with three times-weekly intravenous triapine (25–50 mg/m²) and once-weekly cisplatin (40 mg/m²) with concurrent daily pelvic radiation (45–54 Gy) followed by LDR cervical brachytherapy (30–40 Gy). Overall survival (OS) and recurrence-free survival were evaluated using Kaplan-Meier analysis.

RESULTS: Median follow-up was 27.4 months (range: 2–90 mo). Twenty-eight patients had stage IB2–IIB disease and were treated definitively, and four patients had known distant metastases at the time of diagnosis. One patient had a local recurrence (8 months), and seven patients developed distant recurrences (at 5, 5, 14, 23, 25, 26, and 52 months, respectively). All patients with stage IIB disease died of cancer-related causes (at 3, 13, 34, and 54 months, respectively). OS for all 32 patients at 1 and 2 years was 90.3% (95% CI, 59%–93%) and 86.4% (95% CI, 74%–99%), respectively. For the 28 patients with IB2–IIB disease, OS was 92.6% (95% CI, 82.7%–100%) at both 1 and 2 years. Relapse-free survival (RFS) was 80.8% (95% CI, 76%–100%) at 1 year and 65.6% (95% CI, 59%–93%) at 2 years. Median RFS was 50.9 months. Severe toxicity occurring in the first 2 years included two patients (6.25%) with rectovaginal fistula, one patient (3.1%) with a cerebrovascular accident, and one patient (3.1%) with sigmoid colitis requiring surgery for diversion.

CONCLUSIONS: Two-year follow-up after triapine radiochemotherapy reveals favorable survival outcomes in women with stage IB2–IIB cervical cancer. Further investigation comparing triapine radiochemotherapy with standard cisplatin radiochemotherapy is under way with a prospective randomized phase II National Cancer Institute-sponsored trial (NCT01835171) that has begun accrual.
treatment to a median dose of 54 Gy (range: 24–59.4 Gy) over 30 fractions (range: 12–33 fractions). From the dataset of 2,715 translational table shifts collected from 905 pretreatment cone-beam CTs, a mean translational table shift vector magnitude of 3 mm was calculated. The consortium dataset also allowed for hypothesis generation, with preliminary univariate analyses showing that use of anesthesia was significantly associated with table shift vector magnitudes that were less than the mean value of 3 mm \( (P = .021) \). Conversely, potential predictors, including age, gender, immobilization type, degree of surgical resection, concurrent chemotherapy, KPS, and planning target volume, did not reach statistical significance in the preliminary analyses.

CONCLUSIONS: We describe a method for prospective and real-time data collection that allows for analysis of large datasets of de-identified patient and treatment information across a consortium of multinational institutions. Given the scarcity of data to guide IGRT use in the pediatric population, such methodology provides a novel means for describing breadth of practice and establishing consensus recommendations for IGRT. To our knowledge, this is the first report of the successful deployment of such methodology for analysis of the pediatric population.

(S011) Comparison of Toxicities and Outcomes for Conventional and Hypofractionated Radiation Therapy for Early Glottic Carcinoma

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PURPOSE: The traditional approach to treatment of stage I vocal cord cancer has been to deliver 66–70 Gy in two Gy daily fractions. A Japanese randomized trial (2006) compared hypofractionated radiotherapy (RT) at 2.25 Gy daily with 56.25 Gy for “minimal” T1 and between 63 Gy for larger T1 tumors with 60–66 Gy in 2-Gy fractions. Local control was superior with hypofractionation, and toxicity was reported as extremely low in both arms, leading to widespread adoption of the hypofractionated regimen. However, many US institutions have modified this regimen to deliver a higher total dose (63 Gy for all T1, 65.25 Gy for T2), potentially resulting in more severe acute toxicity. The dose range for comparable conventionally fractionated patients is higher than in Japan, possibly improving local control. Our experience leads us to suspect that hypofractionation, as used in the US, increases toxicity without improving efficacy.

MATERIALS AND METHODS: From 2003–2013, 100 patients with histologically proven early-stage (T1–T2) squamous cell carcinoma of the larynx were treated with RT at our institution and analyzed retrospectively. Median age was 64 years (range: 31–94 yr). Seventy-six patients had T1 tumors, and 24 patients had T2 tumors. Forty-eight patients in the conventional RT group received 2 Gy daily; 52 patients in the hypofractionated group received 2.25 Gy daily. The median RT dose was 66 Gy (range: 54–70 Gy) for conventional RT and 63 Gy (range: 58.5–67.5 Gy) for hypofractionated RT. Fisher’s exact test was used for comparing toxicities between the two groups, and two-sided \( P \) values were reported. Recurrence-free survival (RFS) was estimated using the Kaplan-Meier method, and log-rank test was used to compare RFS curves.

RESULTS: The median follow-up was 28.8 months overall, with 54.7 months (range: 7.1–117.4 mo) for conventional RT and 16.1 months (range: 3–64.7 mo) for hypofractionated RT, after excluding nine patients whose follow-up was less than 3 months from local control analysis. Conventional RT patients had less grade 2 dysphagia [52.1% vs 75%; \( P = .022 \)], grade 2/3 hoarseness [16.7% vs 50%; \( P < .001 \)], and grade 2/3 laryngeal mucositis [27.1% vs 63.5%; \( P < .001 \)] and required less administration of narcotics [43.8% vs 75%; \( P = .002 \)] acutely during treatment. The rates of acute grade 2/3 radiation dermatitis [52.1% vs 63.5%; \( P = .312 \)], grade 2/3 laryngeal edema [25% vs 32.7%; \( P = .266 \)], and weight loss (1.3% vs 2%; \( P = .655 \)) were similar in both groups. Complete response to treatment was 91.7% in the conventional RT group and 90.4% in the hypofractionated group. RFS was comparable at 24 months [86.7% vs 86.6%; \( P = .988 \)] and at 60 months [82.8% vs 78.8%; \( P = .643 \)] in patients receiving conventional and hypofractionated RT, respectively. The \( P \) value of the log-rank test for RFS was .797.

CONCLUSIONS: Our retrospective data suggest that patients receiving hypofractionated RT may experience higher rates of grade 2 dysphagia, grade 2/3 hoarseness, and grade 2/3 laryngeal mucositis and require increased narcotic use, without improvements in complete response to treatment or RFS.

(S012) Prognostic Value of Radiographic Extracapsular Extension in Locally Advanced Non-Oropharyngeal Head and Neck Squamous Cell Cancers

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BACKGROUND: Pathologic extracapsular extension (pECE) in locally advanced head and neck squamous cell cancers (HNCs) is associated with poor prognosis. Previous data from our institution suggest that imaging evidence of extracapsular extension (rECE), identified on pretreatment CT scans, independently predicts for worse distant control and survival for oropharyngeal squamous cell cancer (OPC) patients undergoing radiation therapy. In this present study, we sought to validate these findings in non-OPC HNCs.

METHODS: From our departmental database, 121 patients with locally advanced (cN+) non-OPC HNCs were treated in our department with definitive or adjuvant radiation therapy (± induction chemotherapy and/or concurrent chemoradiotherapy) from 2006–2012. Thirteen patients had recurrent disease at presentation, seven patients discontinued treatment due to noncompliance or other factors, two patients underwent reirradiation of the treated region, and three patients did not have accessible pretreatment CT studies. The remaining 96 patients (nasopharynx \( n = 18 \), hypopharynx \( n = 16 \), larynx \( n = 22 \), oral cavity/lip \( n = 24 \), nasal cavity/sinus...
As previously reported for OPC, presence of rECE, compared with lack of rECE, portends worse prognosis for patients with non-OPC HNCs undergoing definitive or adjuvant radiation therapy. For these patients, presence of rECE is an independent predictor for worse LRC, DC, PFS, and OS. Further studies, with larger cohorts and longer follow-up, are needed to validate these findings and determine how rECE can be used to guide clinical management in these patients.

### (S013) Adjuvant Radiation Therapy and Temozolomide for Anaplastic Gliomas: The Twelve-Year Washington University Experience

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**BACKGROUND:** Anaplastic gliomas represent a heterogeneous group of different pathological entities, and the optimal treatment approach after surgery remains controversial for different subtypes. Recently, long-term results of two randomized studies have shown that radiation therapy (RT) with procarbazine, lomustine, and vincristine (PCV) chemotherapy improved outcomes of those with codeletion of 1p/19q. Another combined modality approach, RT and temozolomide (TMZ), has also gained popularity in the treatment of anaplastic gliomas but has not been validated extensively. In this study, we present our institutional data on the clinical outcomes of RT + TMZ for anaplastic gliomas.

**METHODS:** A single-institutional retrospective review was conducted on patients with intracranial anaplastic oligodendroglioma (AO), mixed anaplastic oligoastrocytoma (AOA), and anaplastic astrocytoma (AA) who were treated with adjuvant RT and TMZ after surgery. RT was delivered with either 3D conformal RT (3DCRT) or intensity-modulated RT (IMRT) to a median total dose of 60 Gy (range: 31.6–63 Gy) in daily fractions (median 2 Gy/fraction; range: 1.8–2.2 Gy/fraction). All patients received standard concurrent TMZ, with (90% of patients analyzed) or without maintenance TMZ (10%). Follow-up time was calculated from the start of RT.

### RESULTS:

From 2000 to 2012, 111 cases met the study criteria and were evaluable: 20% AO, 33% AOA, and 47% AA. Median follow-up time was 2.43 years (range: 0.06–12.1 yr) but was 4.10 years (range: 0.8–12.1 yr) for living patients. All AOs and AOs were

### Table S013  Comparison With Historical Controls

<table>
<thead>
<tr>
<th>Histology/Biomarker Type</th>
<th>Study</th>
<th>Treatment</th>
<th>5-Yr PFS (%) (95% CI)</th>
<th>5-Yr OS (%) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AO/OAOA</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>+1p/19q codeletion</td>
<td>WU</td>
<td>RT + TMZ</td>
<td>70% (51–89)</td>
<td>91% (80–100)</td>
</tr>
<tr>
<td></td>
<td>RTOG 9402</td>
<td>RT + TMZ</td>
<td>57% (40–71)</td>
<td>72% (54–83)</td>
</tr>
<tr>
<td></td>
<td>EORTC 26951</td>
<td>RT + PCV</td>
<td>71% (55–83)</td>
<td>76% (60–86)</td>
</tr>
<tr>
<td>−1p/19q codeletion</td>
<td>WU</td>
<td>RT + TMZ</td>
<td>46% (26–65)</td>
<td>68% (50–85)</td>
</tr>
<tr>
<td></td>
<td>RTOG 9402</td>
<td>RT + TMZ</td>
<td>8% (2–18)</td>
<td>31% (19–45)</td>
</tr>
<tr>
<td></td>
<td>EORTC 26951</td>
<td>RT</td>
<td>14% (8–20)</td>
<td>25% (18–33)</td>
</tr>
<tr>
<td>AA</td>
<td>WU</td>
<td>RT + TMZ</td>
<td>27% (13–40)</td>
<td>37% (23–51)</td>
</tr>
<tr>
<td></td>
<td>Hildebrand et al. (2008)</td>
<td>RT + TMZ + DBD/BCNU</td>
<td>--</td>
<td>36% (26–46)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>RT + TMZ</td>
<td>--</td>
<td>29% (20–38)</td>
</tr>
</tbody>
</table>

**AA** = anaplastic astrocytoma; **AO** = intracranial anaplastic oligodendroglioma; **AOA** = mixed anaplastic oligoastrocytoma; **BCNU** = bis-chloroethyl nitrosourea (carmustine); **DBD** = dibromodulcitol; **PCV** = procarbazine, lomustine, and vincristine; **RT** = radiation therapy; **TMZ** = temozolomide.

Data from Cairncross et al (RTOG 9402) and Van den Bent et al (EORTC 26951).
evaluated for 1p/19q codeletions, and 42% had codeletions of 1p/19q. Pathology subtypes showed distinctively different outcomes. Non-codeleted AOs/AAAs displayed a trend of worse progression-free survival (PFS) than codeleted AOs/AAAs (46% vs 70% at 5 years, respectively; P = .10), while demonstrating significantly worse overall survival (OS) (68% vs 91% at 5 years, respectively; P = .02). Interestingly, AAs had significantly worse PFS and OS than noncodeleted AOs/AAAs (PFS: 27% vs 46% at 5 years, respectively; P = .03; OS: 37% vs 68% at 5 years, respectively; P = .007). Univariate analyses showed that age, Karnofsky performance score (KPS), surgical extent, pathology, and adjuvant TMZ were significant factors for PFS, while age, KPS, surgical extent, and pathology were significant factors for OS. On multivariate analysis, only age, KPS, and pathology (hazard ratio [HR] 6.54 for OS in non-codeleted vs codeleted AOs/AAAs; HR = 15.6 for OS in AAs vs codeleted AOs/AAAs) were significant factors for both PFS and OS.

CONCLUSIONS: In patients treated with surgery followed by RT + TMZ, outcomes were dependent on pathology as follows: codeleted AOs/AAAs > non-codeleted AOs/AAAs > AA. As compared with historical controls from previous randomized studies (Table), codeleted AOs/AAAs treated with RT + TMZ achieved comparable results as those of RT + PCV, while non-codeleted AOs/AAAs that were treated with RT + TMZ appeared to have superior outcomes compared with RT alone. In contrast, AAs that were treated with RT + TMZ had similar results as those of RT alone. RT + TMZ may be a reasonable alternative approach for both codeleted and non-codeleted AOs/AAAs, but may need further validation for AA patients.

(S014) Gamma Knife Stereotactic Radiosurgery in the Treatment of Brainstem Metastases

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PURPOSE: Our single-institution outcomes of linear accelerator (LINAC)-based stereotactic radiosurgery (SRS) for the treatment of metastases located within the brainstem have been previously reported, with a crude local control rate of 76%. The purpose of our study is to report our institutional outcomes in treatment of brainstem metastases with gamma knife SRS for comparison.

MATERIALS AND METHODS: The available records of patients with brainstem metastases treated with gamma knife SRS between 2009 and 2013 were retrospectively reviewed. There were 74 patients who had 80 metastatic lesions located within the brainstem. The endpoints that were assessed included local control and overall survival (OS).

RESULTS: Median age was 58 years. Median follow-up was 5 months (range: 0–47 mo). Tumor histologies included melanoma (32%), lung (32%), breast (16%), renal (7%), and other (13%). The majority of the lesions was located in the pons (78%), followed by the midbrain (14%) and medulla (9%). Two of 74 patients had synchronous brainstem lesions, and 8 had metachronous brainstem lesions. The median lesion volume was 0.111 cc (range: 0.003–5.58 cc), treated with a median dose of 16 Gy (range: 10–20 Gy) prescribed to 50% isodose line (range: 40%–80%). There were three local failures, with a crude local control rate of 95% (66 of 69 patients). Kaplan-Meier OS at 1 year was 27%, with a median OS of 5.5 months (range: 0.55–47.2 mo). Thirty-six percent of lesions were symptomatic. One-third of symptoms (8/24) resolved after SRS. Median volume 2 cc or larger predicted for decreased time to local failure (hazard ratio [HR] = 6.54 for OS in non-codeleted vs codeleted AOs/AAAs; HR = 15.6 for OS in AAs vs codeleted AOs/AAAs) were significant factors for both PFS and OS.

CONCLUSIONS: To our knowledge, there are no available data that provide outcome comparisons between gamma knife versus LINAC-based SRS. Our data suggest possibly improved crude rates of local control with gamma knife SRS (95%) when compared with our historical institutional treatment outcomes with linac-based SRS (76%). Larger brainstem metastases may predict for worse local control with gamma knife therapy alone.

(S015) Temporal Lobe Radionecrosis After Skull Base Radiotherapy: Dose-Volume Predictors

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BACKGROUND AND PURPOSE: Temporal lobe radionecrosis is a potential complication of high-dose radiation therapy for skull base tumors. The risk of radionecrosis increases with absolute doses greater than 60 Gy, but little data are available regarding potential partial volume effects when higher-dose conventionally fractionated radiotherapy is employed.
MATERIALS AND METHODS: Patients who were previously treated with fractionated proton therapy for skull base chordoma, chondrosarcoma, adenoid cystic carcinoma, or paranasal sinus tumors between 2005 and 2012 were analyzed, provided there was a minimum of 6 months of clinical and radiographic follow-up after treatment. The patient factors that were collected were gender, age, hypertension, diabetes, and smoking status. Treatment factors included chemotherapy utilization, whether patients’ temporal lobes had been prospectively contoured or retrospectively contoured for this review, and the absolute dose and absolute volume data for both the right and left temporal lobes, considered separately. Generalized estimating equations were used to test for the association between each patient and treatment factor and radiation necrosis, adjusting for within-subject correlation due to repeated measures. The risk of temporal lobe radiation necrosis as a function of the absolute volume of a single temporal lobe irradiated was modeled using the median effective concentration (EC50) equation. The absolute volume of a temporal lobe receiving 10–70 Gy (relative biological effectiveness [RBE]) in 10-Gy (RBE) increments was analyzed (aV10, aV20, etc).

RESULTS: Sixty-six patients and 131 temporal lobes were included in the analysis. One patient received radiation dose to only one temporal lobe due to a well-lateralized tumor. The median prescribed dose was 75.6 Gy (RBE) (range: 62–79.2 Gy [RBE]) in 1.8–2-Gy (RBE) fractions. Seven patients (11%) received concomitant chemotherapy. The median follow-up time after completion of radiation therapy was 27 months. Thirteen temporal lobes were observed to develop radiation necrosis in 10 patients at a median time of 20 months after radiation. The 2-year Kaplan-Meier estimate of the risk of any-grade temporal lobe radiation necrosis in this cohort was 13% (95% confidence interval [CI], 6%–20%). In the multivariable analysis, only radiation dose-volume relationships were associated with development of radiation necrosis. In the EC50 model, all dose levels from 10 to 70 Gy (RBE) were highly correlated with radiation necrosis, with a 15% 2-year risk of any-grade temporal lobe radiation necrosis when the absolute volume of a temporal lobe receiving 30 Gy (RBE) (aV30) exceeded 16.3 cm³, aV40 >13 cm³, aV50 > 8.8 cm³, or aV60 > 5.2 cm³.

CONCLUSIONS: Dose-volume parameters are highly correlated with the risk of developing temporal lobe radiation necrosis. In the setting of high-dose skull base radiotherapy, larger volumes exposed to lower doses and smaller volumes exposed to higher doses are both highly correlated with the risk of developing temporal lobe radiation necrosis. Treatment planning goals should include reduction in both integral and maximal dose to the temporal lobes. The EC50 model provides suggested dose-volume temporal lobe constraints for conventionally fractionated high-dose skull base radiotherapy.

(S016) Head and Neck Second Primary Cancer Rates in the HPV Era: A SEER Analysis

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PURPOSE: Head and neck (HN) cancer patients are at high risk of second primary cancer (SPC) of the HN or other aerodigestive system sites. HPV-driven tumors are associated with high grade and oropharyngeal (OPC) location. Our objective was to analyze the incidence of SPC limited to the HN (HNSPC) in a population with primary squamous cell carcinoma (SCC) of the HN and its temporal trends in the human papillomavirus (HPV) era.

METHODS: The Surveillance, Epidemiology, and End Results (SEER) database was queried for patients with histopathologically confirmed primary SCC of the HN (excluding skin, salivary glands, nasopharynx, and thyroid) between 1973 and 2008. To assess temporal trends, we defined three time periods: 1973–1989, 1990–1999, and 2000–2008. HNSPCs that occurred within 2 years of initial diagnosis were excluded, since most of the HN recurrences occur within 2 years of diagnosis. Incidence rates of HNSPC, defined as number of HNSPCs per 10,000 person-years (PY10K) of follow-up, were calculated in each time period. The analysis was conducted according to site and grade of the original cancer. Cumulative incidence rates of HNSPC were estimated and compared based on competing risk analysis, with death as the competing risk.

RESULTS: A total of 105,385 cases met our inclusion criteria. The mean age at diagnosis was 61.9 years. Of all patients, 14.7% had OPC, 44.5% had oral cavity cancer (OC), and 40.8% had cancer of the larynx/hypopharynx (LH); 18.9% had low-grade tumor, 37.3% had intermediate-grade tumor, 18.9% had high-grade tumor, and tumor grade was unknown in 24.9%. The incidence of OPC increased over time, constituting 9.5% of the cases in the period 1973–1989 and reaching 18.6% in the period 2000–2008. A total of 5,786 patients had high-grade OPC in the entire cohort.

A total of 4,659 cases of HNSPC were identified, of which 13.5%, 58.3%, 23.3%, and 3% were OPC, OC, LH, and other HN sites, respectively. The estimated incidence rates/PY10K of HNSPC for patients with primary OPC decreased over time: 105.8 (1973–1989), 80.5 (1990–1999), and 50.4 (2000–2008). In contrast, HNSPC in OC patients increased with time: 59.1 (1973–1989), 82 (1973–1989), and 71.8 (2000–2008), respectively. The incidence rates of HNSPC were stable for LH: 33.7 (1973–1989), 39.7 (1990–1999), and 36.0 (2000–2008). High-grade primary HN cases of the OPC showed a decrease of 54% in the person-year incidence rate/ PY10K of HNSPC from the first to the last period (65.1 for 1973–1989, 55.3 for 1990–1999, and 30.2 for 2000–2008). The drop was less for the high-grade OC patients (67.1, 60.3, and 41, respectively) and stable for the high-grade LH cancer (33.0, 39.8, and 36.5, respectively). A competing-risk analysis in the high-grade group showed a larger period effect with decreased cumulative incidence rate of HNSPC for OPC in the period 2000–2008.

CONCLUSIONS: The incidence of HNSPC in patients with primary HN cancer has decreased over time. This reduction is driven by lower rates in patients with high-grade OPC. This finding is temporally related with the increase in HPV-associated OPC over this time period. These results suggest that the incidence rate of HNSPC may be lower for HPV-associated HN cancers compared with his-
toric estimates of HNSPC in non–HPV-related cancers and calls for further study of this issue.

(S017) Long-Term Outcome of Intensity-Modulated Radiation Therapy in Pediatric Craniopharyngioma

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PURPOSE: Although craniopharyngioma is a histologically benign tumor, it is associated with long-term morbidity, secondary to tumor location and treatment. This tumor can present with both cystic and solid components, and response to radiotherapy (RT) for each component may be different. Intensity-modulated radiation therapy (IMRT) may be able to reduce long-term complications of treatment by reducing high doses of RT to the surrounding normal structures. The purpose of this study is to report the long-term progression-free survival (PFS), overall survival (OS), and late-toxicity outcomes in pediatric patients with craniopharyngioma who have been treated with IMRT.

MATERIALS AND METHODS: From 1996 to 2006, 24 children with craniopharyngioma were treated with definitive (13 patients) or salvage (11 patients) IMRT at one institution. The median age at IMRT was 8 years, with an equal gender distribution. Prior to IMRT, surgical intervention included biopsy (5), subtotal resection (18), and gross total resection (1). The clinical target volume encompassed the tumor plus a 1-cm margin. The median prescribed dose was 50.4 Gy (range: 49.8–54 Gy). Median follow-up after IMRT was 107 months.

RESULTS: The 10-year OS rate was 84%, while the 10-year PFS was 63%. The 10-year cystic and solid tumor PFS rates were 70% and 90%, respectively. Eight patients had cystic progression (median: 12 mo) and two patients had solid progression (median: 41 mo), all requiring surgical interventions. There was no difference in OS or PFS, regardless of whether definitive or salvage IMRT was performed. Prior to IMRT, 17 (71%) had endocrine deficiency; including 13 with panhypopituitarism. At the last follow-up, 21 (88%) had panhypopituitarism. Diabetes insipidus (DI) was seen in all patients prior to salvage RT; another five patients developed DI after IMRT. Eight had visual deficits, seven had preexisting visual field deficits prior to IMRT, and two had worsening visual deficit after IMRT. Other late toxicities included two cerebrovascular events (one in a patient with known Moyamoya syndrome prior to IMRT), obesity (9), and seizure disorder (4). One patient developed myelodysplastic syndrome at 6 years after IMRT.

CONCLUSIONS: Treatment with IMRT provides local control and survival rates comparable with 2-dimensional and non-IMRT 3-dimensional techniques. Endocrine and visual problems were common. Many patients had preexisting morbidity prior to starting RT.

(S018) Early Tumor Perfusion Changes Predict Time to Progression in Patients With Recurrent Low-Grade Gliomas Treated With Everolimus Under a Phase II Clinical Trial

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PURPOSE: Low-grade gliomas (LGGs) are slow-growing, primary brain tumors that frequently recur after primary surgical treatment. Recent work has established the activation of the PI3K/mTOR pathway in most LGGs, raising the possibility that mTOR inhibitors, such as everolimus (RAD001), may benefit patients with LGG. Early imaging markers of treatment response and disease progression are
needed to assess patients undergoing investigational therapy.

METHODS: In this phase II clinical trial, 26 patients with recurrent LGG treated with everolimus underwent serial multimodal magnetic resonance imaging every 2 months during treatment. At each time point, the volume of hyperintensity on T2-weighted imaging was manually defined. Maps of imaging parameters were generated, including the fractional blood volume (fBV) and vascular permeability (Kps) from dynamic contrast-enhanced perfusion-weighted imaging, the apparent diffusion coefficient (ADC) and fractional anisotropy (FA) from diffusion-weighted imaging, and MR spectroscopic imaging-derived parameters (peak heights of choline, lipid, and lactate and the choline-to-N-acetylaspartate index, [CNI]). Each parameter was normalized to its median value in normal-appearing white matter, and the median, 10th percentile, and 90th percentile values were computed within the tumor volume, defined by T2 hyperintensity.

RESULTS: At the time of analysis, 11 patients had experienced disease progression (range: 20 d–23.8 mo), 12 had stable disease (median follow-up 18.1 mo), and 3 dropped out of the study due to adverse side effects. Eighteen patients reached the primary study endpoint of freedom from progression at 6 months. Compared with baseline imaging parameters, patients who did not progress in the first 6 months demonstrated a significant decrease in median fBV values within the tumor volume, with a decrease of 17.5% at 4 months and 22.0% at 6 months (P = .010 and .011, respectively, by Wilcoxon signed-rank test). Similarly, these patients demonstrated a decrease in median Kps values of 14.8% at 4 months and 15.7% at 6 months (P = .041 and .070, respectively). Tumor volume, diffusion, and spectroscopic characteristics were not significantly changed during treatment.

Based on these findings, we performed a hypothesis-driven analysis of the relationship between early tumor perfusion changes and time to progression for the 11 patients who experienced disease progression. The change in median fBV at the earliest assessed time point, 2 months after starting treatment, was highly correlated with time to progression (Figure; Spearman's ρ = −.77; P = .014). Baseline imaging characteristics were not correlated with progression time.

DISCUSSION: The finding of significantly decreased tumor perfusion characteristics in patients under treatment with everolimus for recurrent LGG is consistent with the known antiangiogenic properties of mTOR inhibitors. Furthermore, we observe a strong correlation between these early tumor perfusion changes and time to progression. This information could thus be used as an early radiographic marker for response to this targeted molecular therapy, potentially identifying patients who would most benefit from treatment.

(S019) Prospective Evaluation of Stereotactic Radiosurgery for Spinal Metastases in the Postoperative Setting

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BACKGROUND: Stereotactic body radiotherapy (SBRT) has emerged as an effective option in the treatment of metastatic spinal tumors. The technique achieves a steep dose gradient to deliver ablative doses to the tumor while sparing the adjacent spinal cord. Surgical resection is commonly followed by radiation to address residual microscopic disease. When SBRT is used in combination with a surgical approach, the potential for achieving durable symptom and tumor control may be possible for appropriately selected patients, but limited prospective data exist. The purpose of our study is to evaluate the outcomes of patients treated with SBRT in the postoperative setting.

METHODS: The subset of patients who were enrolled in a prospective phase I–II study of SBRT for spinal metastasis treated after undergoing surgical management was included in this study. The initial patients enrolled on protocol were treated to 30 Gy in five fractions, which represented 13 of the 67 tumors treated, while the majority of the remaining tumors was treated to 27 Gy in three fractions. Patients were followed with spinal magnetic resonance imaging (MRI) studies at regular intervals to determine local control (LC). Pain and other symptom data were collected to determine treatment response and toxicity. Toxicity was graded using the Common Terminology Criteria for Adverse Events version 2.0 (CTCAE v2) guidelines and the McCormick neurologic function score. Survival outcomes were calculated using the Kaplan-Meier method, with factors affecting survival determined by log-rank test.

RESULTS: Sixty-two patients with 67 tumors were treated with...
SBRT on protocol between 2002 and 2010. All patients underwent SBRT after spine surgery, which included laminectomy, corpectomy, vertebroplasty, or a combination of these techniques. The median tumor volume was 44.9 cm³ (range: 1.6–358 cm³), with renal cell carcinoma as the most common histology represented (48%). Forty patients (65%) were treated with prior radiation to the spine utilizing conventional fractionation (median dose 31.75 Gy). With a median follow-up of 19 months (range: 1–91 mo), the 1-year imaging LC was 82%, and overall survival (OS) was 71% (median: 25 months). Durable pain control, defined as a score of < 4 of 10 at 6 months, was achieved in 78% of patients. There was no difference in LC between patients treated with different surgical techniques ($P = .47$) or between radiation-naïve patients versus those with prior treatment ($P = .17$). Tumor histology did not significantly correlate with the median time to progression ($P = .35$) or with OS ($P = .30$). Pain control at 1 month and 6 months after treatment was significantly correlated with improved LC ($P < .01$). There was a trend toward improved PFS for tumors below the level of the spinal cord, although this was not statistically significant ($P = .09$). Grade 3 toxicities included pain (four cases), dysphagia (one case), and nausea/vomiting/diarrhea (one case). One patient experienced a grade 4 neurologic toxicity, although this did not correlate with the treatment site.

**CONCLUSION:** This study represents the largest series of prospective data available on patients treated with SBRT in the postoperative setting. The combination of surgery with SBRT can offer patients with metastatic disease to the spine the chance of effective palliation, along with durable tumor control.

**(S020) Availability of Single-Fraction Palliative Radiotherapy for Cancer Patients Receiving End-of-Life Care**

In early 2013, a 12-question survey was emailed to all 78 radiation oncologists currently practicing at VHA radiation oncology facilities. Phone calls were made to nonresponders. Radiation oncologists who did not offer single-fraction palliative radiotherapy were evaluated by Fisher's exact test for associations with a variety of factors.

**RESULTS:** The response rate was 90% (70/78). Half were full-time employees of the VHA, and the majority had thoroughly read either the American College of Radiology (ACR) or American Society for Radiation Oncology (ASTRO) guidelines for palliative radiotherapy of bone metastases. Single-fraction palliative radiotherapy for bone metastasis is currently offered by 75.7% of respondents. Those not offering single-fraction palliative radiotherapy (24.3%) were more likely to be > 10 years out of training (37% vs 10%, $P = .01$) and more likely to have worked in private practice at some point in their career (36% vs 12%, $P = .03$). There were no associations with employment status, history of an academic appointment, or whether they had read the ACR or ASTRO guidelines.

**CONCLUSION:** Single-fraction palliative radiotherapy for bone metastasis appears to be much more available for cancer patients receiving end-of-life care within the VHA when compared with the general US health care system.

**(S021) Central Versus Peripheral Tumor Location: Influence on Survival, Local Control, and Toxicity Following Stereotactic Body Radiotherapy for Primary Non–Small-Cell Lung Cancer**

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**BACKGROUND:** Stereotactic body radiotherapy (SBRT) has been increasingly utilized in the management of medically inoperable non–small-cell lung cancer (NSCLC). However, there is concern that treatment of centrally located tumors could lead to increased toxicity. This has generally led to a treatment with a lower biological equivalent dose (BED) for centrally located tumors, although this could potentially be concerning for decreased local control. The goal of this study is to compare survival, local control, and toxicity outcomes for patients treated with SBRT for centrally versus peripherally located tumors.

**METHODS:** Patients with primary NSCLC treated with SBRT at Yale-New Haven Hospital from 2007 to 2013 were included in this analysis. Central tumor location was defined as within 2 cm of the proximal bronchial tree, heart, great vessels, trachea, or other mediastinal structures. Acute toxicity was defined as occurring within 3 months of treatment, and late toxicity was defined as occurring after at least 3 months of treatment. Toxicity was defined as “severe” if graded as 3 or higher. The association of tumor location with overall survival (OS), progression-free survival (PFS), and local control (LC) was assessed with Kaplan-Meier analysis and Cox regression modeling. For evaluation of toxicity, chi-square analysis and logistic regression modeling were used. Multivariate analyses adjusted for potential covariates, including age, sex, BED, performance status, clinical versus pathologic diagnostic method, tumor histology, tumor size, and total number of targets.

**RESULTS:** There were 253 patients included in this analysis (70 with central tumor location and 183 with peripheral tumor location). Median follow-up was 24.9 months. Patients with central tumors were more likely to have larger tumors (median 2.6 cm vs 1.9 cm; $P < .001$) and be treated with a lower BED (median 112.5 Gy vs 151.2 Gy; $P < .001$) compared with those with peripheral tumors. Univariate analysis revealed that tumor location was not associated with OS (52% vs 56% at 2 years; $P = .56$), PFS (57% vs 65% at 2
years; \( P = .22 \)), LC (83% vs 90% at 2 years; \( P = .33 \)), acute toxicity (23% vs 26%; \( P = .75 \)), acute severe toxicity (1% vs 7%; \( P = .12 \)), late toxicity (17% vs 15%; \( P = .70 \)), or late severe toxicity (7% vs 3%; \( P = .15 \)). After adjustment for demographic and clinical covariates in the multivariate analysis, tumor location did not predict for OS (hazard ratio [HR] = 0.88; \( P = .63 \)), PFS (HR = 1.02; \( P = .94 \)), LC (HR = 1.24; \( P = .73 \)), acute toxicity (odds ratio [OR] = 0.74; \( P = .45 \)), acute severe toxicity (OR = 0.22; \( P = .15 \)), late toxicity (OR = 1.75 at 2 years; \( P = .17 \)), or late severe toxicity (OR = 2.95; \( P = .10 \)). BED did not predict for any of these outcomes overall or within either subgroup of tumor location.

CONCLUSIONS: Despite presenting with larger tumors and being treated with a lower BED, patients with central NSCLC who received SBRT had similar survival, local control, and toxicity outcomes compared with those with peripheral NSCLC. Greater numbers of patients and longer follow-up are needed to further characterize the expected long-term outcomes following SBRT for central NSCLC.

(S022) Influence of Preoperative Radiation Field on Postoperative Leak Rates in Esophageal Cancer Patients After Trimodality Therapy

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PURPOSE: Neoadjuvant chemoradiation is a standard treatment of locally advanced esophageal cancer. Preventive strategies to minimize postoperative morbidity will be important to help improve the clinical outcomes of patients. We investigated the factors associated with an increased incidence of anastomotic leaks among patients treated with neoadjuvant chemoradiation.

MATERIALS AND METHODS: Clinical data were collected from 285 patients treated with neoadjuvant chemoradiation followed by esophagectomy. Dose-volume histograms were analyzed for effect of mean stomach dose on anastomotic leak rates. Postoperative CT scans were examined to determine if the surgical anastomosis was placed in or outside of the preoperative radiation fields. Logistic regression was used to evaluate the factors associated with any or clinically relevant (CR) (≥ grade 2) leaks.

RESULTS: Overall anastomotic leak rate was 11% (31/285), and CR leak rate was 6% (17/285). Using stepwise forward and backward multivariate analysis, body mass index (BMI) (odds ratio [OR] = 1.09, 95% confidence interval [CI], 1.00–1.17; OR = 1.11, 95% CI, 1.01–1.22), three-field surgery (OR = 10.01, 95% CI, 3.83–26.21; OR = 4.83, 95% CI, 1.39–16.71), and within-radiation field (“in-field”) anastomosis (OR = 5.37, 95% CI, 2.21–13.04; OR = 8.63, 95% CI, 2.90–25.65) were independent predictors of both all-grade and CR leaks, respectively. While patients with distal esophageal tumors and Ivor-Lewis surgery had the lowest incidence of all-grade (6.5%) and CR leaks (4.2%), most of the leaks could be accounted for by having the anastomosis constructed within the
field of radiation (in-field: 39% and 30% versus out-of-field: 2.6% and 1.0%, respectively, for total and CR leaks; \( P < .0001 \), Fisher’s exact test).

CONCLUSIONS: Esophagogastric anastomosis placed within the preoperative radiation field was a very strong predictor for anastomotic leaks in esophageal cancer patients treated with trimodality therapy, among other factors. These results have important implications in the preoperative evaluation for the proper anastomotic placement after chemoradiation therapy.

(S023) Stage I Lung SBRT Clinical Practice Patterns

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INTRODUCTION: Stereotactic body radiation therapy (SBRT) is a technique that has become increasingly utilized over the last decade in the treatment of patients with stage I non–small-cell lung cancer (NSCLC). While prior studies have suggested optimal biological effective dose (BED) versus necessary minimum BED for lung SBRT, no standardized clinical guidelines exist. In this retrospective study, we sought to investigate the dose prescription pattern use in the US for patients receiving SBRT.

METHODS: Using the National Cancer Database (NCDB), adult patients aged 19 years and older with a clinical diagnosis of stage I NSCLC (cT1–2, cN0, cM0) between 2003 and 2011 whose primary treatment involved radiosurgery to the lung were identified. BED was calculated for each patient using a lung alpha/beta ratio of 10 and the recorded fraction number and total dose. Patients were excluded if their reported BED was greater than 300 or less than 10 to exclude data entry errors in the database. The most common dose/fraction prescriptions were analyzed during the years 2005, 2008, and 2011.

RESULTS: A total of 6,324 patients were reported to have received radiosurgery to the lung, and 5,582 were analyzed as having reported BEDs within the predefined range. The overall mean and median BEDs were 130.1 and 124.8, respectively. Of these patients, 89.6% was prescribed a regimen with a BED \( \geq \) 100. However, when confined to the three most recent years (2009–2011), the mean BED fell to 127.4, and only 74.5% of patients were prescribed a regimen with BED \( \geq \) 100. The most common prescriptions overall were 60 Gy in 3 fractions (n = 1275, 22.8%), 48 Gy in 4 fractions (n = 937, 16.8%), 50 Gy in 5 fractions (n = 688, 12.3%), and 54 Gy in 3 fractions (n = 674, 12.1%). Analysis of the prescription trends from 2005, 2008, and 2011 revealed decreased utilization of 60 Gy in 3 fractions (26.3% in 2005 to 13.3% in 2011) and increased utilization of 50 Gy in 5 fractions (0% in 2005 to 19.3% in 2011), 54 Gy in 3 fractions (4.2% in 2005 to 13.2% in 2011), and 50 Gy in 4 fractions (0% in 2005 to 8.1% in 2011).

CONCLUSION: Our findings suggest that despite phase II evidence demonstrating the best published local control and overall survival to date with a regimen of 54 Gy in 3 fractions (corrected), over 25% of patients with stage I NSCLC treated with SBRT in recent years have been prescribed regimens that provide a BED of less than 100. Possible explanations for this include the increasing use of SBRT for treating centrally located tumors or tumors near organs at risk and increased adoption of SBRT by physicians who are new to the technology and, consequently, more conservative in their target prescription BED.

(S024) Correlation of Survival to CBCT-Based Tumor Response During Chemoradiation in Patients With Stage III Non–Small-Cell Lung Cancer

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PURPOSE AND OBJECTIVES: Stage III non–small-cell lung cancer (NSCLC) treated with chemoradiotherapy (CRT) results in a median survival of 15–18 months. We evaluated the correlation between patient survival and reduction in gross tumor volume (GTV) using weekly cone-beam computed tomography (CBCT) to assess whether this could be prognostic of survival. We hypothesized that a greater percent decline in primary lung tumor volume during the course of treatment would correlate to improved patient survival.

MATERIALS AND METHODS: Patients with stage III NSCLC who received CRT between July 2009 and September 2012 and had daily CBCTs performed as part of their RT course were included in this institutional review board-approved study. Primary GTVs were contoured from CBCT images obtained on Days 1, 8, 15, 22, 29, 36, and 42. Percentage changes in GTV per patient were determined by calculating \([\text{GTV Day } 1 \text{ } - \text{GTV Day } 42]/\text{(GTV Day 1)}\). MATLAB and Excel 2010 were used to perform t-test analysis of the data, and Kaplan-Meier survival curves were generated based on median GTV reduction with censored patient data. Associations with GTV reduction and time to death were evaluated with a Cox proportional hazards model.

RESULTS: Thirty-seven patients (median age 67.1 years; standard deviation [SD] = 8.8 years) met the criteria for inclusion in this study from December 2009 to May 2013. Median follow-up was 8.2 months (range: 3–32.9 mo). Median GTV reduction was observed to be 39.2% (range: 0%–79.7%) from Day 1 to Day 42 of radio-
therapy. For every 10% decrease in GTV size, the risk of death was lowered by 38.6% \( (P = .0009) \). Local recurrence occurred in 29.7% of patients, and distant recurrence occurred in 72.2%. For every 10% reduction in GTV, the risk of local recurrence and distant metastases was lowered by 29.2% \( (P = .0095) \) and 26.2% \( (P = .027) \), respectively.

**CONCLUSIONS:** Reductions in primary GTV volume, as determined by weekly CBCT, appear to correlate to patient survival, local recurrence, and distant metastases. Further study with additional patients and longer follow-up is necessary. Such findings may help to determine which patients may also benefit from adaptive planning.

**Conclusions:**

Our study demonstrates that PARP1 inhibition improves the therapeutic index of RT in BCa cell lines independent of intrinsic breast cancer subtype or BRCA1 mutational status. Treatment-induced increases in PARP1 activity 24 hours after RT predict for long-term RS by PARP1 inhibition, thus identifying it as a potential biomarker of response. These studies have led to a clinical trial incorporating intratreatment biomarker analyses of PARP1 inhibitors and radiation in BCa patients, which is currently open for accrual through the Translational Breast Cancer Research Consortium (TBCRC 024).

**Purpose and Objectives:**

We queried the SEER database to identify T3N0M0 breast cancer patients diagnosed between 2000 and 2010 who underwent modified radical mastectomy. We performed a Surveillance, Epidemiology, and End Results (SEER) analysis to investigate the benefit of PMRT in these patients.

**Materials and Methods:**

We identified 3,102 patients who we included in this analysis. Statistical analysis was performed utilizing the log-rank test and a Cox proportional hazards model. The primary endpoints were overall survival, breast cancer-specific survival, and distant recurrence occurred in 72.2%. For every 10% decrease in GTV size, the risk of death was lowered by 38.6% \( (P = .0009) \). Local recurrence occurred in 29.7% of patients, and distant recurrence occurred in 72.2%. For every 10% reduction in GTV, the risk of local recurrence and distant metastases was lowered by 29.2% \( (P = .0095) \) and 26.2% \( (P = .027) \), respectively.

**Conclusions:**

Our study demonstrates that PARP1 inhibition improves the therapeutic index of RT in BCa cell lines independent of intrinsic breast cancer subtype or BRCA1 mutational status. Treatment-induced increases in PARP1 activity 24 hours after RT predict for long-term RS by PARP1 inhibition, thus identifying it as a potential biomarker of response. These studies have led to a clinical trial incorporating intratreatment biomarker analyses of PARP1 inhibitors and radiation in BCa patients, which is currently open for accrual through the Translational Breast Cancer Research Consortium (TBCRC 024).

**Results:**

Of the 3,012 patients identified, 1,226 received PMRT; 74% were Caucasian, 18% were African American, and 8% were Asian or Pacific Islander. The median follow-up was 52 months (range: 0–131 mo). The median number of axillary lymph nodes removed was 11 (range: 0–50). The primary was left-sided in 50.7% of cases. Patients who received PMRT were younger; were more likely to be married; more commonly had higher-grade, estrogen receptor positive (ER+), and progesterone receptor positive (PR+) tumors; and had a different geographic distribution compared with those who did not receive PMRT. There were no differences between the groups in terms of the number of nodes removed or the year of diagnosis.

Several disease and patient characteristics were included in the univariate and multivariate analyses, including year of diagnosis, age, grade, race, ER status, PR status, primary quadrant location, number...
**Patients with PRMS, especially those aged ≥ 10 years, present with poor prognostic features and continue to have poor outcomes. Given the high incidence of regional node recurrence, we recommend prophylactic ilioinguinal lymph node irradiation for all patients aged ≥ 10 years. For children aged < 10 years, surgical evaluation of the ilioinguinal lymph nodes to determine the role for nodal irradiation is appropriate.**

**CONCLUSIONS:** Patients with PRMS, especially those aged ≥ 10 years, present with poor prognostic features and continue to have poor outcomes. Given the high incidence of regional node recurrence, we recommend prophylactic ilioinguinal lymph node irradiation for all patients aged ≥ 10 years. For children aged < 10 years, surgical evaluation of the ilioinguinal lymph nodes to determine the role for nodal irradiation is appropriate.

**S028: Figures**
BACKGROUND: A phase II study was recently completed at our institution in which patients with clinical (c) T3 and T4 rectal adenocarcinoma received short-course radiotherapy, followed by 4 cycles of FOLFOX chemotherapy as “near-total” neoadjuvant therapy for rectal cancer. In this analysis, we compared outcomes for patients treated with a near-total neoadjuvant approach with similar patients treated at our institution with standard-of-care preoperative concurrent long-course chemoradiotherapy and postoperative chemotherapy (standard of care).

MATERIALS AND METHODS: A total of 80 patients with cT3–T4, any N, and any M planned for resection of the primary tumor were enrolled on the institutional phase II study of preoperative short-course radiotherapy (25 Gy to the involved mesorectum, 20 Gy to elective nodes in five fractions), followed by 4 cycles of mFOLFOX6 chemotherapy before extirpative surgery. Postoperatively, treatment with 6–8 cycles of adjuvant FOLFOX was suggested at the discretion of the treating medical oncologist. A comparison cohort of 92 patients was identified with locally advanced rectal cancer that was treated at our institution with standard-of-care therapy. These patients had cT3 or cT4 rectal adenocarcinoma and received preoperative concurrent chemoradiotherapy to 45–54 Gy to similar volumes, followed by extirpative surgery. All patients in the comparison group also received postoperative chemotherapy. Kaplan-Meier with log-rank analysis was used to compare local control (LC) and disease-free survival (DFS) outcomes between the two groups, and non-parametric Mann-Whitney Wilcoxon rank sum was used to compare patient and treatment characteristics.

RESULTS: Tumors were converted to ypT0 in 28% in the study cohort compared with 17% of patients in the control cohort (P = .26). T-downstaging was achieved in 68% of patients in the study cohort compared with 50% in the control cohort (P = .015). Median follow-up was 25 months (range: 4.6–46.5 mo) for the study cohort and 16 months (range: 3.9–72 mo) for the control cohort. For all evaluable patients, the 2-year LC was 97% and 96% in the study cohort and control cohort, respectively (P = .89). For all patients with cM0 disease, 2-year DFS was 94% vs 71% (P = .002) for the study vs control cohorts, respectively. The rate of acute G1 toxicity of grade 3 or higher was 9% in the study cohort compared with 21% in the control cohort.

(S029) Patient-Reported Voice and Speech Outcomes and Their Clinical and Dosimetric Predictors after Chemo-IMRT of Oropharyngeal Cancer: A Prospective Longitudinal Study

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PURPOSE AND OBJECTIVES: Although adverse sequelae of chemoradiation (CRT) for head and neck cancer (HNC) have been extensively detailed in recent years, the effects of CRT on voice and speech quality remain poorly characterized. We investigated changes in patient-reported voice and speech quality (VSQ) after CRT in two prospective studies of organ-sparing CRT for locally advanced oropharyngeal cancer (OPC).

MATERIALS AND METHODS: A total of 91 patients with stage III/IV OPC treated at our institution in two prospective studies of definitive CRT from 2003–2011 were included. All received whole-field neck intensity-modulated radiation therapy (IMRT) intended to minimize dose to the pharyngeal constrictors, salivary glands, oral cavity (OC), glottic larynx (GL), supraglottic larynx, and esophagus. Patient-reported VSQ (PRVSQ) was assessed by the Communication Domain of the Head and Neck Quality of Life (HNQOL-C) questionnaire and the speech question of the University of Washington QOL (UWQOL-S) questionnaire at pretreatment and 3, 6, 12, 18, and 24 months after CRT. Factors associated with worsening PRVSQ (defined as a decrease in HNQOL-C or UWQOL-S from baseline) were assessed.

RESULTS: PRVSQ decreased maximally at 1 month, with 68% and 41% of patients reporting worsening HNQOL-C and UWQOL-S scores compared with baseline, and improved thereafter, with recovery of mean population HNQOL-C and UWQOL-S scores to baseline by 12 and 18 months, respectively. At 12 months, however, 33% and 28% of patients continued to report lower HNQOL-C and UWQOL-S scores compared with pretreatment, respectively. In contrast to patient-reported effects, observer-rated larynx toxicity was rare, with only grade 1 toxicity reported by 5% at 6 months and 0% at 12 months. Of patients with mean GL dose of < 20 Gy, > 20–30 Gy, > 30–40 Gy, > 40–50 Gy, and > 50 Gy, 25%, 33%, 59%, 50%, and 64% reported worse HNQOL-C scores at 6 months compared with pretreatment, which persisted at 12 months in 10%, 32%, 25%, 30%, and 63% of patients, respectively (χ2 for trend: P = .02 at 6 months; P = .011 at 12 months). Results using a worsening UWQOL-S score endpoint were similar. Mean GL dose, mean OC dose, N2/3 stage, and shorter time since RT completion were associated with worsening HNQOL-S (P < .05) on univariate analysis. On multivariate analysis, mean GL dose remained independently predictive for worsening HNQOL-S after CRT (odds ratio [OR] = 1.08 per Gy; P < .01).

CONCLUSIONS: In the largest prospective study to assess voice and speech outcomes after CRT for OPC, worsening VSQ was frequently reported by patients, underrecognized by clinicians, and independently associated with dose to the GL. These findings support limiting mean GL dose to < 20 Gy during whole-neck IMRT for HNC when the larynx is not a target.

(S030) Utilization of Postprostatectomy Radiation Therapy at an NCI-Designated Comprehensive Cancer Center

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PURPOSE: To characterize the utilization of postprostatectomy radiation for patients with prostate cancer (CaP) at a National Cancer Institute (NCI)-designated Comprehensive Cancer Center over the past decade, given the introduction of robotic prostatec-
tomy and the publication of multiple phase III trials showing a benefit for adjuvant postprostatectomy radiation.

**METHODS:** We queried our prospective database for patients with CaP who received radiation therapy (RT) to the prostate bed after prostatectomy from 1999–2011. Patients receiving a prescription dose of 60–68 Gy were included. Patients were excluded if they had metastatic disease. Adjuvant RT was defined as initiation of RT within 1 year of surgery and referral for a high-risk factor (T3, positive margin, or Gleason score 8–10). A detectable prostate-specific antigen (PSA) was allowed in the adjuvant definition as long as only a single postoperative PSA was obtained in the setting of the preceding high-risk factors and was < 0.2 ng/mL. Salvage RT was defined as RT in the setting of rising PSA, a single postoperative PSA ≥ 0.2 ng/mL, or documented clinical recurrence via imaging or digital rectal examination. The number of patients with an intact prostate treated with definitive RT was recorded by year as a control for the changing volume in total prostate patients in the department. Chi-square analysis was used to assess differences in patient population between adjuvant and salvage RT cohorts. Spearman correlation was used to assess yearly trends in PSA level at time of referral for RT.

**RESULTS:** A total of 563 patients received postprostatectomy RT between 1999 and 2011: 465 as salvage and 98 as adjuvant. Over time, there was a trend for an increased number of patients treated with postprostatectomy RT. Of all patients treated with RT for localized CaP, postprostatectomy RT constituted a larger proportion, ranging from 5.3% to 9.4% from 1999–2003, 11.9% to 13.3% from 2004–2007, and 18.4% to 26.6% from 2008–2011. There was no increase in the proportion of patients treated with adjuvant RT compared with salvage RT (P = .5). Patients referred for adjuvant RT were younger (P = .001) and had higher pathologic Gleason score (P = .0372), higher pathologic T-stage (P < .0001), and higher rates of positive margins (P < .0001) than patients receiving salvage RT. Pre-RT PSA values were inversely correlated with year (P = .005).

**CONCLUSION:** Postprostatectomy RT utilization now constitutes a larger proportion of patients treated with RT for localized CaP. There has not been an increase in the proportion of patients treated with adjuvant compared with salvage RT. There is a trend over time for CaP patients to be referred for postprostatectomy RT with lower PSAs.

**(S031) A Phantom-Based Simulator Approach to Improving the Quality of Prostate Brachytherapy Training**

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**PURPOSE AND OBJECTIVES:** Permanent prostate brachytherapy (PPB) is a well-established treatment for localized prostate cancer. The future of PPB relies upon the quality training of future residents; however, current training requirements are frequently inadequate. Our objective was to design and implement a unique training program that utilized a phantom-based simulator to teach the process of quality assurance (QA) and improve PPB education.

**MATERIALS AND METHODS:** Trainees in our simulator program were radiation oncologists, radiation oncology residents, and fellows of the American Brachytherapy Society. The simulator program emphasized six core areas of PPB QA: patient selection, simulation, treatment planning, implant technique, treatment evaluation, and outcome assessment. Trainees used the iodine-125 preoperative treatment planning technique to implant their prostate phantoms using a transrectal ultrasound (TRUS) device. Preimplant and postimplant dosimetric parameters were compared and correlated using regression analyses.

**RESULTS:** Thirty-one trainees successfully completed the simulator training program. The mean phantom prostate size, number of seeds, and total activity were consistent among trainees, with some differences based on phantom heterogeneity. All trainees met the V100 > 95% objective both preimplant and postimplant. V150 and D90 were higher in the postimplant setting as compared with preimplant, and the standard deviations of all parameters were slightly higher postimplant. The mean planned D90 was 183.6 Gy (range: 162.6–196.5 Gy), while the postimplant D90 achieved was 191.2 Gy (range: 158.5–215.4 Gy), suggesting that trainees achieved excellent heterogeneity control. Preimplant and postimplant V100 and V150 vs TRUS prostate volume showed strong correlation (r = 0.99 for V100 and r = 0.59 for V150). A comparison of preimplant and postimplant V100 and V150 similarly demonstrated good correlation (r = 0.99 for V100 and r = 0.37 for V150). As expected, the range of V100 values was quite narrow and very closely related to the initial prostate volume. The V150 values had a broader range and slightly lower concordance with prostate gland size, likely due to variations in planning, implantation, and trainee experience.

**CONCLUSIONS:** Analysis of implants from the phantom-based simulator shows that there is a high degree of consistency among trainees and that implants are uniformly high-quality with respect to parameters used in actual clinical practice. This training program provides a valuable educational opportunity for those learning the PPB process and likely accelerates the learning curve inherent to PPB. Prostate phantom implantation can be a valuable first step in the acquisition of the required skills to safely perform PPB. Given the current healthcare environment and increased scrutiny on benefits, costs, and impact of technology on cancer care, our approach to PPB training will impact the future of patient care, and the phantom-based simulator is an excellent tool to educate the next generation of brachytherapists.

**(S032) Stereotactic Body Radiation Therapy for Low-, Intermediate-, and High-Risk Prostate Cancer: Disease Control and Quality of Life at Six Years**

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**ARS PROCEEDINGS 2014 19**
OBJECTIVES: Stereotactic body radiation therapy (SBRT) takes advantage of the low alpha-beta (α/β) ratio in the prostate to deliver a large radiation dose in few fractions. Initial studies on small groups of low-risk patients support the potential of SBRT for clinical efficacy while limiting treatment-related morbidity and maintaining quality of life (QOL). This prospective study expands upon prior studies to further evaluate SBRT efficacy and QOL for a large patient population that includes low-, intermediate-, and high-risk prostate cancer patients.

METHODS: A total of 515 patients with organ-confined prostate cancer (471 T1c and 44 T2a, all N0M0) received CyberKnife SBRT. The mean age was 69 years, and the mean PSA was 6.48 ng/mL. 343 patients were low-risk (PSA = 10 ng/mL and Gleason < 7), 134 were intermediate-risk (PSA 10–20 ng/mL or Gleason = 7), and 38 were high-risk (PSA > 20 ng/mL or Gleason > 7). Androgen deprivation therapy was administered to 70 patients for up to 1 year. A total of 158 patients received 35 Gy delivered in five daily fractions. These patients were either low-risk or low–intermediate-risk. The remaining patients, from all risk groups, received a total dose of 36.25 Gy in five daily fractions. The dose was prescribed to a planning target volume (PTV), created by a 5-mm expansion of the prostate gross tumor volume (GTV), with a 3-mm posterior expansion. The proximal seminal vesicles were included for intermediate- and high-risk patients. The PTV was covered by the 83% to 87% isodose line; real-time intrafractional motion tracking was used. Biochemical failure was assessed using the Phoenix criterion.

RESULTS: At a median follow-up of 63 months (range: 9–84 mo), 49 patients died of other unrelated causes and 39 were lost to follow-up. The median PSA at 60 months was 0.11 ng/mL. Biochemical failures occurred for 10 low-risk patients (2 locally), 10 intermediate-risk patients (2 locally), and 10 high-risk patients (2 locally). The actuarial 6-year freedom from biochemical failure was 97%, 90.8%, and 71.8% for the low-, intermediate-, and high-risk groups, respectively (P < .001). For low- and low–intermediate-risk patients, there was no difference in terms of median nadir or biochemical control between doses of 35 and 36.25 Gy. Late Radiation Therapy Oncology Group (RTOG) toxicity was mild, with 4% grade 2 rectal, 7.8% grade 2 urinary, and 1.4% grade 3 urinary (all with 36.25 Gy). Late grade 2 urinary toxicity for 35 Gy was 5.1% versus 9.9% for 36.25 Gy (P = .01). Mean Expanded Prostate Cancer Index Composite (EPIC) urinary and bowel QOL declined at 1 month posttreatment and returned to baseline by 2 years, where it remains. Mean EPIC sexual QOL declined by 25% at 72 months. Seventy-three percent of the patients who were potent at baseline remain potent.

CONCLUSIONS: CyberKnife SBRT produces excellent biochemical control rates at up to 7 years, with mild toxicity and minimal impact on QOL. Median PSA levels compare favorably with other radiation modalities and strongly suggest durability of response. Further follow-up is needed to determine if these results are durable in the long term. These results also strongly suggest that 35 Gy is as effective as 36.25 Gy for low- and low–intermediate-risk patients with less urinary toxicity.

(S033) Dose-Escalated Radiation Therapy With or Without Short-Course Androgen Deprivation for Intermediate-Risk Prostate Cancer

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BACKGROUND AND PURPOSE: To investigate outcomes in intermediate-risk prostate cancer patients receiving dose-escalated external beam radiation therapy (RT) with or without short-course androgen deprivation therapy (ADT).

MATERIALS AND METHODS: This study comprised 203 intermediate-risk prostate cancer patients who were treated at a single institution to a dose of ≥ 7,560 cGy from 2003–2010. Of these patients, 62 (30.5%) received ADT in addition to their RT. Comparisons of patient characteristics were performed using chi-square analysis. Biochemical recurrence, distant metastatic-free survival (DMPFS), prostate cancer-specific survival (PCSS), and overall survival (OS) were analyzed using the Kaplan-Meier method. Multivariate Cox regression was used to analyze the impact of covariates on biochemical outcomes.

RESULTS: The median follow-up was 62 months, and the median duration of ADT was 6 months. Patients with a prostate specific antigen (PSA) above 10 ng/mL or lessthan those with PSA values of 10 ng/mL or less (P < .001). There was a trend toward reduced ADT usage for those who were aged younger than 70 years compared with those who were older (P = .10), as well as for those who were treated with further dose escalation above 7,560 cGy (P = .06). There were no differences in ADT use based on race or the Gleason score of the biopsy. There were a total of 33 biochemical failures (16.3%), and the median time to biochemical failure was 42 months (range: 4–98 mo). Biochemical failure occurred in 4 of the 62 patients who were treated with RT and ADT (6.5%) and in 19 of the 141 patients who were treated with RT alone (13.4%). The 6-year biochemical control was 92.9% for those receiving RT plus ADT vs 76.7% in those receiving RT alone (P = .02). There were three distant failures—one in patients who received RT alone and one in a patient who received RT + ADT; the time to distant failure was 22 and 47 months for the patients who received RT alone, respectively, and was 109 months for the patient who received RT + ADT. The 6-year DMPFS, PCSS, and OS rates were 98.2%, 99.0%, and 82.3% for those receiving RT alone and 100%,100%, and 72.3% for those receiving RT + ADT, respectively (respective P values = .91, .50, and .67). On multivariate analysis, only ADT use was associated with improved biochemical outcomes (hazard ratio [HR] = 0.24; 95% confidence interval [CI], 0.08–0.70; P = .01), while perineural invasion was associated with worse biochemical outcomes (HR = 2.94; 95% CI, 1.36–6.34; P = .01).

CONCLUSIONS: Dose-escalated RT and short-course ADT result in improved biochemical outcomes for intermediate-risk prostate
cancer patients. Perineural invasion appears to be an important prognostic factor that portends worse biochemical control.

**DO**\textsuperscript{S034} Do Sociodemographic Factors Influence Outcome in Prostate Cancer Patients Treated With External Beam Radiation Therapy (EBRT)?

**OBJECTIVES:** To determine if there is an influence of sociodemographic factors on biochemical control (bNED) and overall survival (OS) in prostate cancer (CaP).

**METHODS:** CaP patients treated with definitive EBRT ± hormone therapy (HT) from 1997–2006 were analyzed. Patient demographics, treatment (Tx), and clinical outcomes were obtained from electronic medical records. Median household income (mHHI) at the census block group level was obtained from the 2000 census data. Data on disease and Tx parameters included Gleason score, pre-Tx prostate-specific antigen (PSA), T-stage, year of Tx, EBRT dose and technique, and use of HT. Patients were categorized as having low-, intermediate-, or high-risk disease. Sociodemographic factors included age, race, marital status, and mHHI. Biochemical failure was defined as nadir PSA + 2 ng/mL. OS was based on death from any cause.

**RESULTS:** A total of 788 consecutive patients were studied, with a median follow-up of 7 years. African Americans (AAs) constituted 48% of the patients, while 46% of patients were white and 6% was other. Whites had an average mHHI of $59,235 compared with $36,917 for AAs ($P < .001). After multivariable modeling, only radiation dose was predictive for bNED or OS. For biochemical failure, compared with radiation dose < 70 Gy, the hazard ratio (HR) was 0.69 (95% confidence interval [CI], 0.49–0.98) for 70–74 Gy and 0.68 (95% CI, 0.31–0.74) for ≥ 75 Gy; for mortality, the HR was 0.67 (95% CI, 0.50–0.89) for 70–74 Gy and 0.62 (95% CI, 0.43–0.89) for ≥ 75 Gy. No sociodemographic factors were predictive of either outcome.

**CONCLUSIONS:** This analysis suggests that sociodemographic factors are not prognostic in determining outcome in prostate cancer, as long as patients have access to current standards of care. Rather, only a treatment factor—the radiation dose—predicted for bNED and OS.

**Do**\textsuperscript{S035} Peripheral and Lymphatic Radiation (RT) Doses With Treatment on RTOG 9413: Immunosuppression or Scattered Doses and Death From Second Cancers?

**OBJECTIVES:** To determine whether the findings might explain these observations.

**METHODS:** We generated 6 and 18 MV WPRT (50-Gy pelvic irradiation plus boost) and PORT plans for an adult male phantom in accordance to protocol guidelines, with a total prostate dose of 70 Gy for all four plans. The plans were delivered, photon doses were measured using thermoluminescent dosimeters within the phantom, and Monte Carlo dose calculations were performed. Neutron dose equivalents for 18 MV plans were estimated using literature-reported values. To explore possible RT effects on the immune system, dose-volume histograms for the major lymphatic regions were calculated for WPRT and PORT and compared with an 8-Gy total lymphoid irradiation (TLI) technique, used for immune suppression in patients experiencing heart transplantation rejection.

**RESULTS:** Ranges of total dose equivalent were estimated for organs associated with death from SCs. Lung and esophageal doses were on the order of 70 mSv for six MV PORT and 70–150 mSv for six MV WPRT. The dose equivalent ranges for 18 MV plans were on the order of 100–250 mSv. The pancreas dose ranged from 150–250 mSv for PORT and approximately doubled for WPRT. Large ranges were calculated for bladder and rectum, which lay within the treatment field. The colon dose extended to 50 Gy for WPRT but was below 3 Gy for PORT. Approximately one-fourth of the major lymphatics received 8 Gy with WPRT, while one-tenth did so with PORT. The mean lymphatic dose with WPRT was higher than with TLI.

**CONCLUSION:** The estimated scattered doses to organs associated with SC were generally low, and there was large overlap between the dose ranges for WPRT and PORT treatment. This may be reflected in the statistically insignificant difference in SC incidence that was observed. The mean dose to the lymphatics was comparable to mean doses delivered under TLI. This suggests a new hypothesis—that the increased risk of death from SCs may be in part due to pre-existing second cancers that grew more quickly when immune surveillance was compromised. More work in this area is needed.

**Do**\textsuperscript{S036} The Low Alpha-Beta Ratio of Bladder Cancer: A Rationale for Hypofractionation

**OBJECTIVES:** Long-term results from Radiation Therapy Oncology Group (RTOG) 9413 show an improvement in biochemical (PSA) failure for patients treated with neoadjuvant androgen suppression (NHT) and whole-pelvis radiotherapy (WPRT) compared with NHT and prostate-only radiation (PORT) but no improvement in survival. There appears to be an increased risk of death from second cancers (SCs), most notably among patients treated with WPRT and adjuvant hormone therapy (AHT), despite the fact that the incidence of SCs is not statistically higher for WPRT. The biologic processes underlying these unexpected results are presently not understood and merit further exploration. This study estimates RT doses received by organs of interest during protocol treatment to determine whether the findings might explain these observations.
We hypothesized that the promising outcomes with partial-bladder treatment might be due to the effects of hypofractionation. We thus aimed to analyze the clinical impact of hypofractionation on local control and to characterize the radiation response of a bladder cancer cell line with regard to clonogenic survival.

MATERIALS AND METHODS: We retrospectively reviewed our institutional experience with clinical stage T2–4 N0–2 bladder cancer patients treated with definitive organ preservation chemoradiation from 2009–2012. Patients who were treated with a hypofractionated course (HF; 2.5 Gy/fx to a total tumor dose of 62.5 Gy; n = 16) were compared with conventionally fractionated patients (CF; 1.8 Gy/fx to a total tumor dose of 59.4–70.2 Gy; n = 7). All patients received pelvic nodal irradiation (45–50.4 Gy at 1.8–2 Gy/fx). Treatment was delivered via intensity-modulated radiation therapy with cone-beam CT image guidance (daily for HF). Concurrent radiosensitizing chemotherapy (typically platinum) was administered. Mean follow-up was 20 ± 3 months. Local control was defined as absence of progressive or recurrent disease within the bladder.

An immortalized human bladder cancer cell line, SW780 (ATCC), was used for in vitro studies. Clonogenic survival assay was performed on exponentially growing cells, which were trypsinized, counted, and diluted accordingly. Cell suspensions were irradiated at doses of 0, 1.8, 2, 2.5, 4, 6, and 8 Gy using a 137Cs laboratory irradiator at a dose rate of 4.21 Gy/min. Cells were then plated in 100-mm dishes in triplicate. After 21 days, colonies were fixed and stained with crystal violet in 70% ethanol. Colonies consisting of > 50 cells were counted to determine surviving fractions.

RESULTS: No patients who received hypofractionated treatment had local failure in the bladder. There were only three LENT-SOMA late grade 3 ureteral toxicities (2 CF, 1 HF) and one acute grade 4 renal toxicity (CF), all of which resolved with management of ureteral obstruction. There appeared to be a difference in 2-year local control: 100% HF (7/7) vs 82% CF (13/16) [see Figure 1A]. The alpha-beta ratio was calculated to be 4.5 Gy for SW780 cells [Figures 1B, 1C].

CONCLUSIONS: Hypofractionated chemoradiation is an effective and well-tolerated treatment for bladder cancer. In fact, hypofractionation appears to provide better local disease control than conventional fractionation, although the study was underpowered to validate this observation. In vitro data suggest that bladder cancer cells have a lower alpha-beta ratio than most tumors, more closely approximating normal tissue values. The low alpha-beta ratio of bladder cancer may provide a radiobiological explanation for the efficacy of hypofractionation. Future studies of the effects of chemotherapy may provide valuable insight into enhancing the therapeutic ratio with radiosensitization as well as altered fractionation.

S037: Changes in Mass Transport as an Early Marker of Response to Cytotoxic Therapy in Human Pancreatic Adenocarcinoma

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BACKGROUND: Identifying a biomarker of local tumor response in pancreatic cancer has proven elusive, because the disease is usually unresectable, which limits the use of pathological response as a readout and because blood-based biomarkers, such as CA19-9, are not necessarily specific to local tumor control. One clinical observation is that a decrease in tumor enhancement on CT scans after cytotoxic therapy is generally regarded as a good response. We hypothesized that measuring this phenomenon would correlate with local control of human pancreatic adenocarcinoma (PDAC).

METHODS: We developed an imaging-based biomarker using principles of mass transport. Using systematic measurements of density of pancreatic tumors at each of the timed phases of contrast-enhanced pancreatic protocol CT scans, we applied a mathematical model to derive a mass transport parameter that quantified the area under the enhancement curve (AUC) for patients with PDAC. We defined a “normalized AUC ratio” as the post-therapy AUC (4–8 weeks after treatment) divided by the pre-therapy AUC. This parameter was correlated with clinical outcome in patients treated on two prospective trials. The first trial originally included 48 patients with locally advanced PDAC treated with radiation to 50.4 Gy with concurrent bevacizumab and capecitabine. The second trial originally included 69 patients with locally advanced PDAC treated with induction cetuximab, gemcitabine, and oxaliplatin, followed by radiation to 50.4 Gy with concurrent cetuximab and capecitabine. A total of 84 patients (36 from Trial 1 and 48 from Trial 2) had both post-therapy and pre-therapy pancreatic protocol CT scans to analyze. The others did not have pancreatic protocol CT scans for one or either of the tests.

RESULTS: There were 30 patients with clinical and radiographic evidence of local progression. The 2-year local control rate was 50% for all patients. We found that the normalized AUC ratio correlated significantly with local progression-free survival (PFS) (hazard ratio [HR] = 1.81; 95% confidence interval [CI], 1.01–3.03; P = .048). Furthermore, patients with a measurable decrease in tumor mass transport (normalized AUC ratio < 1) after chemoradiation had significantly better local control (86% with tumor control at 2 years) compared with those without a decrease in tumor mass transport (normalized AUC ratio ≥ 1; 34% with tumor control at 2 years; P = .002). As a continuous or discrete variable (with a cutoff of 1), the normalized AUC ratio correlated with local PFS, independent of therapy regimen, change in tumor size after therapy, and receipt of curative-intent surgery.

CONCLUSIONS: After cytotoxic therapies, decreased enhancement in human PDAC tumors correlated with improved local control. This phenomenon can be quantified using our systematic methodology and mathematical model. With further validation, this method may serve as an early readout of response to new therapies, which could help accelerate promising treatments and enable rational management decisions. Ongoing work will address the hypothesis that a decrease in tumor enhancement correlates with pathological response for patients who have resectable PDAC and receive neoadjuvant cytotoxic therapy.

(S038) Patient Tolerability and Acute Toxicity of Intensity-Modulated Radiation Therapy for Treatment of Carcinomas of the Biliary Tract

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PURPOSE AND OBJECTIVES: Chemoradiation for biliary tract cancers (BTCs) has been associated with substantial toxicities due to the large, irregular target volumes surrounded by critical normal tissues. The purpose of this study was to evaluate patient tolerability and acute toxicity of chemoradiation with intensity-modulated radiation therapy (IMRT) for BTCs.

MATERIALS AND METHODS: Patients receiving chemoradiation with IMRT for resected or locally advanced BTCs between March 2006 and July 2010 were retrospectively evaluated on an institutional review board (IRB)-approved protocol. Patients received radiation therapy to 50.4 Gy with concurrent 5-FU or capecitabine. Toxicity was scored using Common Toxicity Criteria version 3.0 (CTC v3.0). Adverse events were defined as hospitalization, emergency department visits, and treatment breaks/inability to complete therapy. Dose-volume histogram (DVH) parameters for liver, small and large bowel, and stomach were collected. Correlation of toxicity with DVH parameters was estimated and tested using Kendall’s nonparametric correlation coefficient. Disease-specific outcomes were estimated using the Kaplan-Meier method.

RESULTS: A total of 28 consecutive patients were identified. Median age was 62 years (range: 38–81 yr), including 17 male (61%) and 11 female (39%) patients. Twelve patients had gallbladder cancer (43%), 12 had cholangiocarcinoma (CCA) of the common bile duct (43%), 8 had intrahepatic CCA (29%), and 4 had perihilar CCA (14%). Twenty-four patients received adjuvant radiation therapy (86%), while four patients were treated with definitive intent (14%). Of the resected tumors, 10 patients had negative surgical margins (36%), 8 patients had close margins (< 1-mm margin) (29%), and 4 patients had grossly positive margins (22%). Thirty-six percent had positive nodes. Median follow-up was 36.7 months (range: 4.6–76.2 mo). Local control (LC), progression-free survival (PFS), and overall survival (OS) rates at 1 year were 90%, 56%, and 76%, respectively. Grade 3–4 toxicity occurred in only two patients (7%). Three patients (11%) required treatment breaks, three patients (11%) had ED visits, and four patients (14%) required hospitalization. One patient died of a postoperative arterio-enteric fistula (4%) during the first week of radiation. There were no cases of radiation-induced liver disease. Analysis of dosimetric data for normal tissue structures revealed no significant correlations with toxicity or adverse events.
CONCLUSIONS: In one of the largest cohorts of such biliary tract cancers reported to date, chemoradiation with IMRT was well tolerated with minimal acute treatment-related toxicities. Due to the small number of adverse events, we were unable to determine dosimetric correlation of toxicity with DVH parameters. These data suggest that future prospective studies may safely evaluate radiation dose escalation as a means of improving BTC outcomes.

(S039) ALDH-Expressing Cancer Stem Cells Are Associated With Inferior Survival in Patients With Resected Pancreatic Adenocarcinoma Treated With Adjuvant Chemoradiation

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INTRODUCTION: We and others previously identified aldehyde dehydrogenase (ALDH) activity as a marker of pancreatic cancer stem cells (or tumor-initiating cells). The presence of cancer stem cells (CSCs) has been associated with decreased survival and treatment resistance in pancreatic adenocarcinoma. In this study, we investigate the role of ALDH expression in predicting survival and patterns of disease recurrence in patients treated with chemoradiation (CRT) following pancreatectomy.

METHODS: Tissue microarrays using pancreatectomy specimens from 1998–2002 at our institution were made, stained for ALDH1, and scored as ALDH-positive or ALDH-negative by two expert pancreatic cancer pathologists blinded to patient outcomes. Physician documentation and radiology reports were used to document patient follow-up information. Time to local failure (TLF), time to distant metastases (TDM), progression-free survival (PFS), and overall survival (OS) were analyzed using SPSS software.

RESULTS: Previously, we found that ALDH expression was associated with worse OS in a cohort of 269 patients with resected pancreatic adenocarcinoma (Rasheed, JNCI 2009). From this original cohort, adjuvant treatment information was available for 87 patients with ALDH-negative tumors (48.6%) and 41 patients with ALDH-positive tumors (45.6%). In patients treated with adjuvant CRT, median OS was superior in the ALDH-negative cohort versus the ALDH-positive cohort (26.3 mo vs 18.2 mo; P = .011). Further, in patients treated with adjuvant CRT, ALDH-negative patients had statistically greater TLF, TDM, and PFS than their ALDH-positive counterparts (see Table). On multivariate analysis, ALDH-positive tumor staining (hazard ratio [HR] = 1.94; P = .004) and tumor grade (HR = 1.54; P = .041) predicted lower OS, and ALDH-positive tumor staining (HR = 1.83; P = .008), tumor grade (HR = 1.52; P = .038), and tumor size > 3 cm (HR = 1.65; P = .023) predicted decreased PFS.

DISCUSSION: This study suggests that adjuvant CRT improves TLF, TDM, PFS, and OS in patients with localized pancreatic ade

<table>
<thead>
<tr>
<th>Parameter</th>
<th>ALDH-Negative (n = 69)</th>
<th>ALDH-Positive (n = 35)</th>
<th>P Value</th>
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<tr>
<td>OS (months)</td>
<td>26.3</td>
<td>18.2</td>
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<td>TLF (months)</td>
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<td>TDM (months)</td>
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<tr>
<td>PFS (months)</td>
<td>18.4</td>
<td>12.3</td>
<td>.022</td>
</tr>
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**Table S039**

OS = overall survival; PFS = progression-free survival; TDM = time to distant metastases; TLF = time to local failure.

(S040) Outcomes, Costs, and Patient Satisfaction in a Pancreatic Multidisciplinary Clinic: Can Multidisciplinary Oncology Models Deliver Higher Value Care?

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BACKGROUND: Multidisciplinary clinics (MDCs) are novel delivery models for disease-based oncologic care. MDCs involve simultaneous initial evaluation by three oncologic specialists, radiologists, pathologists, and others. The costs and overall value (defined as quality relative to costs) of care delivered in MDCs are not well described. For patients with pancreatic cancer, we compared direct care costs, patient retention rates, and survival outcomes for patients treated in our institution’s pancreatic MDC with those evaluated within the institution but outside the MDC.

METHODS: Two groups of patients with pancreatic cancer were analyzed and compared retrospectively: patients evaluated in a pancreatic MDC versus through individual referrals. Demographics, region of origin, disease stage, and patient retention rates (defined as > 3 encounters for pancreatic cancer, a surrogate for patient satisfaction) were collected using electronic health records. Cost information was obtained using claims data and stratified by inpatient, outpatient, physician, OR, pharmaceutical, radiology, and lab charges and compared using Fisher’s exact tests. Logistic regression was used to compare retention rates between MDC and non-MDC patients, correcting for region of origin, disease stage, and demographics. Cox proportional hazards models facilitated comparisons of hazard ratios (HRs) of death, correcting for similar variables. Kaplan-Meier curves compared long-term survival between the two groups.

RESULTS: Between 2008 and 2010, 252 consecutive MDC patients...
were compared with 764 consecutive non-MDC patients (total n = 1,100). Gender was similar between the groups. MDC patients were slightly older (64 vs 62 y; \( P = .02 \)). A greater percentage of MDC patients traveled from nonadjacent states (49\% vs 23\%, \( P < .001 \)) and had more advanced disease stages (10\%, 25\%, and 23\% of MDC patients with borderline resectable, locally advanced, and metastatic disease, respectively, vs 5\%, 9\%, and 18\% of non-MDC patients). Adjusting for demographics, disease stage, and region of origin, MDC patients had 2.816 times the odds of being retained over non-MDC patients (\( P < .001 \)). Mean total charges per patient were higher for non-MDC patients than MDC patients ($58,458 vs $43,318, \( P < .001 \)), and all cost subcategories were statistically higher for non-MDC vs MDC patients except for outpatient charges ($19,762 vs $22,606, \( P = .612 \)). Across all patients, the non-MDC group had a higher HR for death than the MDC group, trending toward but not reaching statistical significance (HR = 1.182; \( P = \) ...)
.117); this difference remained non-significant after stratifying by patient retention status. At 3 years, unadjusted overall survival (OS) rates were approximately 20% for both MDC and non-MDC patients (log-rank test \( P = .845 \)); differences also remained non-significant after stratifying by patient retention status (Figure).

**CONCLUSIONS:** Even after adjusting for region of origin, patients who were evaluated in the MDC were more likely to continue their care at our institution, suggesting higher patient satisfaction for MDCs. Mean costs per patient were higher for non-MDC patients, even despite lower retention rates. Outpatient costs were higher for MDC patients, suggesting that greater outpatient engagement in MDCs can supplant more costly inpatient encounters. Because survival outcomes were similar for both groups despite higher costs for non-MDC patients, these data suggest that multidisciplinary models offer higher-value care for patients with pancreatic cancer.

**(S041) The Effect of High-Dose Stereotactic Body Radiation Therapy on Liver Function in the Treatment of Primary and Metastatic Liver Malignancies Utilizing the Child-Pugh Score Classification System**

**Pawel T. Dyk, MD, Shahed N. Badiyan, MD, Robert Myerson, MD, Parag Parikh, MD, Jeffrey R. Olsen, MD; Washington University**

**PURPOSE:** Evaluation of liver function following high-dose liver stereotactic body radiation therapy (SBRT) in the treatment of metastatic and primary malignancies of the liver utilizing the Child-Pugh score classification system.

**MATERIALS AND METHODS:** Retrospective analysis of 46 patients treated with SBRT for metastatic and primary malignancies of the liver. Patient, disease, prior treatment, and SBRT dosimetric factors were analyzed to correlate with decline in Child-Pugh score following liver SBRT.

**RESULTS:** Median follow-up was 11.0 months for patients alive at last follow-up. Twenty-four patients (52%) had primary liver malignancies. Median delivered dose was 55 Gy in 5 fractions (range: 36–60 Gy in 3–6 fractions) to 1 lesion (1–4 lesions) measuring 4.0 cm (range: 1.3–12.4 cm). Forty-one patients (89%) received ≥ 50 Gy in 3–6 fractions. Child-Pugh score classification was A in 42 patients (91%). Seven patients (15%) received adjuvant chemotherapy or targeted therapy. Twenty-nine patients (63%) experienced an intrahepatic recurrence following treatment. Ten patients (22%) experienced a decline in Child-Pugh score at a median time of 1.6 months (range: 0.2–6 mo). Eighty percent experienced a one-category decline. Only the V20, V25, V30, and V50 were correlated with decline in Child-Pugh score on univariate analysis, with V25 being most significant (\( P = .027 \)). A V25 > 2% was associated with a 41% incidence of Child-Pugh score decline, compared with 10% for V25 ≤ 2% (\( P = .021 \)). For primary liver malignancies, a V25 > 36% was associated with a sevenfold increase in the incidence of Child-Pugh score decline (70% vs 10%; \( P = .006 \)).

**CONCLUSIONS:** Approximately one-quarter of patients experience a decline in Child-Pugh score following high-dose liver SBRT. The V25 may be an important dosimetric parameter predicting decline in liver function following treatment.

**(S042) Changing Practice Patterns for Breast Cancer Radiotherapy With Clinical Pathways: An Analysis of Hypofractionation in a Large Integrated Cancer Center Network**

**Malolan S. Rajagopalan, MD, John C. Flickinger, MD, Sushil Beriwal, MD, Dwight E. Heron, MD, FACRO, FACR; University of Pittsburgh Cancer Institute**

**PURPOSE:** Hypofractionated whole-breast irradiation (HF-WBI) following breast-conserving surgery has produced excellent outcomes, but utilization remains limited. We evaluated the impact of a clinical pathway on adoption of HF-WBI in a large integrated radiation oncology network.

**METHODS:** We identified patients aged ≥ 70 years treated for breast cancer or ductal carcinoma in situ (DCIS). Excluded patients were those treated with palliative intent; accelerated partial breast radiation following mastectomy; or with axillary, supraclavicular, or internal mammary fields HF-WBI was defined as ≤ 20 fractions with a dose/fraction ≥ 2.5 Gy. Multivariate analysis identified variables associated with increased HF-WBI utilization.

**RESULTS:** We identified 2,426 patients meeting the inclusion criteria. HF-WBI utilization increased from 6.5% before pathway modification to 33.8% afterwards (\( P < .001 \)). For academic physicians, the odds of utilizing HF-WBI increased 4.1 times following publication of the seminal HF-WBI trial and an additional 3.2 times following pathway modification (\( P < .001 \) and \( P = .001 \), respectively). For community physicians, the odds of HF-WBI did not change following publication but increased 20 times following pathway modification (\( P < .001 \)). The increased adoption of HF-WBI saves $377,000 annually in our network and $51 million annually if extrapolated nationally.

**CONCLUSIONS:** We found that our implementation of clinical pathways dramatically increased adoption of HF-WBI for breast cancer in a large integrated cancer network. We found no significant change in utilization of HF-WBI among community physicians following publication of a seminal trial for HF-WBI until after clinical pathway implementation, which led to a 20-fold increase. Clinical pathways can be highly effective in changing practice patterns, disseminating evidence, and realizing health care savings.

**(S043) RadiotypeDx: Validation of a Radiation Sensitivity Signature in Human Breast Cancer**

**Corey Speers, MD, PhD, O. Alejandro Balbin, PhD, Meilan Liu, MD, Prasanna Aluri, MD, PhD, Lori J. Pierce, MD, Felix Y. Feng, MD; Department of Radiation Oncology, Comprehensive Cancer Center, University of Michigan**

**PURPOSE:** An unmet clinical need in breast cancer (BC) manage-
ment is the identification of which patients will respond to radiation therapy (RT). We hypothesized that the integration of post-RT clonogenic survival data with gene expression data across a large spectrum of BC cell lines would generate a BC-specific RT sensitivity signature predictive for RT response in BC patients and allow identification of patients with tumors refractory to conventional therapy.

METHODS: Using clonogenic survival assays, we identified the range of surviving fraction (SF) after 2 Gy of RT across 21 BC cell lines. Using SF as a continuous variable, the RT sensitivity score (RSS) was correlated to gene expression using a Spearman correlation method on an individual gene basis. Genes were selected for the signature based on positive or negative correlation with a P value < .05 and false discovery rate (FDR) of < 0.01. Unsupervised hierarchical clustering identified differences in gene expression across resistant and sensitive cell lines to generate a radiation sensitivity (RS) signature. This signature was trained and validated in a separate human breast tumor dataset (n = 185 patients) containing early-stage, node-negative patients treated with surgery and RT alone without adjuvant chemotherapy to assess the predictive effect of RS signature on recurrence risk after RT. Gene function and potentially actionable targets from the signature were validated using clonogenic survival and DNA damage assays.

RESULTS: Clonogenic survival identified a range of radiation sensitivity in human BCC lines (SF 77%–17%) with no significant correlation (r value < .3) to the intrinsic BC subtype. Using Spearman’s correlation method, a total of 126 genes were identified as being associated with radiation sensitivity (72 positively correlated, 54 negatively correlated). Unsupervised hierarchical expression discriminated gene expression patterns in the RT-resistant and RT-sensitive cell lines and were enriched for genes involved in cell cycle arrest and DNA damage response (enrichment P value = 5.0 E-22). Knockdown of genes associated with the radiosensitivity signature identified previously unreported radiation resistance genes, including TACCI and RND3, with enhancement ratios of 1.25 and 1.37 in BCC lines, respectively. Application of this RS signature to an independent breast cancer dataset with clinical outcomes validated the signature and accurately identified patients with decreased rates of recurrence compared with patients with high expression of the radiosensitive signature (P < .0001; misclassification error rate 0.31; 12/13 patients with locoregional recurrence accurately identified). This signature was then externally validated on another independent dataset of patients treated with adjuvant RT with locoregional recurrence data (P < .001; misclassification error rate 0.33; 26/28 patients with locoregional recurrence accurately identified).

CONCLUSION: In this study, we derived a human BC-specific RT sensitivity signature (RadotypeDx) with biologic relevance from preclinical studies and validated this signature for prediction of recurrence in two independent clinical datasets. The signature is not correlated with the intrinsic subtypes of human breast cancer and thus provides useful information beyond traditional breast cancer subtyping. By identifying patients with tumors refractory to standard RT, this signature has the potential to allow for personalization of radiotherapy, particularly in patients for whom treatment intensification is needed.

(S044) Repeated Measures Analyses of the Common Terminology Criteria for Adverse Events (CTCAE v3.0)-Based Dermatitis Toxicities in Breast Cancer Patients Receiving Radiotherapy in a Phase III Randomized Trial of Mometasone Furoate, N06c4 (Alliance)

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PURPOSE: The evolution of dermatological symptoms over time as measured by provider-assessed Common Terminology Criteria for Adverse Events version 3.0 (CTCAE v3.0) and patient-reported outcomes (PROs) is not well quantified. Using repeated measures analyses, we analyzed the data from the originally published N06c4 prospective trial and present here the CTCAE-based temporal profile of acute skin toxicities, when time factor was considered. The PRO results were previously reported (Abstract, ASTRO 2013, TT Sio and RC Miller et al).

PATIENTS AND METHODS: A total of 176 breast cancer patients (including ductal carcinoma in situ) undergoing external beam radiotherapy (RT) to the breast or chest wall were randomized to receive daily mometasone or placebo cream. Temporal symptoms were assessed for up to 10 cycles; the provider-reported CTCAEs, including radiation (XRT)-induced dermatitis, pruritus, skin burn, skin disorder, skin striae, skin hypopigmentation, skin atrophy, and skin infection, were collected. The analyzed groups included XRT-induced dermatitis, dermatitis-related symptoms (seven items, excluding XRT-induced dermatitis), and worst dermatitis-related symptoms (eight items included). We applied repeated measures analyses of variance with mixed models (Proc Mixed), Pearson’s correlation, and risk analyses methodologies. Adverse event (AE) grades were modeled using arm and cycle as classification variables with interaction effects. A maximum grade of any dermatitis-related symptom was calculated per patient per evaluation cycle.

RESULTS: One hundred sixty-nine (96%) patients were evaluable for toxicity. CTCAE symptoms typically started during Cycles 3 and 4, peaked between Cycles 4 and 7, and subsided after Cycles 8 and 9. Of the evaluable patients at each cycle, the grade 2+ (2 or higher) AE rates were: 26 (16%) of 167 patients in Cycle 4; 47 (28%) of 165 patients in Cycle 5; 58 (38%) of 151 patients in Cycle 6; 39 (36%) of 109 patients in Cycle 7; 4 (22%) of 18 patients in Cycle 8; and 1 (50%) of 2 patients in Cycle 9. For dermatitis-related symptoms, 110 (20%) of 537 events were grade 2 or higher in the mometasone arm versus 124 (18%) of 688 events in the placebo arm; 7 (1%) and 16 (3%) grade 3 toxicities were reported in the
mometasone and placebo arms, respectively. Similar trends were observed for radiation-induced dermatitis, with event frequencies about half of that for dermatitis-related symptoms. Repeated measures analysis results showed that significant differences were detected across cycles in five out of nine symptoms and in the interaction between arms across cycles in two out of nine symptoms, including radiation-induced dermatitis and the maximum grade of dermatitis-related symptoms ($P < .001$, favoring mometasone). The CTCAE scales correlated weakly with the PRO tools by Pearson’s statistics. Risk analyses confirmed these results.

**CONCLUSIONS:** The CTCAE tools captured a detailed range of patient experience and symptoms, when the time variable was taken into consideration. Our results strengthened the conclusion drawn from the original report that mometasone reduced acute skin toxicities. The use of frequent CTCAE-based assessments, along with PRO surveys, to accurately assess a patient’s experience of symptom types and intensity over time should be encouraged in the design of future clinical trials.

**RESULTS:** The analysis included 9,686 patients with a median follow-up (based on survivors) of 111.0 months (range: 0.10–155.0 mo). Overall, patients with stage I or II breast cancer who underwent breast conservation surgery or mastectomy from 1998–2003. Cause-specific survival (CSS) was evaluated by Kaplan-Meier survival analysis, and the log-rank test was used to compare CSS between treatment categories of interest. Multivariable Cox regression model analysis was performed to estimate the predictors of CSS. Adjusted hazard ratios (AHRs) and 95% confidence intervals (95% CIs) were calculated for risk of breast cancer-related death.

**CONCLUSIONS:** Patients aged 40 years and younger with stage I and II invasive breast cancer treated with BCT had noninferior CSS than mastectomy, regardless of ER status. Our data suggest that young age and/or ER status is not a contraindication to BCT in early-stage breast cancer patients.

**RESULTS:** A total of 87,528 patients undergoing breast conservation therapy were identified. Of this total, 4,253 patients (4.9%) received APBI using brachytherapy. The percentage of BCT patients receiving APBI did not change after guideline publication (4.9% vs 4.8%; $P = .361$). The analysis was then limited to patients who were not missing data that would affect their ASTRO CS classification.
the ASTRO CS, the proportion of "unsuitable" patients treated with APBI decreased after guideline publication (15.8% vs 11.1%; *P* < .001), and the proportion categorized as suitable increased after guideline publication (37.7% vs 42.1%; *P* = .005), while the proportion categorized as cautionary did not change (46.5% vs 46.7%; *P* = .859). The proportion treated for cautionary or unsuitable disease went from 62.3% prior to guideline publication to 57.9% following publication (*P* = .005). Significant decreases were seen in the number of patients receiving APBI aged younger than 50 years (2.5% vs 1.7%; *P* < .001), without nodal evaluation (4.7% vs 3.4%; *P* = .036), and with estrogen receptor-negative tumors (10.4% vs 8.2%; *P* = .022) after publication of the guidelines. Additionally, there was a trend toward a decrease in the proportion of patients with node-positive tumors receiving APBI (2.5% vs 1.7%; *P* = .086). There was no significant change in the percentage of APBI patients treated for DCIS (16.4% vs 16.7%; *P* = .80).

CONCLUSIONS: In the period directly following the publication of the ASTRO CS, the proportion of "unsuitable" patients treated with brachytherapy-based APBI decreased, and the proportion of "suitable" patients increased. Nonetheless, nearly 60% of patients treated would be considered cautionary or unsuitable.


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BACKGROUND: Screening has led to a decrease in the number of women diagnosed with late-stage breast cancer, but there are limited studies assessing stage at diagnosis over time for black and Hispanic patients, who historically have been more likely to present with advanced disease. We examined whether presenting stage at time of breast cancer diagnosis has changed over time in Florida and whether there is variation in this change with respect to race, ethnicity, and socioeconomic status (SES).

METHODS: Data were obtained from the Florida Cancer Data System (FCDS), which was linked with Florida’s Agency for Health Care Administration (AHCA) and with information from the US census track. Our sample included female breast cancer patients in Florida during 1981–2009 (n = 364,303). We excluded non-Florida residents aged < 18 years and with carcinoma in situ (n = 63,974). Patients with missing values for race, ethnicity, SES, or surgery (n = 73,678) were excluded, resulting in a total sample size of 226,651. Associations between categorical variables were examined using chi-square tests. Predictors of Surveillance, Epidemiology, and End Results (SEER) stage at diagnosis (local, regional, distant) were modeled with multinomial ordinal logistic regression models to obtain adjusted odds ratios (ORs) and corresponding 95% confidence intervals (95% CIs) for race, ethnicity, and SES. The model includes the year of diagnosis to take into account the trend over time for stage at diagnosis. Type I error rate was set at 5%. SAS v9.3 (SAS Institute Inc., Cary, NC) was used to perform all analyses.

RESULTS: In total, 145,494 (64%) patients presented with local disease, 68,167 (30%) had regional disease, and 12,990 (6%) presented with distant disease. There were 206,994 (91%) white patients, 17,787 black patients (8%), and 1,920 (1%) of other races. A total of 207,311 (91%) were identified as non-Hispanic Latino, and 19,340 (9%) were Hispanic Latino. In the entire cohort, there was a significant increase in local disease and a decrease in regional and distant disease at presentation over the time period examined (*P* < .0001). The increase in local stage at diagnosis was greater for black than for white patients, as was the decrease in regional and distant disease (*P* < .001). Hispanic women also had a significant increase in localized disease and a decrease in regional and distant disease (*P* < .001), but there was little difference in the rate of change compared with non-Hispanic women. Multivariable analysis showed that race, ethnicity, and SES were all significantly associated with change in stage of diagnosis over time. Despite a greater rate of change for black patients, whites continued to have greater odds of local presentation (OR = 1.78; 95% CI, 1.69–1.88), and
Hispanic patients continued to have lower odds of local presentation compared with non-Hispanic patients (OR = 0.80; 95% CI, 0.76–0.84).

CONCLUSIONS: Trends in Florida from 1981 to 2009 show that early-stage breast cancer diagnosis is more common over time in all race and ethnic groups. While there remains a significant disparity, with black and Hispanic patients being less likely to present with early-stage disease, the rate of change appears to be greater for black patients. Thus, this disparity may be decreasing over time, particularly for black patients.

(S048) Impact of Breast Cancer Subtype in Locoregional Outcomes in Stage III Locally Advanced Breast Cancer (LABC) Treated With Modern Multimodality Therapy

Jonathan Verma, MD, Deukwoo Kwon, PhD, Isildinha M. Reis, PhD, Joan L. Wright, MD, Cristiane Tokita, MD; Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine

BACKGROUND: The use of molecular profiling in breast cancer for local risk assessment and local therapy decision is not well understood. The goal of this study is to assess locoregional outcomes associated with breast cancer subtype in stage III locally advanced breast cancer (LABC) patients after surgery, radiation therapy (RT), and modern systemic therapy.

MATERIALS AND METHODS: We retrospectively collected the data from patients treated at our institution for stage III breast cancer from 1998–2008. Biologic subtype was approximated using receptor status: luminal A (estrogen receptor positive [ER+] or progesterone receptor positive [PR+], human epidermal growth factor receptor 2 negative [HER2−]), luminal B (ER+ or PR+, HER2+), basal (ER−, PR−, HER2−), and HER2 (ER−, PR−, and HER2+). Progression-free survival (PFS) and overall survival (OS) were estimated by the Kaplan-Meier method. The method of cumulative incidence allowing for competing risk was applied to the first failure event categorized as locoregional (LRR), distant metastasis (DM), simultaneous (LRR + DM within 4 months of each other), and death with no evidence of disease (NED). Local control (LC) was defined as the complement of the combined rate of LRR and simultaneous LRR + DM failures. Log-rank test was used to compare OS and PFS by biologic subtype, and Gray’s test was used to compare incidence rates of failure events by biologic subtype. Prognostic effects relative to first failure and cause-specific death were evaluated by fitting competing risk regression models by the method of Fine and Gray.

RESULTS: The data for 188 patients were reviewed, with a median follow-up of 74.9 months (range: 7–205 mo). The median age at diagnosis was 49 years. The subtypes included luminal A (51.6%), luminal B (10.6%), HER2 (11.7%), and basal (26.1%). Tumor grade was high in 63.8% of patients. Seventy-eight percent of patients had mastectomy, and 22% had lumpectomy. Axillary surgery was performed in all patients. Surgical margins were negative in 95.7%. Further, 93.6% of the patients received chemotherapy—adjuvantly (43.1%), neoadjuvantly (23.9%), or both (26.6%). Hormone therapy was given to 53.7% of the patients. Trastuzumab was used in 90% of patients with HER2+ disease. All patients received RT. The first failure event was LRR in 19 patients (10.1%), DM in 22 (11.7%), LRR + DM in 5 (2.7%), and deaths with NED in 9 (4.8%). The 8-year locoregional control rates were 88.4%, 90%, and 78.9% in patients with luminal A, luminal B/HER2, and basal tumors, respectively. The 8-year OS was 84%, 92.4%, and 68.8% in patients with luminal A, luminal B/HER2, and basal tumors, respectively (P = .015). In the multivariate analysis, the significant predictors for worsened locoregional recurrence were basal subtype (hazard ratio [HR] = 3.26; P = .017), tumor size > 5 cm (HR = 2.93; P = .012), and positive nodal status (HR = 5.38; P = .02). The predictors for breast cancer-specific mortality included basal subtype (HR = 6.0; P < .001), size > 5 cm (HR = 3.44; P = .008), and positive nodal status (HR = 27; P = .003).

CONCLUSION: Basal subtype, tumor size > 5 cm, and nodal positivity were predictive of LRR and breast cancer-specific mortality in this cohort of patients with stage III LABC treated with modern multimodality therapy. Prospective studies are needed to improve locoregional control and survival in patients with the basal subtype.
SCIENTIFIC POSTERS

(P001) Triapine Radiochemotherapy Improves Survival in Women With Stage IIb Cervical Cancer
Charles A. Kunos, MD, PhD; Tracy Sherertz, MD; Case Western Reserve University; Summa Health System; University Hospitals of Cleveland

PURPOSE: The Surveillance Epidemiology and End Results (SEER) registry has published a 3-year cancer-related survival rate of 55% among the 2,236 cases of stage IIIB squamous cell cervical cancer between 1988 and 2001. Triapine irreversibly blocks ribonucleotide reductase, the de novo rate-limiting generator of DNA building blocks, and enhances cytotoxic effects of cisplatin chemotherapy and radiation therapy. Whether triapine radiochemotherapy reduces extrapelvic disease progression and disease-related death is not known.

MATERIALS AND METHODS: Between 2006 and 2011, 12 women with clinical stage IIIB cervical cancer underwent three-times-weekly intravenous triapine (25 mg/m²), once-weekly cisplatin (40 mg/m²), and daily pelvic irradiation (45 Gy) followed by brachytherapy (30–40 Gy) on phase I and phase II trials. Lymph node positivity was determined by CT and positron emission tomography (PET) with [18F]-fluoro-2-deoxy-D-glucose (FDG). Cancer-related survival was evaluated by the Kaplan-Meier method.

RESULTS: Median follow-up was 30 months (range: 4–90 mo). Pretheraphy FDG-PET/CT detected abnormal FDG uptake in pelvic lymph nodes in 9 (75%) of the 12 stage IIIB women. One local (8 mo) and three distant (5, 23, and 24 mo) relapses have occurred after triapine radiochemotherapy. Two (17%) cervical cancer-related deaths and two (17%) non-cancer-related deaths have been observed. The 3-year cancer-related survival rate for women with stage IIIB cervical cancer was 74% (95% confidence interval [CI], 58%–90%), which compares favorably with a 55% SEER control.

CONCLUSIONS: Findings suggest that triapine radiochemotherapy provides improved cancer-related survival in women with stage IIIB cervical cancer. A prospective National Cancer Institute–sponsored (NCT01835171) randomized phase II trial of triapine radiochemotherapy vs radiochemotherapy has begun accrual nationwide.

(P002) Impact of Three Decades of Screening on Cervical Cancer Incidence
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BACKGROUND: Effective cancer screening should detect disease at an earlier, more curable stage and thus reduce the incidence of late-stage diagnosis. In the last 3 decades, the Pap smear has become widely practiced in the US and is effective in the early diagnosis and prevention of cervical cancers. However, the overall number of cases of cervical cancer prevented by screening is unknown.

METHODS: We obtained cervical cancer incidence data spanning 1976 to 2009 from the Surveillance, Epidemiology, and End Result (SEER) database. Additionally, screening utilization data from 1951 to 2010 were obtained from literature reports and from the National Cancer Institute (NCI) Progress Reports. We examined trends in early (localized)- and late (regional, distant)-stage cancer incidence and sought to estimate the number of cancers prevented due to screening over the past 3 decades.

RESULTS: From 1951 to 1973, there was a steady increase in screening utilization. Screening rates rose from under 1% in 1951 to 63.7% in 1973. However, over the past 3 decades, the percentage of adult women who received cervical cancer screening remained steady at 71.7% in 1982 and rising to 73.8% in 2010. From 1976 to 2009, there was a statistically significant decrease in the incidence of early-stage cervical cancer, from 10.2 cases to 5.4 cases per 100,000 women (P < .001). Late-stage disease incidence also decreased from 5.2 cases to 3.7 cases per 100,000 women (P < .001). After adjusting for “prescreening era” rates of cervical cancer, we estimated that Pap smears were associated with a reduction of between 102,000 and 452,000 cases of cervical cancer over the past 3 decades in the US.

CONCLUSIONS: There has been a statistically significant decline in both early- and late-stage cervical cancer incidences during an era of widespread screening.

(P003) Isolated Port-Site Metastases Following Laparoscopic Hysterectomy for Endometrial Cancer: Outcomes of Patients Treated With Radiotherapy
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INTRODUCTION: Laparoscopic hysterectomy is increasingly replacing total abdominal hysterectomy as the standard approach in the management of endometrial cancer. An uncommon but reported complication of this minimally invasive approach is the recurrence of disease at the surgical entry site, known as port- or trocar-site metastasis. The optimal management of isolated port-site metastasis is unknown, and the outcomes of very few patients with port-site metastasis have been reported in the literature. We report here on the outcome of seven patients with isolated port-site metastases who were treated definitively with or without resection and radiotherapy.
METHODS: We retrospectively reviewed all cases of endometrial adenocarcinoma treated at UT MD Anderson Cancer Center from 1996–2013 who were treated with external beam radiation to the abdomen or pelvis without brachytherapy. Seven patients were identified as having isolated port-site metastases following laparoscopic surgery. Clinical and treatment characteristics were obtained from the medical chart, along with follow-up and outcome data.

RESULTS: Patients presented with stage Ia (5), Ib (1), or II (1) endometrial cancer with endometrioid (4) or serous (3) histology. All patients underwent a total laparoscopic hysterectomy and bilateral salpingo-oophorectomy with or without a node dissection. The median interval from initial surgery to port-site recurrence was 15 months. Six of the seven patients underwent surgical resection of the recurrence, and all received radiotherapy. Patients with negative margins were treated to 45–50.4 Gy (4), one patient with a close margin (< 0.5 mm) received 60 Gy, and patients with a positive margin (1) or gross disease (1) received 66 Gy. Two patients were treated with electrons alone, three were treated with photons alone, and two received a combination of photons and electrons. Photon treatment was delivered with wedge pair (1), tangent fields (1), or intensity-modulated radiation therapy (IMRT) (1). Electrons were delivered appositionally with 9, 12, 18, and 16 MeV. At a median follow-up of 2 years from the time of the port-site recurrence, the rate of disease-free survival (DFS) at 1 and 2 years after the recurrence was 100% and 71%, respectively. The rate of overall survival (OS) at 2 years was 100%. One patient with stage Ia, grade 2 endometrioid adenocarcinoma developed lung metastases at 17 months following port-site recurrence. Another patient developed contralateral abdominal wall and lymph node metastases at 22 months following the recurrence.

CONCLUSION: High rates of DFS after definitive treatment of surgical entry-site recurrences support aggressive treatment with curative intent. The optimal integration of surgery, chemotherapy, and radiation is unknown.

(P004) Definitive Radiation in Early-Stage Endometrial Carcinoma
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INTRODUCTION: The purpose of this study is to describe the outcomes of definitive radiation in medically inoperable early-stage endometrial carcinoma. Although early-stage disease usually results in favorable overall survival (OS) after surgery, there is a growing cohort of patients who are medically inoperable secondary to morbid obesity.

METHODS: In this retrospective study, we analyzed the outcomes of 30 patients with International Federation of Gynecology and Obstetrics (FIGO) clinical stage I or II disease who were treated definitively between 2002 to 2011 with either high-dose-rate (HDR) brachytherapy to 36 or 48 Gy utilizing tandem, ovoids, and Simon-Heyman capsules or combined brachytherapy and external beam radiation therapy (EBRT). Prior to 2005, external beam radiation was delivered to the whole pelvis with a split field to a total dose of 50.4 Gy. After 2005, IMRT was utilized to deliver 50.4 Gy to the pelvic and para-aortic nodes and 20 Gy to the uterus or [18F]-fluoro-2-deoxy-D-glucose (FDG)-avid uterus if positron emission tomography (PET)/CT was available. The primary endpoint was overall survival (OS).

(P004) Figure: Overall Survival of Patients Treated with EBRT + Brachytherapy vs Brachytherapy Alone. EBRT = external beam radiation therapy; HDR = high dose rate; LAD = lymphadenopathy; MMI = myometrial invasion; MMT = mixed Müllerian tumor.
RESULTS: Nineteen patients underwent HDR brachytherapy alone, all of whom were stage I. Eleven patients underwent brachytherapy and EBRT, 64% of whom was stage I. Mean follow-up time was 36.5 months in the brachytherapy group and 56.5 months in the combined modality group. Three-year OS was 72% in the brachytherapy group and 42% in the combined modality group (Figure). Patients who received combined modality therapy did have more advanced disease than those who received HDR brachytherapy alone. Two patients in the HDR brachytherapy group presented with symptomatic local recurrence at 7 months and at 2 years, respectively.

CONCLUSION: In conclusion, in our limited retrospective series, medically inoperable patients with FIGO clinical stage I endometrial carcinoma treated with modern-era HDR brachytherapy have a 3-year OS of 72% in the absence of surgery. Patients with more advanced disease have a worse outcome; however, it is unclear whether this is cancer-specific, as these patients have multiple comorbidities (listed in Table). Further investigation into cause-specific mortality in a larger cohort of patients is warranted.

(P005) Time to Cervical Stent Placement as a Predictor of Prolonged Treatment Course in Patients Treated With Definitive Chemoradiation Therapy for Cervical Cancer

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BACKGROUND: While it is known that definitive chemoradiotherapy (CRT) for cervical cancer should be completed within 56 days, many patients experience delays which prolong treatment. At many institutions, a cervical stent is inserted 1 or more days prior to start of high-dose-rate brachytherapy (HDR), though optimal time of placement is unknown. Placement early on, as the cervix is responding to therapy, may compromise the positioning of the stent, suture integrity, and dosimetry at the time of brachytherapy, whereas late placement may prolong overall treatment length. Our objective is to evaluate factors predictive of prolonged treatment time, including time of stent placement, in this patient population.

METHODS: After institutional review board (IRB) approval, 71 consecutive patients treated from 2008 to 2013 for cervical cancer with CRT followed by HDR were identified. Medical records were reviewed to gather demographic, clinical, and treatment data. Prolonged treatment was defined as > 56 days per the American Brachytherapy Society guidelines. In addition to the time of stent placement, the following variables were evaluated using paired t-tests and univariate logistic regression: age, race, use of intensity-modulated radiation therapy (IMRT) vs conventional technique, time to first HDR, genitourinary (GU) or gastrointestinal (GI) toxicity, and the presence of a boost.

RESULTS: Median age was 50 years. Thirty-nine percent of patients had International Federation of Gynecology and Obstetrics (FIGO) stage 1 disease, 39% had stage II, 16% had stage III, and 6% had stage IV. Median external beam radiation therapy (EBRT) dose was 45 Gy with a 5.4-Gy sidewall or parametrial boost. The median HDR dose was 27.5 Gy in five fractions. Sixty-six percent was treated with a four-field technique, and 34% was treated using IMRT. Sixty-eight women had HDR with a ring and tandem applicator, whereas three underwent an interstitial implant. For the 68 patients requiring a cervical stent, the median time from start of EBRT to cervical stent placement and first HDR was 29 and 38 days, respectively. The median treatment length for all patients was 59 days. Factors associated with prolonged treatment were time to cervical stent placement (P = .001), delay ≥ 2 days between final EBRT and initial HDR (P = .0195), any grade GU toxicity (P = .0007) or GI toxicity (P = .0002), and the presence of a boost (P = .0006). Age, stage, and IMRT vs conventional technique were not significantly associated with prolonged treatment time. Excluding patients with any treatment breaks, the following factors remained associated with prolonged treatment: time to cervical stent placement, with a mean of 31 days vs 27 days in patients completing treatment in ≤ 56 days (P = .05), and time to initial HDR (mean, 47 vs 34 days; P = .01).

CONCLUSION: In this series of patients, acute toxicity, increased time to cervical stent placement, and time to first HDR treatment were associated with prolonged treatment time. Patients who completed treatment in ≤ 56 days had a lower average time to cervical stent placement, 27 vs 31 days. Preventing and treating acute toxicity in order to minimize treatment breaks remains essential. Additionally, our results suggest that cervical stent placement during the fourth week of treatment is also an important factor in facilitating timely completion of treatment.

(P006) Comorbidities and Senior Oncology Patients: How Comorbidities Affect Older Women With Cervical Cancer

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Despite improvements in public health and important advances in clinical care, cervical cancer is still an important condition among older women.

OBJECTIVES: Analyze a cohort of older women with cervical cancer and explore the role of comorbidities on the rates of late gastrointestinal (GI) and urinary (GU) toxicities after treatment.

METHODS: Using the Surveillance Epidemiology and End Results (SEER) database linked to Medicare claims, we analyzed rates of GI and GU toxicities over a 60-month period among women aged over 65 years diagnosed with stage I and above cervical cancer between 1992 and 2005. All 2,080 women were treated with radiation therapy. We initially compared women who reported any GI or GU toxicity with those who reported no toxicity using chi-square tests. Using the Charlson index, we then compared mortality rates by Charlson index score to determine if number of comorbidities affected mortality. Time-to-event analysis was used to compare rates of survival by Charlson score.

RESULTS: Death rates progressively increased as the Charlson index score increased, with women reporting a score of 3 having the highest mortality rate (81.5%) after 60 months from diagnosis of cervical
cancer. Time-to-event analysis by type of toxicity showed significant differences in survival rates among those with score 0 and those with score 3 in the index for GI but not for GU toxicity.

CONCLUSIONS: Comorbidities play an important role in survival of women with cervical cancer. Physicians need to carefully evaluate comorbidities among older women with cervical cancer and discuss the benefits of cancer treatment based on the clinical profile for each patient.

(P007) Safety and Tolerability of Adjuvant Radiation “Sandwiched” Between Carboplatin and Paclitaxel in Women With Uterine Carcinosarcoma

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OBJECTIVE: Carcinosarcoma (CS) is a rare uterine tumor with a poor prognosis and a high recurrence rate, even in early-stage disease. Adjuvant treatment includes radiotherapy (RT), systemic chemotherapy, or both; however, the optimal sequence and agents remain undefined. We report the initial analysis on the tolerability and toxicity of radiotherapy “sandwiched” with carboplatin and paclitaxel in surgically staged CS.

METHODS: After institutional review board (IRB) approval, women with surgically staged CS with no evidence of gross residuum were enrolled into a protocol. Carboplatin (AUC 6) and paclitaxel (175 mg/m²) every 3 weeks for 3 cycles, followed by intensity-modulated radiation therapy (IMRT) and brachytherapy, followed by 3 additional cycles of carboplatin (AUC 5) and paclitaxel (175 mg/m²) every 3 weeks. Toxicities were graded by Common Toxicity Criteria and Adverse Events version 4.0 (CTCAE v4.0). Of note, IMRT was utilized in the planning and treatment delivery. This allowed placing constraints of radiation dose to the bone marrow, bladder, rectum, and bowel with the goal of reducing toxicity in the setting of multimodality therapy.

RESULTS: There are seven patients enrolled thus far, and six patients have completed the protocol. One patient declined further chemotherapy after the first cycle. All patients completed IMRT and brachytherapy. Median age at diagnosis was 70 years (range: 46–78 y); mean BMI was 28.7 kg/m² (range: 19–38 kg/m²); and five out of seven patients had stage I A disease. Of the 37 cycles of chemoradiotherapy administered, there were 10 (27%) grade 3/4 neutropenia, 2 (5.4%) anemia, and 4 (10.8%) thrombocytopenia, most of which were self-limiting. There were only one (2.7%) grade 3/4 nonhematologic toxicity and one radiation-related toxicity. Two patients required growth factor support following Cycle 2 and each subsequent cycle. An additional two patients required growth factor support following Cycle 4 and each subsequent cycle.

CONCLUSIONS: Carboplatin and paclitaxel “sandwiched” with IMRT and brachytherapy are well tolerated, with the majority of toxicities being grade 1 or 2 and self-limiting. Accrual of patients on this regimen will continue in order to delineate the efficacy of these findings as well as the long-term toxicity of this regimen.

(P008) The Effect of Body Mass Index on Chemoradiation Treatment Outcomes in Cervical Carcinoma

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PURPOSE AND BACKGROUND: Obesity is a significant problem in the US, and an increase in body mass index (BMI) has an unclear effect on outcomes for patients with cervical carcinoma who receive definitive chemoradiation.

METHODS: This retrospective cohort included 490 patients with International Federation of Gynecology and Obstetrics (FIGO) stage IB1 or greater cervical carcinoma who received definitive chemoradiation therapy consisting of both external beam radiotherapy (EBRT) and brachytherapy between January 1998 and June 2012 at a single institution. The mean follow-up was 50 months. BMI was calculated using the National Institutes of Health online calculator. Primary outcomes were rates of overall survival (OS) and grade 3 or greater complications.

RESULTS: Underweight patients (BMI < 18.5 kg/m²) had an inferior OS when compared with normal-weight (18.5–24.9 kg/m²) and overweight (> 24.9 kg/m²) patients (P = .04) on log-rank analysis. The 5-year OS rate was 58% (15/26) for underweight, 69% (99/143) for normal-weight, and 71% (228/321) for obese patients. Overweight patients had the lowest risk of toxicity (P = .05) on log-rank analysis. The rates of grade 3 or greater bowel or bladder toxicity were 23% for underweight (6/26), 18% for normal-weight (26/143), and 12% for overweight patients (38/321).

CONCLUSIONS: Underweight patients have inferior OS and greater complication rates when compared with normal-weight and overweight patients.

(P009) Early-Stage Carcinosarcoma Treated With Adjuvant Radiotherapy and Chemotherapy

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PURPOSE AND OBJECTIVES: To report a single-institution experience using adjuvant chemoradiation for early-stage carcinosarco-
ma (CS) of the uterus.

**MATERIALS AND METHODS:** We retrospectively reviewed 31 women with completely resected stage I–II CS following hysterectomy/bilateral salpingo-oophorectomy (BSO) who received adjuvant radiotherapy (RT) and chemotherapy from 2000–2010. Exclusions were lack of residual disease after diagnostic biopsy, positive washings, or prior abdominopelvic malignancy.

**RESULTS:** Of the 31 patients, 24 (77%) were stage IA, 4 (13%) were IB, and 3 (10%) were stage II. Pelvic node sampling was performed in 97% of patients (median, 17 nodes), and para-aortic node sampling was performed in 81% (median, 6 nodes). None of the patients had positive pelvic cytology. The chemotherapy regimen was carboplatin/taxane in 26 patients (84%), ifosfamide-based doublet in 3 patients (10%), or carboplatin alone in 2 patients (6%). Adjuvant RT was primarily given as intravascular RT (IVRT) in 30/31 patients (97%) to a median dose of 21 Gy, and only 1 patient (3%) received pelvic RT. Median follow-up was 48 months. The 5-year actuarial rate of pelvic recurrence was 11% (95% confidence interval [CI], 0%–23%) and 11% for para-aortic recurrence (95% CI, 0%–22%). There were no vaginal recurrences, and the 5-year rate of isolated pelvic recurrence was 3.7% (95% CI, 0%–10%). The 5-year actuarial rate of peritoneal relapse was 11% (95% CI, 0%–22%) and 26% for other distant metastases (95% CI, 10%–42%). The 5-year disease-free survival (DFS) was 66% (95% CI, 50%–82%), and the 5-year overall survival (OS) was 79% (95% CI, 61%–96%).

**CONCLUSIONS:** Adjuvant chemotherapy coupled with intravaginal RT (given to 30/31 patients) seems to provide a good outcome in terms of low rate of isolated pelvic recurrence (3.7%). However, given the rate of distant metastasis, further intensification of systemic therapy is still needed in this group of patients.

**P010** Clinical Outcomes in Patients With Early-Stage Uterine Clear-Cell Carcinoma

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**PURPOSE AND OBJECTIVES:** There is a paucity of data on the clinical outcomes in women with uterine clear-cell carcinoma. The purpose of this study is to report single-institution clinical outcomes in patients with early-stage uterine clear-cell carcinoma. The results demonstrate a local recurrence rate of 12.5%, Kaplan-Meier estimate was used to assess overall survival (OS) and disease-free survival (DFS).

**RESULTS:** The median follow-up was 63 months. The 5-year vaginal recurrence rate was 6.4% (95% confidence interval [CI], 0%–14.6%), and the pelvic recurrence rate was 6.4% (95% CI, 0%–14.6%). There were no isolated vaginal or pelvic recurrences. The 5-year rates of para-aortic and distant recurrence were 4.7% (95% CI, 0%–11.3%) and 9.7% (95% CI, 1.0%–18.9%), respectively. The site of distant relapse was lung in four (8.7%) patients, peritoneum in three (6.5%) patients, thoracic lymphadenopathy in one (2.2%) patient, and bone in one (2.2%) patient. The 5-year DFS rate was 85.3% (95% CI, 74.1%–96.5%), and the OS rate was 90.3% (95% CI, 81.1%–99.5%). In the subset of patients who received adjuvant chemotherapy, the 5-year rate of distant relapse was 7.7% (95% CI, 0%–22.5%), compared with 18.5% (95% CI, 3.3%–33.7%) in patients who did not receive chemotherapy.

**CONCLUSIONS:** With a median follow-up of 63 months, we observed reasonable disease control and survival at 5 years in 46 women with early-stage uterine clear-cell carcinoma. The lack of isolated vaginal/pelvic recurrence observed in this study seems to justify the growing interest in utilizing systemic therapy in early-stage clear-cell carcinoma of the uterus.

**P011** Efficacy and Morbidity of Temporary Iodine-125 Brachytherapy in Pediatric Rhabdomyosarcomas

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**PURPOSE:** Rhabdomyosarcomas are the most common soft tissue tumors in the pediatric population, and they have a high propensity for local recurrence. Adjuvant radiation therapy is often used in their management and has a vital role in maximizing local control. Brachytherapy has advantages over external beam radiation therapy (EBRT) that are important in the pediatric population—namely, the ability to provide a high dose of radiation to the most susceptible areas of recurrence, while delivering a much lower dose to surrounding normal tissue. Since the pediatric population is at increased risk for long-term complications of radiation therapy (RT) affecting growth and development, it is important to establish the best radiation treatment regimen with minimal exposure to healthy tissue and optimal local control. Iodine-125 brachytherapy, in particular, has the advantage over iridium-192 of being of lower energy, permitting easier shielding, and is more accommodating for patient interaction during treatment. This study examined a group of pediatric patients with rhabdomyosarcomas who were treated with temporary, low-dose-rate iodine-125 brachytherapy and investigated the efficacy and side effects of such treatment. This is the first report of patients exclusively with rhabdomyosarcomas being treated exclusively with iodine-125 brachytherapy.

**METHODS:** This study examined a group of eight pediatric patients with new or recurrent rhabdomyosarcomas who were treated with adjuvant temporary, low-dose-rate iodine-125 brachytherapy, total dose 3,600–4,500 cGy to the target volume, and investigated the efficacy and late side effects of such treatment.

**RESULTS:** The results demonstrate a local recurrence rate of 12.5%,
with minimal side effects occurring in the patients who had no prior radiation history. There was an 88% disease-free survival (DFS) and overall survival (OS). Three patients with prior radiation exposure experienced early and/or late adverse events, and all patients without prior radiation experienced no significant late adverse events.

**CONCLUSIONS:** This study demonstrates good local control and survival in pediatric patients with rhabdomyosarcomas treated with iodine-125 brachytherapy, with a low rate of side effects in patients without prior radiation exposure and a notable increase in radiation toxicity with a history of prior radiation. Radiation therapy has an important role in maximizing local control of rhabdomyosarcomas, and the high efficacy and ease of radiation protection for visitors establish iodine-125 brachytherapy as an effective treatment that is logistically convenient for patients and families. This is the first report of patients exclusively with rhabdomyosarcomas being treated exclusively with iodine-125 brachytherapy and demonstrates promising results.

**(P012) National Trends in Surgery for Sinonasal Malignancy: The Effect of Hospital Volume on Short-Term Outcomes**

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**BACKGROUND:** Sinonasal carcinomas are rare, highly morbid neoplasms originating in the nasal cavity and paranasal sinuses. The mainstay of treatment over the past 2 decades has been a combination of surgery, radiation, and chemotherapy. We sought to characterize trends in the initial management of sinonasal malignancy in the National Inpatient Sample (NIS) within 30 days.

**METHODS:** A retrospective cohort study was conducted, examining time trends among patients admitted for surgical resection of sinonasal malignancy in the National Inpatient Sample (NIS) between 1988 and 2009. Subset analysis of high-risk cases was performed on patient cohorts with skull base involvement or orbital or maxillary sinus involvement or those who underwent neck dissection. Patient characteristics as well as hospital attributes were correlated with patient morbidity and mortality.

**RESULTS:** Over the course of 22 years, we identified 3,850 cases of sinonasal surgery patients from 879 hospitals—24.3% of patients had complications, ranging from infections, cardiopulmonary complications, neuropathy, visual disturbances, and electrolyte abnormalities, and 0.8% of hospitalizations resulted in mortality. High-risk cases with skull base or orbital or maxillary sinus involvement or including neck dissection had more complications (29.4% vs 23.2%; \(P < .001\)) and a longer length of stay (9.34 d vs 6.13 d, \(P < .001\)). There was an increase in the number of cases with neck dissection over the time period studied.

Thirty-two hospitals averaged more than five cases per year, accounting for 28% (1,097) of all sinonasal surgeries. These high-volume centers were predominantly large (73.3%), urban (96.7%), teaching (90%) institutions and performed more high-risk cases, accounting for 32.4% of cases, including neck dissection, 44.6% of cases with orbital involvement, and 43.1% of cases with skull base involvement. Compared with low-volume centers, high-volume centers had more cardiopulmonary complications (21.1% vs 17.8%; \(P = .024\)), electrolyte abnormalities (10.4% vs 7.2%; \(P = .018\)), and longer lengths of stay for both high-risk cases (10.58 d vs 8.59 d; \(P = .003\)) and non–high-risk cases (6.84 d vs 5.89 d; \(P = .004\)). Over the time period studied, a greater proportion of cases were recently performed at high-volume centers.

**CONCLUSIONS:** This study characterizes current trends in the initial management of sinonasal cancer. There is an increased likelihood that complicated surgeries are performed at higher-volume hospitals, which also entails a higher complication rate. High-risk cases resulted in higher rates of complications but were not associated with a higher mortality rate.
data from two large academic centers that utilize PrT and conventional RT, we found that there was no difference in the use of PrT when compared with RT for EOL. These results were evident, despite extreme patient selection inherent in the use of PrT.

(P014) Age and Gender Patterns in the Use of Anesthesia for Children Receiving Radiotherapy

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OBJECTIVE: Complications in pediatric patients receiving anesthsia-assisted radiation therapy (AART) are rare, but the procedure is time-, space-, and resource-consuming. Influencing the decision to use AART may include ill-defined patient functional or psychological factors, as well as parent/physician discretion. We analyzed our experience with AART for identifiable patterns regarding age and gender in children receiving daily proton radiation therapy.

MATERIALS AND METHODS: After institutional review board (IRB) approval, we reviewed our records from the Indiana University Health Proton Therapy Center for patients requiring AART between January 9, 2004 and June 30, 2013 with respect to age and gender in our pediatric patients (defined as patients ≤ 18 years of age).

RESULTS: A total of 390 pediatric patients were treated in this era. Of them, 182 were girls and 208 were boys. The median age at start of treatment for pediatric patients treated with AART was 4 years vs 13 years for those not requiring AART. Similarly, the median age at start of treatment for pediatric boys and girls treated with AART compared with those not requiring AART was 4 years vs 13 years and 3 years vs 12 years, respectively. Overall, the likelihood of requiring AART by age is shown in the figure. All children ≤ 3 years of age and the majority of children ≤ 6 years of age required AART. There was no significant difference in any age group by gender.

CONCLUSION: While children aged ≤ 3 years invariably require AART in our experience, not surprisingly, the need for AART decreases with increasing age. A small cadre of older children has functional or other issues that require them to receive AART for daily radiation treatment. There is no difference in AART requirement by gender. This pattern of care data may assist centers in pre-planning needs for pediatric radiation therapy cases referred from distant referral sites. Additionally, it establishes a baseline curve for AART requirements in the pediatric population upon which future studies can build.

(P015) Delayed Cerebrovasculopathy Due to Cranial Radiation Therapy for Pediatric Tumors

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BACKGROUND: Radiation-induced cerebrovascular injury in the form of accelerated arteriosclerosis of blood vessels is a well-known phenomenon. Delayed cerebrovasculopathy in pediatric cancer patients as a result of cranial irradiation has been reported to present as Moyamoya disease or intracerebral hemorrhage. In this study, we propose to analyze reported cases of delayed radiation-induced cerebrovasculopathy that presents as Moyamoya disease and/or intracerebral hemorrhage and investigate the relationship between radiation dose and the interval between radiation and the presentation of cerebrovasculopathy.

METHODS: Patients under 21 years of age at the time of radiation were included in analysis. Manuscript review yielded 77 cases of delayed radiation-induced cerebrovasculopathy, consisting of 45 cases of Moyamoya disease, 30 cases of intracerebral hemorrhage, and 2 cases of both. The total prescribed radiation dose and the interval between radiation and the onset of cerebrovasculopathy were determined for each case.

RESULTS: The median age at radiation was 4.8 years, with a range of 0.5 to 20 years. Approximately 75% of these patients received radiation at less than 9 years of age. The median interval period from radiation to presentation for intracerebral hemorrhage cases was 7.5 years (range: 0.8–27 yr), whereas the median interval period for Moyamoya disease cases was 3.3 years (range: 0.3–20 yr) (P < .001). There was no significant association between radiation dose and interval from radiation to intracerebral hemorrhage presentation (P = .31), while for Moyamoya patients, the association was significant (P < .001).

CONCLUSIONS: Pediatric patients who presented with Moyamoya disease generally presented earlier than those who presented with intracerebral hemorrhage. This supports the possibility that Moyamoya may be an earlier manifestation of cerebrovasculopathy that precedes intracerebral hemorrhage. Furthermore, in patients who presented with Moyamoya, there was a statistically significant correlation between increasing doses of radiation and shorter time from radiation to disease presentation.

(P016) Management of Pediatric Intracranial Low-Grade Gliomas: Long-Term Follow-up After Radiation Therapy

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INTRODUCTION: The treatment of pediatric low-grade gliomas...
(LGGs) generally begins with maximal safe resection. Radiation therapy (RT) and chemotherapy are typically reserved for patients with incomplete resection and/or disease progression. We report long-term treatment outcomes and toxicities in a cohort of pediatric patients with LGG after RT.

**METHODS:** A retrospective single-institution study was performed for pediatric patients with intracranial LGG. Thirty-three patients aged <21 years at diagnosis who received RT between 1982 and 2010 were included in this analysis. Patients were evaluated for overall survival (OS) after RT, progression-free survival (PFS) after RT, timing of RT, patterns of failure, and toxicity. Descriptive statistics and the Kaplan-Meier method were used for analysis. A Cox proportional hazards regression analysis was performed to determine which parameters were significant under multivariate analysis.

**RESULTS:** The mean age at diagnosis was 7.7 years (range: 1.2–18.3 yr), and mean age at time of radiation was 10.7 years (range: 3.0–28.9 yr). The median follow-up time was 9.4 years after radiation (range: 0.8–22.1 yr). Seventeen patients were male (52%). Twenty-five patients (76%) had World Health Organization (WHO) grade I pilocytic astrocytomas, seven (21%) had grade II astrocytomas, and one (3%) had LGG not otherwise specified.

At the time of diagnosis, 2 patients (6%) underwent gross total resection (GTR), 18 (55%) underwent subtotal (STR), 4 (12%) underwent partial resection (PR), and 9 (27%) underwent biopsy alone. Fifteen (45%) patients received chemotherapy. Chemotherapy regimens varied but included treatment with temozolomide, vincristine, and/or carboptatin. Ten patients (30%) received chemotherapy before RT, three (9%) received concurrent chemoradiation, and two (6%) received chemotherapy after RT.

All patients in the cohort received RT; 18 (55%) received conventional, 9 (27%) received intensity-modulated RT (IMRT), 3 (9%) received 3D-conformal, 2 (6%) received fractionated stereotactic radiotherapy, and 1 (3%) received stereotactic radiosurgery. Patients received a median radiation dose of 53.4 Gy (range: 38.0–55.8 Gy). The patient who received SRS was treated with 15 Gy in a single fraction. Twenty patients (61%) received adjuvant radiation after surgical resection, seven (21%) received radiation after a biopsy, and six (18%) received salvage radiation at time of progression. Estimated 10-year OS and PFS were 91% and 73%, respectively. Eleven patients had disease progression after RT, and all failures were local. The median time to progression was 3.6 years (range: 0.5–16.4 y) after RT. One of the 11 patients who progressed after RT developed malignant transformation to a high-grade glioma 16.4 years after RT. Two patients died due to disease progression 2.3 and 9.1 years after RT, respectively. At last follow-up, all other patients had stable disease. No significant predictors of PFS were identified on univariate or multivariate analysis. Late effects that were seen were endocrine hormone deficiencies in 15 patients, hearing loss in 4 patients, and special education requirements for 4 patients. One patient developed a grade I falx meningioma 22 years after RT.

**CONCLUSION:** In this retrospective single-institution series of pediatric LGG patients treated with RT, excellent OS and PFS were attained at long-term follow-up. Our study suggests that the use of radiation is important for tumor control in pediatric LGG, with acceptable toxicity.

(P017) Prolonged Progression-Free Survival for Surgically Managed P16-Negative Squamous Cell Carcinoma of the Oropharynx

_Eva M. Suarez, MD, Anxand Sharma, MD, Kent Armeson, MS, Terry Day, MD; Medical University of South Carolina_

**PURPOSE:** It is well known that survival of patients with p16-negative oropharyngeal squamous cell carcinoma has a poor prognosis with standard chemoradiation. Studies have not compared the addition of surgery to chemoradiation as a method to improve survival. This study was designed to assess the benefit in progression-free survival (PFS) based on p16 status when surgery is included as part of the treatment paradigm for patients with squamous cell carcinoma of the oropharynx.

**METHODS:** A single-institution retrospective analysis identified 120 patients who were treated for stage III or IV oropharynx squamous cell carcinoma that was tested for p16 overexpression. Patients either received surgery followed by postoperative radiation or chemoradiation, as indicated by final pathology (S + RT/CRT), or definitive chemoradiation (CRT). PFS, defined as the time from the completion from treatment until the first evidence of local or distant recurrence, was summarized and plotted using Kaplan-Meier methods. The log-rank test was used to compare survival distributions across treatment groups, with \( P < .05 \) indicating statistical significance.

**RESULTS:** The median follow-up was 19 months. A total of 32 patients tested negative and 88 tested positive for p16 overexpression. In the p16-negative group, 10 were treated with S + RT/CRT and 22 had definitive CRT. In the p16-positive group, 37 patients were treated with S + RT/CRT and 51 had definitive CRT. In the p16-negative group, 62.5% of patients had recurrence of disease (3 in S + RT/CRT arm and 17 in CRT arm) compared with 15.9% in the p16-positive group (5 in S + RT/CRT arm and 9 in CRT arm). PFS for the p16-negative patients was statistically better for the S + RT/CRT group (mean PFS, 24.7 mo) versus CRT (mean PFS, 21.1 mo) \( (P = .031) \). Two-year PFS for the S + RT/CRT arm and CRT arm was 68.6% and 22%, respectively. This difference was not seen in the p16-positive population (mean PFS 46.8 mo for S + RT/CRT vs 36.0 mo for CRT; \( P = .440 \)). Two-year PFS for the S + RT/CRT arm and CRT arm was 94.6% and 79.7%, respectively. There was no statistical difference in overall survival (OS) among the S + RT/ CRT arm and CRT arm within the p16-negative group or the p16-positive group.

**CONCLUSION:** Surgery followed by RT or CRT improved PFS for patients with p16-negative oropharynx squamous cell carcinoma compared with those who received definitive chemoradiation. A prospective clinical trial is warranted and is in development to further assess treatment options in this group of patients.

(P018) Micronucleus Score in Buccal Smear of Premalignant Lesions of Oral Cancers in Smokers

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INTRODUCTION: Oral squamous cell carcinoma encompasses 90% of all oral malignancies. It is considered the sixth most common malignancy and is a major cause of cancer morbidity and mortality worldwide. Early detection of pre-malignant lesions or cancerous oral lesions would improve the survival to a greater extent.

The micronucleus (MN) is the small fragment of the nucleus situated around the periphery of the main nucleus. The number of micronucleated cells (MNCs) per 1,000 epithelial cells in oil immersion magnification (1,000 ×) is known as MN score. The MN score from buccal mucosa may be helpful in detecting premalignant lesions of the oral cavity in smokers.

OBJECTIVES: To evaluate the role of MN score in buccal smears of premalignant lesions of the oral cavity in smokers.

MATERIALS AND METHODS: It was a prospective cross-sectional study including 60 patients with ages ranging from 15–70 years. They were divided into three groups. Group 1 (control) included 20 nonsmokers with lesions other than premalignant lesions, Group 2 included 20 smokers with lesions other than premalignant lesions, and Group 3 included 20 smokers with premalignant conditions of the oral cavity.

In each patient, smears were taken from the lesion with the help of sterile, clean, blunt scalpel blades. Smears were immediately seen under a fluorescent microscope, and MNCs were counted per 1,000 epithelial cells. In all patients, a biopsy was also done.

Chronic alcoholics, postradiotherapy cases, and cases exposed to any cytotoxic drug were excluded from the study.

OBSERVATIONS: Overall, 85% was male and 15% was female. Mean MN scores in all groups (acridine orange stain) were 0.1052, 0.2725, and 0.855, respectively. Mean scores for Groups 1, 2, and 3 in Papanicolaou staining were 0.1365, 0.395, and 1.12, respectively. Pearson's correlation coefficient was done between smoking and MN score. Smoking was found to be positively correlated to MN score. MN score was not statistically significant between Group 1 and Group 2 (> .5). However, MN score was highly statistically significant (P < .0001) between Group 2 and Group 3 and also between Group 1 and Group 3.

CONCLUSIONS: We found a gradual increase in MN score from nonsmokers with no premalignant lesions (Group 1) to smokers with no premalignant lesions (Group 2) and smokers with premalignant lesions (Group 3). MN scoring can be used as a biomarker for screening premalignant conditions.

(P019) Fractionated Robotic Stereotactic Radiosurgery for the Treatment of Benign Meningioma

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PURPOSE: Fractionated stereotactic radiosurgery (SRS) may offer several benefits in the treatment of symptomatic or growing meningioma but has not been examined extensively in the literature. Our primary aim was to describe the rates of tumor control and side effects in patients treated with CyberKnife SRS for meningioma.

METHODS: We retrospectively reviewed 75 symptomatic or growing lesions treated in 72 consecutive patients who were unsuitable for or declined surgery (61 tumors, 83%) or had residual disease after resection (14 tumors, 17%) from 2008 to 2013. The study group included 31 skull base tumors, 27 falci/neoparagangliomas, 7 tentorial tumors, 6 convexity tumors, 2 intraventricular tumors, and 2 spinal tumors. Patients were treated with a prescription dose of 25 Gy in five fractions. We calculated actuarial local control (LC) and progression free-survival (PFS) using the Kaplan-Meier method and recorded the rates of early adverse effects of treatment that may be related to peritumoral edema or proximity to cranial nerves or sinuses.

RESULTS: The median follow-up was 21 months (range: 1–61 mo). Sixteen tumors (21%) were larger than 3 cm. The median conformation index was 1.5 (range: 1.2–2.2). At last follow-up, a decrease in tumor volume was seen in 5 tumors (7%), and 68 tumors (91%) were stable. Two-year LC was 98.6%. Overall, two tumors (3%) progressed, both in patients with grade 2 meningioma treated with SRS for progression after surgical resection. Two-year PFS was 97.2%. Early adverse effects were mostly temporary. Patients with parasagittal tumors experienced fatigue (14.8%), hair loss (11.1%), dizziness (11.1%), headache (3.7%), tinnitus (3.7%), facial pain (3.7%), near-syncope (3.7%), and temporary blurred vision (3.7%). Patients with nonparasagittal tumors experienced fatigue (26.7%), nausea (11.1%), headache (4.4%), and dizziness (2.2%). In three patients with optic nerve involvement, vision was unchanged at last follow-up.

CONCLUSIONS: CyberKnife radiosurgery resulted in a 97.2% 2-year PFS, but longer follow-up is needed to fully evaluate clinical efficacy. Patients who were poor candidates for surgery or single-fraction SRS were effectively treated with minimal adverse effects.

(P020) The Effect of Dose on Pain Relief and Numbness With Robotic Stereotactic Radiosurgery for Trigeminal Neuralgia

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PURPOSE: CyberKnife stereotactic radiosurgery (SRS) is a minimally invasive alternative for patients with trigeminal neuralgia (TN). The purpose of this project is to determine the effects of dose and other clinical parameters on the rate of pain relief, duration of response, and rate of adverse effects in the treatment of TN using CyberKnife SRS.

METHODS: Between October 2008 and April 2012, 56 patients were treated with 66 courses (including 10 re-treatments) of CyberKnife SRS for classical (idiopathic) TN at our institution. Of the 66 SRS courses, 22 were prescribed to 70 Gy (Dmax 86 Gy), 37 were pre-
scribed to 60 Gy ($D_{max}$ 74 Gy), and 6 were prescribed to 50 Gy ($D_{max}$ 62 Gy). Clinical characteristics were retrospectively retrieved from the medical record. Pain level was documented at consultation and at follow-up, and adverse effects were recorded at follow-up. Logistic regression was used to test for correlations of clinical parameters, including dose, gender, age, pretreatment pain level, treatment order (first or second), and TN type, with the rates of pain relief and adverse effects. We also described the characteristics of patients who achieved an "optimal outcome" (continued pain relief with no numbness at 12 months).

RESULTS: The median follow-up was 15 months. Of 66 treatments administered, 57 (86%) resulted in pain relief. Twenty-six patients (46%) had pain relief with no recurrence at last follow-up. A higher rate of pain relief was seen in patients with typical, type 1 TN features ($P = .05$). The other parameters tested, including dose ($P = .15$), did not correlate with response rates. The actuarial median duration of pain relief was 21 months. Thirty patients (54%) experienced mild (16%), moderate (18%), or severe (20%) facial numbness at last follow-up. Other side effects were not seen. There was a trend toward lower rates of numbness in patients treated with 60 Gy compared with 70 Gy ($P = .07$). In patients treated only once, the relative numbers of patients with pain relief and numbness are shown below by prescription dose. Ten patients with sufficient follow-up had an optimal outcome. Of these, all had type 1 TN, seven were treated to 60 Gy, and eight had severe pretreatment pain (Barrow Neurological Institute [BN1] V).

CONCLUSIONS: CyberKnife SRS is safe and effective for the treatment of trigeminal neuralgia. A prescription dose of 60 Gy provides similar pain relief to higher doses, with a trend toward decreased numbness. The majority of patients who achieved an optimal outcome received 60 Gy. This study is among the largest to demonstrate effectiveness with this low-dose SRS.

(P021) Long-Term Survival in Patients With Brain Metastases: Fact or Fallacy?
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BACKGROUND: The diagnosis of a brain metastasis (BM) is usually a devastating one for patients and their families. Perceptions of major morbidity and impending mortality are widespread. Indeed, a typical patient with a BM dies within an average of 8 months following the initial treatment of his or her brain tumor(s). Cause-specific mortality is rarely assessed or recorded, and the BM is often assumed to be the culprit.

METHODS: We reviewed data on patients with newly diagnosed BM treated with a resection or stereotactic radiosurgery at UT MD Anderson Cancer Center between June 1993 and May 2008. Out of a total of 2,170 patients, 1,931 (89%) died and 76 (3%) were lost to follow-up less than 5 years from treatment, and 163 (8%) were known to have survived 5 or more years from the date of initial BM treatment (long-term survival [LTS]). The 2,094 patients with known outcome were included in the study. Variables, such as patient age, functional status (assessed by the Karnofsky Performance Scale [KPS] score), primary cancer type, time lag between diagnosis of the primary and the BM, status of primary and extracranial systemic metastasis at the diagnosis of the BM, as well as factors related to BM, such as number of tumors, largest tumor volume, and worst tumor functional grade, were assessed. Of them, factors impacting long-term survival were sought out. Standard statistical methods were utilized. The study was conducted under an institutional review board (IRB)-approved protocol.

RESULTS: The median age among the patients with LTS was 53 years (range: 17–77 yr), and 47% were male; 72% were symptomatic at the time of initial BM treatment, and 98% had a pretreatment KPS > 70. The primary cancer was lung in 30%, melanoma in 20%, breast in 18%, and renal in 11%. The interval from primary to diagnosis of BM was 14.3 months (range: 0.0–299.7 mo). Further, 77% had a stable primary or no evidence of disease at the time of treatment, with a recursive partitioning analysis (RPA) score of I in 59%. With regard to the BM, 31% were in eloquent brain areas and 41% were near eloquent areas. Single tumors were seen in 80% of patients, and two or three tumors were seen in 18%. The median largest tumor volume was 4.5 cm$^3$ (range: 0.05–100.4 cm$^3$). Seventy-one percent was treated with a resection. In the multivariate analysis, a KPS score > 70 was by far the factor most strongly associated with LTS, followed by a stable primary or no evidence of disease. Additional associations with treatment type and adjuvant radiation within subgroups of patients with specific characteristics at initiation of BM treatment will be presented.

CONCLUSIONS: Among patients with BM, there were long-term survivors in all typically unfavorable categories. However, good functional status was most strongly associated with LTS, followed by a nonprogressing primary. The use of modern and effective neurosurgical and radiosurgical techniques may have enabled BM patients with good functional status and a controlled primary to survive for a prolonged period of time.

(P022) Modern Management of Lymphoepithelioma of the Head and Neck
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BACKGROUND: Lymphoepithelioma is a rare tumor of the head and neck region, the optimal management of which remains to be defined. Treatment may include surgery, radiation, and chemotherapy. We evaluated and reported on management outcomes from a large cohort of patients with modern management for this diagnosis.

MATERIALS AND METHODS: An institutional review board (IRB)-approved retrospective chart review for primary lymphoepithelioma of the head and neck region returned 28 histologically proven cases diagnosed and treated between January 2001 and July 2012. Patient age ranged from 19–81 years, including 18 males and 10 females, with the majority being Caucasian. Most patients presented with an enlarging mass. Tumor originated in the nasopharynx in 12 patients (43%); tonsil in 5 (18%); base of tongue in 3; and 1 each in the pharynx, pyriform sinus, submandibular gland, and vallecula. Four patients presented with unknown primaries. Surgery beyond biopsy was undertaken in 54% (15 patients), including excision of the primary alone in 7 patients, with neck dissection in 6 additional patients, and nodal excision alone in 2 patients. All patients underwent photon external beam radiation therapy (EBRT), most commonly intensity-modulated radiation therapy (IBRT) (75%), and with image guidance in 32%. The mean XRT dose was 67 Gy, with 10 patients receiving more than 70 Gy. Chemotherapy was delivered to 24 patients (86%), and was most commonly platinum-based.

RESULTS: All patients have been followed a mean of 45 months. Acute treatment-related complications were generally grade 1/2 (57%), most commonly radiation dermatitis (61%), mucositis (50%), and dysphagia (36%). Late complications were all grade 1/2, most commonly xerostomia (32%). At last follow-up, 21 patients (75%) had no evidence of disease. One patient experienced locoregional failure alone, three had distant metastases alone, and three had both locoregional and distant failure. Statistical analysis reports chemotherapy as the only variable improving survival (P = .02).

CONCLUSIONS: Based on this series, modern management for lymphoepithelioma appears to favor definitive chemoradiation, as this allows for high local control and survival rates. Radiation dose escalation did not improve local control or survival. The addition of chemotherapy offered a statistically improved outcome and, if possible, appears to be part of any curative treatment regimen. Distant failure for this diagnosis is relatively high and needs to be addressed to improve outcomes.

(P023) The Importance of Surgery and the Role of Radiation Therapy and Chemotherapy for Treatment of Oral Tongue Cancer

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BACKGROUND: Oral tongue cancers have been classically managed with upfront surgical resection, whereas radiation therapy (RT) and chemotherapy (CT) have been generally reserved in the adjuvant setting for patients who possess high-risk features and those with unresectable disease. Although surgical resection is a vital component for management of oral tongue cancer, CT and RT have been shown to be beneficial in both early-stage patients with high-risk features and those with locally advanced disease as well. We wanted to determine the role of RT, surgery, and CT for patients with oral tongue cancer.

MATERIALS AND METHODS: A retrospective chart review of 94 patients was conducted for patients diagnosed with and treated for oral tongue cancer at SUNY Upstate University Hospital between 2001 and 2011. Institutional review board (IRB) approval was obtained prior to initiation of the study. The primary endpoint was overall survival (OS). Secondary endpoints included local relapse (LR) rates at both the primary site and the neck. Early-stage patients were classified as stage I/II, and late-stage patients were classified as stage III/IV. OS and LR were calculated using Kaplan-Meier curves and log-rank testing. Univariate and multivariate proportional hazards regression analyses were conducted to determine prognostic features affecting OS and LR rates. Treatment results were analyzed with respect to surgery, RT, and CT as part of the overall management.

RESULTS: The median follow-up for the entire cohort was 61.1 months. The breakdown for stages was I (n = 31), II (n = 14), III (n = 8), and IV (n = 31); 53% of the patients were early-stage and 47% was late-stage. The 2-year and 5-year OS for the entire cohort was 67.5% and 52.2%, respectively. The median survival for the entire cohort was 61.1 months. Further, 77.8% of the early-stage patients were treated with surgery alone, and 13.3% was treated with surgery/RT, and their survival was 80% and 50%, respectively. For late-stage patients, the OS for those treated with surgery/RT/CT (n = 15), surgery alone (n = 7), and RT/CT (n = 6) was 66.7%, 42.9%, and 16.7%, respectively. Multivariate analysis for OS showed a hazard ratio (HR) of 2.663 (95% CI 0.91–7.62) for patients who did not have surgery. Alcohol (HR = 2.354; 95% CI 1.054–5.255), higher grade (HR = 2.779; 95% CI 1.059–7.294), and higher T-stage (HR = 3.77; 95% CI 1.622–8.797) were statistically significant for poor prognostic features for OS. The median time to local recurrence to either the primary site or neck for the entire cohort was 7.4 months. Multivariate analysis for local recurrence showed that not having surgery (HR = 8.113; 95% CI 1.599–41.172) and positive margins after resection (HR = 8.365; 95% CI 1.682–41.596) conferred a worse prognosis.

CONCLUSION: Oral tongue cancer is an infrequently encountered malignancy that requires a multidisciplinary approach. Surgery remains the cornerstone for management of these patients. Early-stage patients do well with surgery alone, whereas late-stage patients tend to do better with CT and RT in addition to surgery.

(P024) Proton Radiotherapy for Midline CNS Lesions: A Class Solution

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OBJECTIVE: Midline and central lesions of the brain requiring conventional radiation therapy (RT) present complex difficulties in dose avoidance to organs at risk (OAR). In either the definitive or adjuvant setting, proper RT coverage of these lesions involves unnecessary treatment of large volumes of normal brain. We propose a class solution for these lesions using proton therapy (PrT).

MATERIALS AND METHODS: The records of the IU Health Proton Therapy Center were reviewed for patients presenting between January 1, 2009 and March 1, 2013 with midline central nervous system (CNS) lesions. Nine patients were identified. After institutional review board (IRB) approval was granted, their dosimetry was reviewed for target volume doses and OAR dose avoidance.

RESULTS: Most of these cases were craniopharyngiomas (five cases); the others were meningiomas (four cases). In all nine cases, fields that were formed by the vertex and anterior and/or posterior superior oblique PrT beams along the midsagittal plane were used to provide coverage with minimal dose to the brainstem deep or to the cerebral hemispheres. The median prescribed dose using only midsagittal fields to target planning target volume (PTV) was 52.2 Gy relative biological effectiveness (RBE) (range: 48.6–61.2 Gy RBE), with a mean dose of 53.2 Gy RBE. The average of the mean doses to the brainstems using these fields in the nine plans was 18.0 Gy RBE (range: 0.0–40.1 Gy RBE). Similarly, the average of the mean doses to the hippocampi was 17.1 Gy RBE (range: 0.0–45.9 Gy RBE).

CONCLUSIONS: We consider these patients to be optimally treated with PrT and preferentially refer patients whenever possible. The use of modified midsagittal PrT schemas allows for treatment of midline CNS lesions with sparing of most of the uninvolved brain.

(P025) Outcomes of Nonmelanoma Skin Cancer in Immunosuppressed Patients Treated With Surgery and Radiation Therapy

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PURPOSE: To evaluate and compare the outcomes of nonmelanoma skin cancer (NMSC) in immunosuppressed and immunocompetent patients treated with surgery and radiation therapy (RT).

METHODS: Between January 2004 and October 2013, 75 NMSCs in 74 patients were treated with surgery and RT with curative intent. Patients with distant metastasis at diagnosis were excluded. Patients with HIV, chronic lymphocytic leukemia (CLL), or solid-organ transplantation were classified as immunosuppressed. Rates of locoregional control and distant metastasis-free survival were estimated using the Kaplan-Meier method. Cox proportional hazards model was used for univariate and multivariate analysis. A P value < .05 was considered statistically significant.

RESULTS: Mean follow-up was 18.6 months (range: 2–71 mo). The mean age was 67 years (range: 41–91 yr). Of the 75 lesions, 61 (81%) were squamous cell carcinomas (SCCs) and 14 (19%) were basal cell carcinomas (BCCs); 72 lesions (96%) were in the head and neck. Staging was as follows: stage I 8%, stage II 42.7%, stage III 13.3%, and stage IV 36%. Lymph nodes were pathologically involved in 17 cases (22.7%). Disease was recurrent in 44 cases (58.6%). Perineural invasion was present in 38 cases (50.6%). In-transit metastases were present in six patients with SCC, four of whom were immunosuppressed.

RT was delivered to a median dose of 64 Gy (range: 45–74.8 Gy) in a median of 30 fractions (range: 5–45 Gy). Six patients also received adjuvant chemotherapy. Twenty-three patients were immunosuppressed, including 7 patients with HIV, 5 with CLL, and 11 with solid-organ transplantation. There were no significant differences in the patient- and treatment-related characteristics between the immunosuppressed and immunocompetent groups.

The Kaplan-Meier–estimated local control, regional control, and distant metastasis-free survival at 2 years were 77.4%, 87.1%, and 93.6%, respectively. Univariate analysis to identify variables associated with recurrence included the following variables: histology, primary tumor stage, nodal stage, stage grouping, margin status, recurrent tumor, perineural invasion, named nerve involvement, in-transit metastasis, extranodal extension, dose, and immunosuppression. In-transit metastasis was the only significant predictor of local recurrence (hazard ratio [HR] = 6.94; 95% confidence interval [CI], 1.82–26.3; P = .004). Both immunosuppression and in-transit metastasis were significant predictors of regional recurrence on univariate analysis. However, only in-transit metastasis remained significant on multivariate analysis (HR = 12.7; 95% CI, 3.04–52.6; P < .001). In-transit metastasis was the only predictor of distant metastases (HR = 45.5; 95% CI, 4.69–500; P = .001). Of the six patients with in-transit metastases, four developed locoregional recurrence and three developed metastatic disease, all within 4 months of the completion of RT. Three of the four patients with in-transit metastases who developed recurrence were immunosuppressed. Testing for sets of multiple negative factors other than in-transit metastases revealed no combinations predictive of recurrence.

CONCLUSIONS: In patients with high-risk NMSC treated with surgery followed by RT, in-transit metastasis is significantly associated with worse locoregional control and with a higher risk of distant metastasis. In-transit metastases were only observed in SCC and were more common in immunosuppressed patients. Intensification of therapy and reduction of immunosuppression should be part of the treatment strategy for patients with in-transit metastases.

(P026) Limiting Radiotherapy to the Contralateral Retropharyngeal and High Level II Lymph Nodes in Head and Neck Squamous Cell Carcinoma Is Safe and Improves Quality of Life

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PURPOSE: To report the results of using intensity-modulated radiation therapy (IMRT) to limit treatment of the contralateral retropharyngeal lymph nodes (RPLNs) in the clinically uninvolved neck for patients diagnosed with head and neck squamous cell carcinoma (HNSCC) in terms of safety and quality of life (QOL).

MATERIALS AND METHODS: A retrospective institutional database was used to identify patients treated using IMRT with primary oral cavity, oropharynx, hypopharynx, larynx, and unknown primary HNSCC between 1997 and 2010. There were three temporal treat-
Recurrence of low-risk oral tongue cancer can be successfully salvaged in the majority of cases. Neck failures have a worse prognosis than local failures.

(P028) Efficacy and Tolerability of Chemoradiation for Lymph Node–Positive Cutaneous Nonmelanoma Skin Cancer

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**INTRODUCTION:** To investigate the efficacy and tolerability of chemoradiation (CRT) for locoregionally advanced cutaneous nonmelanoma skin cancer (NMSC).

**METHODS:** We retrospectively reviewed the charts of all patients treated for high-risk NMSC from 2000–2012. Patients were included if they had pathologic NMSC and evidence of regional lymph node (LN) spread and received an LN dissection and/or parotidectomy. Exclusions were: less than 6 months of follow-up or having received palliative treatment only. The primary endpoints for analysis included locoregional control (LRC), progression-free survival (PFS), and overall survival (OS). Kaplan-Meier curves and Cox regression analysis were used for statistical analysis. The study was approved by the institutional review board (IRB).

**RESULTS:** A total of 53 patients met our inclusion criteria, 15 (28%) of whom received CRT—cefoxitin (6), cisplatin (7), carboplatin (1), and paclitaxel (1). Patients treated with chemotherapy were significantly younger (P = .001), had larger LNs (P = .024), and a trend toward a greater number of LNs involved (P = .075) and LNs dissected (P = .069). With a median follow-up for 2.2 years (range: 0.5–8.5 yr), 20 (38%) patients had evidence of recurrence, with 16 out of 20 patients failing locoregionally as a component of their disease relapse. At 5 years, LRC was 70%, PFS was 61%, and OS was 47%. The PFS of patients who received RT alone was significantly better than those who received CRT (72% vs 32%; P = .009), although the OS was not significant (P = .22). CRT patients had evidence of aggressive disease: 10 of the 15 in the CRT group (67%) had recurrence of their disease at one or more sites, despite both systemic and locoregional treatment. Eight of the 10 (80%) patients in the CRT group with disease recurrences had distant metastasis as part of their recurrence. CRT was generally well tolerated, although not free of side effects, including acniform rash, neutropenia, tinnitus, decrease in creatinine clearance, severe dehydration, and/or failure to thrive. There was one grade 4 asymptomatic thrombocytopenia but otherwise no other grade 3 or higher toxicities.

**CONCLUSIONS:** In this series, patients who were treated with multimodality therapy for high-risk NMSC did not do well, and those
who were selected for trimodality therapy did exceptionally poorly. The natural history of high-risk NMSC is poorly understood, and appropriate patient selection for the intensification of adjuvant therapy needs clarification.

(P030) Peritumoral Lymphatic Vessel Density as a Predictor of Progression-Free Survival in Locally Advanced Laryngeal/Hypopharyngeal Cancer
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PURPOSE AND OBJECTIVES: The clinical significance of tumor lymphangiogenesis continues to be an area of active research. We hypothesize that high peritumoral and intratumoral lymphatic vessel density (LVD) predict for inferior oncologic outcomes, including local failure (LF), progression-free survival (PFS), and overall survival (OS).

MATERIALS AND METHODS: Selected blocks from formalin-fixed, paraffin-embedded laryngectomy specimens were sectioned and stained with hematoxylin-eosin and immunostained with D2-40, a specific lymphatic endothelial cell marker. Peritumoral and intratumoral LVD was determined in tumor vessel "hot spots" using light microscopy (20× magnification) by four observers. The mean vessel counts in three "hot spots" per section were recorded. All surgical specimens were from patients with T3/T4 laryngeal or T4 hypopharyngeal cancer treated at our institution from 1999 through 2010. Charts were retrospectively reviewed for demographic, patient characteristic, and oncologic outcome data. All patients had undergone laryngectomy followed by concurrent chemoradiotherapy. Radiation therapy (RT) was delivered using a 3-field or intensity-modulated RT (IMRT) technique to a prescribed dose of 60–66 Gy. Chemotherapy was generally platinum-based, with patients receiving up to three cycles. LF was fitted with a competing risks model, with death as the competing risk. PFS and OS were calculated with Cox regression. Recursive partitioning analysis (RPA) was used to identify thresholds for peritumoral LVD and intratumoral LVD for association with PFS.

RESULTS: A total of 43 patients who underwent laryngectomy followed by 1) concurrent chemoradiotherapy (40 patients) or 2) radiotherapy alone (3 patients) and whose tissues were evaluable for staining at our institution were included in the present analysis. Mean age of this cohort was 56.8 years, with 11 females (25.6%) and 32 males (74.4%). Nineteen patients had T3 disease (44.2%), while 24 (55.8%) had T4 disease. Fourteen had N0, 5 had N1, 21 had N2, and 3 had N3 disease. Twelve-month OS, PFS, and LF for the cohort were 8 months (95% confidence interval [CI], 6.6–9.8), 7.1 months (95% CI, 5.5–9.0), and 1.1 months (95% CI, 0.36–2.3), respectively. Patients identified as having peritumoral LVD > 0 demonstrated a better median PFS (3.04 years; 95% CI, 1.05–5.35) than those with 0 peritumoral LVD (0.80 years; 95% CI, 0.48–NR; P = .03). When we evaluated those patients with intratumoral LVD with RPA, no statistical significance was reached for PFS (P = .24).

CONCLUSIONS: Patients with locally advanced laryngeal/hypopharyngeal cancer treated with laryngectomy and concurrent chemoradiotherapy who have any staining for peritumoral lymphatics have a statistically significantly better PFS than patients in whom the specimen shows no staining for peritumoral lymphatics. Our findings do not support our hypothesis and may reflect the advanced nature of disease in the patient population examined. Further study in this area examining earlier-stage patients is under way to further characterize the potential utility of this staining technique.

(P031) Disease Control and Toxicity Outcomes for T4 Carcinoma of the Nasopharynx Treated With Intensity-Modulated Radiotherapy
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BACKGROUND: Treatment of T4 nasopharyngeal carcinoma (NPC) is challenging due to the close proximity of the tumor to the central nervous system. We evaluated our disease control and toxicity outcomes for patients with T4 NPC treated with intensity-modulated radiation therapy (IMRT) and chemotherapy.

METHODS: The medical records of 66 patients with T4 NPC treated from 2002–2012 with IMRT were reviewed. Endpoints included tumor control and toxicity, as assessed by Common Terminology Criteria for Adverse Events version 4.0 (CTCAE v4.0). Preliminary prospective patient-reported quality-of-life outcomes were obtained from survivors who completed the MD Anderson Symptoms Inventory and Brief Fatigue Inventory (BFI). For both scoring systems, a score of 0 represents absence of the symptom, while a score of 10 is most severe.

RESULTS: Median follow-up was 38 months. On institutional pathology review, 13 patients were identified as having World Health Organization (WHO) I NPC, 6 patients were WHO II, and 46 patients were WHO III. WHO classification was unavailable for one patient. Fifteen patients were N0, 10 had N1 disease, 27 patients had N2 disease, and 14 had N3 disease. Epstein-Barr virus (EBV) status was available for 28 patients, 17 of whom were positive. Sixty-five patients received chemotherapy—2% induction, 26% concurrent, and 71% both. Actuarial 5-year rates of locoregional control (LRC), distant metastasis-free survival (DMFS), progression-free survival (PFS), and overall survival (OS) were 80%, 82%, 57%, and 69%, respectively. There was a trend toward improved OS (P = .056) and LRC (P = .050) in patients with WHO III disease compared to patients with WHO I/II disease. Evidence of EBV infection was associated with improved OS (P = .023) and PFS (P = .003). Nodal involvement was associated with worse PFS (P = .015), while advanced nodal disease (N2/N3) was associated with worse DMFS (P = .044) compared to N0/N1 disease. PTV volume > 400 cm³ was associated with worse OS (P = .024), PFS (P = .001), and DMFS (P = .024). Ototoxicity was the most common toxicity (n = 42), with 19
(P032) Clinical Outcomes for Hybrid Forward and Inverse Planned IMRT for Supine Craniospinal Irradiation

Stephanie K. Childs, MD; Jon J. Kruse, PhD, Kevin L. Kisrow, CMD, RTT; Nadia N. Laack, MD; Mayo Clinic

BACKGROUND: Conventional matching techniques of craniospinal irradiation (CSI) require patients to be in the prone position in order to use skin surface markers to align matched or gapped adjacent fields. Small setup misalignments of even 1 mm can lead to large deviations in delivered dose of up to 40%. In addition, the prone position is cumbersome for patient positioning, especially for pediatric patients requiring anesthesia for treatment. Because of safety concerns regarding field overlap with a blind match, there has been reluctance to treat patients supine. Here, we present the clinical outcomes of patients treated with our supine CSI technique using a gradient match of brain and spinal fields.

METHODS: We retrospectively reviewed the charts of all patients who received CSI at Mayo Clinic from 2009–2013. All patients were simulated in the supine position, and all radiotherapy plans were created using a hybrid of forward and inverse planned intensity-modulated radiation therapy (IMRT). The inferior borders of the brain fields and superior border of the lower spine field are designed with long, gradual dose gradients created by sequential closing of the 5-mm multileaf collimator (MLC) leaves using forward planned, multiple static segment IMRT delivery. Next, a sliding window upper spine IMRT field is created by the inverse planning system to match the gradients of the brain and lower spine fields. Daily patient localization is confirmed by kV On-Board imaging of the cranial fields and a single posterior spine image. Subsequent shifts are calculated based on couch coordinates and planned isocenter shifts, not skin markings. To verify the robustness and safety of the CSI plans, dose was calculated, assuming a systematic setup error of 3 mm. Resulting dose deviations were +/- 15%.

RESULTS: We identified 26 patients with a median age of 16 years (range: 3.4–65.5 y). Thirteen patients had medulloblastoma, nine had primitive neuroectodermal tumors (PNETs), two had pure germinomas, one had a mixed germ cell tumor, and one had an anaplastic gliomeurotumoral tumor. The median dose delivered to the neuraxis was 36 Gy (range: 18–39.6 Gy), and the median boost dose to the tumor bed, posterior fossa, or ventricles was 55.8 Gy (range: 30.6–60 Gy). At a median follow-up of 2.8 years (range: 0.2–4.7 y), no patient had an isolated spinal recurrence and no patient had a clinically or radiographically apparent spinal myelopathy. One patient with medulloblastoma who presented with diffuse leptomeningeal disease and one patient with a supratentorial PNET recurred with diffuse leptomeningeal disease throughout the neuraxis. Seven of the nine patients with PNETs had an intracranial recurrence, five of which were in the primary tumor bed.

CONCLUSIONS: We saw no clinical evidence of isolated spinal recurrences or myelopathies at the field gradients using our hybrid forward and inverse planned IMRT supine CSI technique. Smooth field transitions obviate the need for match line shifts, allowing patients to be treated more comfortably in the supine position. In addition, the hybrid IMRT plans are less susceptible to geometric inaccuracies and the resulting dose deviations.

(P034) Ethnic and Gender Disparities Among Limb Salvage Rates in Pediatric Sarcoma Patients

Jeremy S. Somerson, MD, Isaac Kim, Rajiv Rajani, MD; University of Texas Health Science Center at San Antonio

INTRODUCTION: Racial and ethnic disparities in limb salvage surgery for limb salvage or amputation. Statistical analysis of patient demographics (age, sex, ethnicity, and body mass index [BMI]) was performed to assess for factors associated with limb salvage surgery.

RESULTS: A total of 51 records were identified as pediatric patients who underwent surgery for extremity sarcoma in the defined study period. Five records were excluded due to inadequate availability of body site or surgery type documentation. A total of 46 patients. Hispanic patients were more likely to undergo amputation compared with non-Hispanics (5 of 10; P = .03). Female patients were more likely to have had limb salvage surgery (8 of 17) than males (7 of 29; P = .04). Logistic regression analysis showed no difference between likelihood of limb salvage and amputation by BMI or age.

CONCLUSIONS: Hispanic ethnicity and male gender were predictors of amputation in a cohort of pediatric sarcoma patients undergoing surgical treatment. Further study should be devoted to identifying underlying factors for ethnic and gender discrepancies between treatment groups.
(P035) Outcomes in Patients With Hypopharyngeal Cancer Treated With Intensity-Modulated Radiation Therapy

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BACKGROUND: Intensity-modulated radiation therapy (IMRT) is increasingly used in the treatment of hypopharyngeal carcinoma for functional organ-sparing. Due to the relative rarity of this diagnosis, particularly at early stages, few reports of outcomes exist. We retrospectively reviewed our single-institution experience treating stage I–Iva hypopharyngeal cancer (HPC) patients with definitive IMRT +/- chemotherapy.

MATERIALS AND METHODS: Fifty-seven patients who were treated with definitive IMRT from 2003–2013 met our inclusion criteria. The Kaplan-Meier method was used to estimate locoregional control (LRC), distant metastasis-free survival (DMFS), progression-free survival (PFS), and overall survival (OS) of this cohort of patients.

RESULTS: Median age at treatment was 65 years. American Joint Committee on Cancer (AJCC) clinical stages were: I, 1 (T1 N0); II, 12 (10 T2 N0 and 2 T1 N1); III, 15 (6 T2 N1, 4 T3 N0, and 5 T3 N1); and IV A, 29 (5 T1 N2, 13 T2 N2, and 11 T3 N2). Patients were treated to a dose of 66–72 Gy (1.8–2.2 Gy per fraction). Forty-four patients (77%) received chemotherapy: 43 concurrent and 38 induction. The median follow-up was 28.8 months (range: 3–105 mo). The 2- and 5-year OS was 74% and 60%, respectively; LRC, DMFS, and PFS at 2 years were 77%, 88%, and 62%, respectively. There was no significant difference in OS (P = .7) or PFS (P = .4) when comparing patients by AJCC stage or nodal status. However, smaller primary tumors did trend toward improved 2-year OS (86% for T1 vs 72% for T2–T3; P = .2), which was independent of nodal status. There was a trend toward improved LRC in patients who received chemotherapy (P = .07). Three patients had postradiotherapy neck dissection for persistent nodal disease. Feeding tubes (FTs) were placed in 38 patients (67%): 9 prior to treatment (16%), 26 during treatment (46%), and 3 (5%) after treatment. Of those with FTs placed during or after treatment who became FT-independent (97%), median FT duration was 2.8 months (range: 1.2–13.9 mo). Twelve grade 3 toxicities were observed: nine dysphagia, two fatigue, and one pain. Actuarial 2-year and 5-year grade 3 toxicities were 18.4% and 23.2%, respectively.

CONCLUSIONS: These preliminary data suggest acceptable disease outcome and toxicity rates for hypopharyngeal carcinoma patients treated with definitive IMRT +/- chemotherapy. Smaller primary size and use of chemotherapy may predict for better prognosis. Further analysis of this cohort and of patients with T4 or N3 disease is ongoing to validate these findings.

(P036) The Significance of Different Dose Fractionations in the Management of Optic Nerve Sheath Meningioma

Veronica A. Finnegan, MD, Seung Hahn, MD, Anna Shapiro, MD, Luis Mejico, MD; SUNY Upstate Medical University

BACKGROUND: Optic nerve sheath meningiomas (ONMs) typically present with unilateral vision loss, visual disturbance, and/or eye pain or pressure. The diagnosis is usually made by clinical and imaging findings without biopsy. ONMs are generally not amenable to surgery due to morbidity, visual deterioration. For this reason, radiation is often used as primary treatment. Different dose fractionations have been used, without clear consensus on optimal treatment. The number of fractions can also be influenced by accessibility to treatment centers and is a significant factor for patients in rural areas treated with conventional-dose fractionation, which requires over 5 weeks of treatment.

MATERIALS AND METHODS: A retrospective review of patients treated with radiation therapy (RT) for ONMs was performed to analyze tumor control, symptom improvement, and treatment complications according to different dose fractionations. Patients had documented vision testing before and after treatment, which was performed by a neuro-ophthalmologist.

RESULTS: Data were collected on 8 patients, 2 of whom had bilateral disease, for a total of 10 cases treated for ONM between 2006 and 2012. Vision loss was the presenting symptom in eight cases, one patient had eye pain, and the other was asymptomatic and was found to have an abnormal eye exam with increased optic nerve pressure. The patient who was asymptomatic had biopsy consistent with meningioma. Median follow-up was 43 months. Six optic nerve tumors were treated by conventional fractionation (≤ 2 Gy/fraction to a total dose of 45–54 Gy). They were considered standard fractionation. Four cases were treated with hypofractionated radiotherapy using 25 Gy in five fractions. All patients had local control based on the most recent imaging with MRI. In follow-up vision testing by neuro-ophthalmologic evaluation, 6 of 10 eyes achieved long-term vision improvement. Three patients had stable vision, and one had worse. With conventional fractionation, three of six had improvement, two were stable and one was worse. For the hypofractionated radiotherapy group, four of four had initial improvement, and three had long-term improvement. One patient developed radiation retinopathy 3 years after treatment, resulting in vision loss. In this case, the retina received full dose due to extension of the tumor. Six of nine patients, excluding the one who was asymptomatic, had resolution of subjective symptoms. Vision in the contralateral eye was unaffected in the majority of cases and actually improved in one patient, possibly due to radiotherapy to the area of involvement of the optic chiasm.

CONCLUSION: RT for ONM is an effective treatment to prevent visual deterioration and often improves visual loss that has already happened. Our study indicates that hypofractionated radiation is at least as effective as conventional radiation in preventing visual loss but seems to be more effective for improving visual changes caused by ONM. Hypofractionated radiation can be safely applied to patients with limited access to radiation centers. This should be further tested in a nationwide large-scale study in the future.

(P037) Impact of Serial DWI and ADC Measurements in Assessment of Brain Metastases Treated With Neurosurgical Resection and Intraoperative Cesium-131 Brachytherapy: Results of a Prospective Trial
brain metastasis treated with surgical removal and brachytherapy might be very useful in differentiating ischemic necrotic inflammatory processes from residual or local recurrent neoplasms. A new enhancement observed around the surgical cavity after brachytherapy should be interpreted in the context of the serial DWIs, including preoperative evaluation.

**CONCLUSION:** Serial DWI and measurement of ADC values on brain metastasis treated with surgical removal and brachytherapy are important for assessing surgical cavity enhancement and differentiating ischemic necrotic inflammatory processes from residual or local recurrent neoplasms. New enhancement observed around the surgical cavity after brachytherapy should be interpreted in the context of the serial DWIs, including preoperative evaluation.

Menachem Z. Yondorf, BS, A. Gabriella Wernicke, MD, MSc, Bhupesh Parashar, MD, Theodore H. Schwartz, MD, John A. Boockvar, MD, Phillip Stieg, MD, Susan Pannullo, MD, Dattatreyudu Nori, MD, K.S. Clifford Chao, MD, Ilhami Kovancikaya, MD, Weill Cornell Medical College

**BACKGROUND AND OBJECTIVES:** Intraoperative Cs-131 brachytherapy has been demonstrated to be safe, well tolerated, and convenient for patients, rendering high local control and minimal toxicity for patients with brain metastases (Wernicke et al.). Early identification of residual or recurrent metastasis is crucial to apply potentially more effective therapy. Interpretation of conventional magnetic resonance imaging (MRI) is a challenge in differentiating residual tumor and possible inflammatory reactions. In this study, we reviewed serial MRI images along with diffusion-weighted images (DWIs) for distinct local changes and assessed their clinical relevance and measured apparent diffusion coefficient (ADC) values.

**MATERIALS AND METHODS:** As part of the institutional review board (IRB)-approved prospective study, 26 patients with brain metastases treated with Cs-131 brachytherapy were evaluated with MRI exams, which included: T2-weighted, flair, diffusion-weighted, gradient recalled echo (GRE), or susceptibility weighted imaging (SWI); and T1-weighted sequences with and without contrast, before and after the surgery (the first within 48 hours and subsequent ones every 4–8 weeks). GRE/SWI images were used to rule out hemorrhage or other sources of susceptibility artifacts that cause high signal intensities on DWI. ADC values were measured and normalized by dividing contralateral normal-appearing brain parenchyma.

**RESULTS:** On follow-up MRI, delayed enhancement was seen in previously ADC low areas immediately postoperatively and was interpreted as ischemic/inflammatory changes due to surgical trauma. Depending on its size and localization, some of these changes ended up as encephalomalacia in the brain parenchyma. Contrast enhancement (CE) in lower ADC areas other than the previously low ADC should be considered suspicious for a local recurrent tumor (there have been no cases of local recurrent tumor). There were nine cases that showed increased enhancement 4–7 weeks after implantation, with higher ADC values other than surgical changes in the parenchyma around the cavity. The enhancement pattern was mostly rim-shaped, but some nodular pattern was noticed. These cases were interpreted as being suspected for recurrent tumor, and follow-up MRI was recommended. Mean ADC ratio was 1.71 (range: 1.46–1.78). In all cases, CE revealed decreased enhancement in the follow-up exams, with higher ADC values. We propose that this enhancement pattern with high ADC values is due to the inflammatory effects of Cs-131 seeds in the cavity. All of the higher ADC values seen due to surgical trauma decreased on the follow-up exams. New restricted diffusion was found in two patients: one with an abscess in the cavity and one with an additional subdural metastasis in the surgical incision. T2 hyperintensities, which reflected vasogenic edema around the metastatic tumor, decreased in 24/26 cases, mostly in 4 weeks after surgery. In two cases, T2 hyperintensities increased in the follow-up studies due to additional metastasis close to the region of original metastasis.

**CONCLUSION:** The serial DWI and measurement of ADC values on brain metastasis treated with surgical removal and brachytherapy might be very useful in differentiating ischemic necrotic inflammatory processes from residual or local recurrent neoplasms. A new enhancement observed around the surgical cavity after brachytherapy should be interpreted in the context of the serial DWIs, including preoperative evaluation.
except in four patients with tumors encasing the carotid artery, where only doses to the carotid artery were increased.

**CONCLUSIONS:** 4π plans yielded significantly and consistently improved tumor coverage and critical organ-sparing. Given the risk of late toxicities with SBRT, especially in patients with previously irradiated HNC, 4π radiotherapy using conventional C-arm linear accelerators (LINACs) may enhance locoregional control by allowing safe dose escalation while potentially reducing toxicity.

(P039) Reirradiation for Recurrent Gliomas: The University of Miami Experience

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**PURPOSE:** Treatment options for recurrent gliomas include surgery, chemotherapy, and radiotherapy. The majority of patients receive radiotherapy as part of their primary treatment, and multiple reirradiation fractionation schedules have been used in an attempt to decrease toxicity. We sought to report our institutional experience with reirradiation in the management of recurrent gliomas.

**METHODS:** A retrospective review was performed of adult patients with recurrent gliomas who received reirradiation between 2000 and 2013 with at least partial overlap of the initial radiation fields. Progression-free survival (PFS), overall survival (OS), and toxicity were evaluated. Hyperfractionated radiotherapy (HFR) was delivered at 1.2-Gy fractions bid. Standard radiotherapy (SRT) was delivered at 1.8–2.15 Gy once daily. Hypofractionated radiotherapy (HOR) was delivered at daily doses of 2.5 Gy or larger. Stereotactic radiosurgery (SRS) was delivered in a single fraction. Comparisons among fractionation schedules were performed.

**RESULTS:** A total of 27 patients met our inclusion criteria. The mean age at initial diagnosis was 45 years (range: 20–81 yr), 59.3% were male, and all patients underwent at least subtotal resection (STR) at the time of initial diagnosis. The mean total radiotherapy dose at initial treatment was 58.5 Gy, and median dose was 60 Gy (range: 32–60 Gy). Concurrent chemotherapy (temozolomide) with initial radiotherapy was given in 70.8% of patients. World Health Organization (WHO) grade 4 glioma was diagnosed in 59.3% of patients at the time of recurrence.

The percentages of patients who received HFR, SRT, SRS, and HOR were 51.9%, 22.2%, 14.8%, and 11.1%, respectively. The dose range (median) was 39.2–60 Gy (39.6 Gy), 30–60.2 Gy (56.65 Gy), 18–21 Gy (19 Gy), and 25–30 Gy (25 Gy) for HFR, SRT, SRS, and HOR, respectively. For the purpose of this analysis, HOR and SRS outcomes were reported as a group, referred to as hypofractionated (HPR). There was no difference on initial grade (P = .35), grade at recurrence (P = .863), age (P = .486), sex (P = 1.00), or type of surgery between groups (P = .877). Two patients in the HPR group received a third course of radiotherapy, with one patient receiving HFR to a total dose of 39.6 Gy and the other one receiving SRS with 21 Gy.

Three cases of radiation necrosis were reported: two of them in patients who received HFR (one after a third radiotherapy course with HFR) and one case in the HFR group. Chemotherapy was received by 74.1% of patients as part of their salvage treatment. The median PFS and OS after reirradiation were 2.03 and 6.8 months, 3.8 and 10 months; and 5.1 and 8.1 months for the HFR, SRT, and HPR patients, respectively. There was no difference in OS (P = .58) or PFS (P = .23) among groups.

**CONCLUSIONS:** Reirradiation is safe and feasible for the treatment of recurrent gliomas. Radiation necrosis was observed infrequently and occurred after HPR or HFR. No significant difference between fractionation groups was found in this cohort. Given the shorter treatment time, hypofractionation or SRS may be preferable for reirradiation of recurrent gliomas. SRT is a reasonable alternative in patients with large-volume disease or significant overlap of radiation fields.

(P040) Gastrointestinal Impact of Proton Radiation to the Spine in Pediatric Patients

**Christine E. Hill-Kayser, MD, Stefan Both, PhD, Zelig Tochner, MD, Robert A. Lustig, MD; Perelman School of Medicine, University of Pennsylvania**

**INTRODUCTION:** Radiation to the spine may be associated with gastrointestinal (GI) toxicity, including nausea, vomiting, anorexia, and esophagitis. Proton therapy is expected to reduce this due to decreased exposure of the GI system when posterior-anterior beams are utilized.

**METHODS:** A consecutive series of 31 pediatric patients received proton therapy to the spine using posterior beams at the Children's Hospital of Philadelphia/Robarts Proton Therapy Institute. Gastrointestinal dosimetry was evaluated at the time of radiation planning. Acute toxicities were evaluated weekly during proton therapy.

**RESULTS:** A total of 32 patients (15 male) were evaluated; average age was 12 years (range: 2–20 yr). Of them, 25 received radiation to the total spine, and 6 received radiation to the partial spine (4 thoracic, 2 lumbar, 1 cervical). For those requiring total spine radiation, matchline changes were performed after each 900 cGy relative biological effectiveness (RBE). Proton radiotherapy dose ranged from 2,340 cGy (RBE) to 7,200 cGy (RBE), depending on clinical factors, and 19 patients received concurrent chemotherapy. Proton dosimetry to the esophagus, stomach, and bowel was evaluated at the time of radiation planning. Dose to the stomach and bowel was essentially 0 for all patients. Esophageal dose was very heterogeneous, with maximum ranging from near 0 to 6,180 cGy (RBE), and mean dose was < 1,000 cGy for all patients. Anorexia was the most common acute GI toxicity, affecting 16 patients (50%), followed by nausea (15, 47%) and constipation (10, 31%) (Table). The majority of GI effects were grade (G) 1 or 2, although four patients experienced G3 anorexia, one experienced G3 esophagitis, and one experienced G3 nausea. Dosimetry for the patient with G3 esophagitis demonstrated a maximum radiation dose of 2,120 cGy; however, the patient required daily intubation for anesthesia and also received chemotherapy concurrently. No patient experienced G4 acute GI toxicity.

**CONCLUSIONS:** Pediatric patients who were treated with proton therapy to the spine using posterior fields developed relatively mild acute toxicity, with > grade 2 acute toxicity rare. Some patients did experience bothersome anorexia and nausea. These side effects will
**RESULTS:** At time of analysis, median follow-up was 4.6 years, and 61% of patients had developed clinical or subclinical hypothyroidism. Under univariate analysis, none of the demographic variables was statistically different in the euthyroid and hypothyroid groups, but thyroid volume and many of the dosimetric parameters were significantly different. Patients with initial thyroid volumes of less than 8 cc experienced very high rates of hypothyroidism in this study, with an estimated risk of hypothyroidism of 75% 3 years post-RT. In a subanalysis of the patients with thyroid volumes of 8 cc or greater, patients with resV45Gy of at least 3 cc, resV50Gy of at least 5 cc, resV50Gy of at least 6 cc, V50Gy below 45%, V50Gy below 55%, or mean thyroid dose below 49 Gy demonstrated significantly lower rates of hypothyroidism development than their counterparts on a log-rank test. At 3 years post-RT, the patients in the lower-dose groups had a 30% to 38% estimated risk of hypothyroidism compared with a 55% risk for the entire study group. Although there was some qualitative agreement between the hypothyroidism rates observed in this study with the rates predicted by various NTCP models, all comparisons showed a lack of fit using the Hosmer-Lemeshow test.

**CONCLUSION:** In a large retrospective review of 123 patients treated with definitive IMRT for OPC, a significant reduction in hypothyroidism rates at 3 years post-RT was found for patients with initial thyroid volumes over 8 cc and at least 3 cc of thyroid-spared radiation doses of 45 Gy or more. Similar patient stratification was obtained using related dosimetric parameters and thresholds, such as mean thyroid dose less than 49 Gy. To reduce the risk of hypothyroidism in these patients, it is recommended that IMRT optimization objectives be used to reduce the volume of thyroid receiving 45 Gy.

**Table P040** Acute Gastrointestinal Toxicity Associated With Spinal Proton Therapy

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<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
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<tbody>
<tr>
<td>Anorexia</td>
<td>14 (44%)</td>
<td>6 (19%)</td>
<td>8 (25%)</td>
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<tr>
<td>Bloating</td>
<td>32 (100%)</td>
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<tr>
<td>Constipation</td>
<td>22 (69%)</td>
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<tr>
<td>Dehydration</td>
<td>32 (100%)</td>
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<tr>
<td>Diarrhea</td>
<td>27 (81%)</td>
<td>4 (13%)</td>
<td>1 (3%)</td>
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<tr>
<td>Esophagitis</td>
<td>28 (88%)</td>
<td>2 (6%)</td>
<td>1(3%)</td>
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<tr>
<td>Nausea</td>
<td>16 (50%)</td>
<td>10 (31%)</td>
<td>4 (13%)</td>
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<tr>
<td>Vomiting</td>
<td>23 (72%)</td>
<td>8 (25%)</td>
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**Acute Gastrointestinal Toxicity**

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continue to require support from the clinical team, despite improved dosimetry to the GI tract with use of proton radiotherapy.

**(P041) Dosimetric Predictors of Hypothyroidism Development in Oropharynx Cancer Patients Treated With IMRT**

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**PURPOSE:** Radiation therapy delivered to the lower neck has long been associated with an increased risk of subsequent development of hypothyroidism. The purpose of this study was to define dosimetric predictors of increased hypothyroidism risk for oropharyngeal (OPC) patients treated with intensity-modulated radiation therapy (IMRT) to be used to guide treatment planning.

**MATERIALS AND METHODS:** In a retrospective study of patients treated at a single institution with conventionally fractionated IMRT, 123 patients with confirmed thyroid status were analyzed. Patients were categorized as hypothyroid if diagnosed with hypothyroidism by the attending physician or if laboratory test results showed elevated thyroid-stimulating hormone (TSH) levels. Univariate analysis was performed, comparing the hypothyroid with the euthyroid patient groups. Along with patient demographic parameters, thyroid volume, mean thyroid dose, the percent of thyroid volume receiving at least various levels of dose (VxxGy [%]), and the residual absolute thyroid volume receiving less than various levels of dose (resVxxGy [cc]) were analyzed. Kaplan-Meier curves for freedom from hypothyroidism and the log-rank test were used to compare subgroups of patients. The frequency of hypothyroidism observed in the study was compared with predicted outcomes for several literature-proposed Normal Tissue Complication Probability (NTCP) models using the Hosmer-Lemeshow test.

**RESULTS:** At time of analysis, median follow-up was 4.6 years, and 61% of patients had developed clinical or subclinical hypothyroidism. Under univariate analysis, none of the demographic variables was statistically different in the euthyroid and hypothyroid groups, but thyroid volume and many of the dosimetric parameters were significantly different. Patients with initial thyroid volumes of less than 8 cc experienced very high rates of hypothyroidism in this study, with an estimated risk of hypothyroidism of 75% 3 years post-RT. In a subanalysis of the patients with thyroid volumes of 8 cc or greater, patients with resV45Gy of at least 3 cc, resV50Gy of at least 5 cc, resV50Gy of at least 6 cc, V50Gy below 45%, V50Gy below 55%, or mean thyroid dose below 49 Gy demonstrated significantly lower rates of hypothyroidism development than their counterparts on a log-rank test. At 3 years post-RT, the patients in the lower-dose groups had a 30% to 38% estimated risk of hypothyroidism compared with a 55% risk for the entire study group. Although there was some qualitative agreement between the hypothyroidism rates observed in this study with the rates predicted by various NTCP models, all comparisons showed a lack of fit using the Hosmer-Lemeshow test.

**CONCLUSION:** In a large retrospective review of 123 patients treated with definitive IMRT for OPC, a significant reduction in hypothyroidism rates at 3 years post-RT was found for patients with initial thyroid volumes over 8 cc and at least 3 cc of thyroid-spared radiation doses of 45 Gy or more. Similar patient stratification was obtained using related dosimetric parameters and thresholds, such as mean thyroid dose less than 49 Gy. To reduce the risk of hypothyroidism in these patients, it is recommended that IMRT optimization objectives be used to reduce the volume of thyroid receiving 45 Gy.

**(P042) Patterns of Failure in Node-Positive Thyroid Cancer**

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**BACKGROUND:** We reviewed a cohort of patients with node-positive thyroid cancer treated at a single institution surgically with or without radioactive iodine to evaluate patterns of failure.

**MATERIALS AND METHODS:** After approval by the institutional review board (IRB), records of patients with node-positive thyroid cancer treated surgically with or without radioactive iodine between 1998 and 2012 were retrospectively reviewed. Patients with anaplastic histology, no positive nodes, or distant metastases at presentation or those who received external beam radiation in initial management were excluded. A total of 256 patients remained for analysis. Recurrences were scored if biopsy-proven or if radiographic/clinical evidence initiated a change in management. Locoregional recurrence (LRR) was assessed via Kaplan-Meier graphic/clinical evidence initiated a change in management. Loco/regional recurrence (LRR) was assessed via Kaplan-Meier analysis.

**RESULTS:** Median follow-up of patients alive at last contact was 40 months. Median age was 43 years (range: 14–92 yr). Females (n = 163, 63.7%) were more common than males (n = 93, 36.3%). Histology included papillary variants (n = 238, 93.4%), medullary (n = 14, 5.8%), follicular (n = 3, 1.2%), and oxyphilic (n = 1, 0.4%). Total thyroidectomy was performed in 241 (94.1%), and lobectomy without radioactive iodine to evaluate patterns of failure.
4 (1.6%). Central neck dissections were performed in 171 (66.8%), cervical neck in 129 (50.4%), and mediastinal in 35 (13.7%). Radioactive iodine was used in 217 (84.8%) with a median dose of 148.3 mCi. American Joint Committee on Cancer (AJCC) staging was TX–2 in 128 (50%) and T3–4 in 128 (50%), with 92 cases (36%) of N1a and 164 cases (64%) of N1b. Median number of nodes examined was 16 (intraquartile range: 7–32), with a median number of positive nodes of 4 (intraquartile range: 2–10). Margins were positive in 72 (28.1%) while negative in 145 (56.6%) and unreported/unknown in 54 (21.1%). Extracapsular extension (ECE) was seen in 98 (38.3%) while not seen in 124 (48.4%) and unknown in 34 (13.3%). Lymphovascular space invasion (LVSI) was positive in 90 (35.2%) while negative in 112 (43.8%) and unknown in 54 (21.1%). Local recurrence in the thyroid bed developed in 6 (2.3%), regional in neck or upper mediastinum in 49 (19.1%), local and regional in 52 (20.3%), and distant in 6 (2.3%). Regional recurrence was more likely in the lateral neck compartment (n = 33, 67.3%) than central (n = 21, 42.8%) or mediastinal (n = 6, 12.2%); failure occurred in more than one compartment in 11 (4.3%). Actuarial risk of LRR for the entire cohort was 20.1% at 3 years, 24.3% at 5 years, and 35.2% at 10 years. LRR risk at 3 years was elevated in patients with follicular histology (100%; P < .007), T3–4 (28.7%; P = .015), N1B (24.6%; P = .006), ECE (28.3%; P = .001), LVSI (34.2%; P = .015), and increasing number of positive nodes (33.5%; P < .001 for ≥ 5 vs < 5). On multivariate analysis, only ≥ 5 lymph nodes (hazard ratio [HR] = 3.63; 95% confidence interval [CI], 1.99–6.63; P < .001) remained significant for LRR.

CONCLUSIONS: At median follow-up of 40 months, patients with node-positive thyroid cancer were most likely to recur in the neck rather than in the thyroid bed or distantly. Increasing nodal burden is associated with significantly increased risk of locoregional recurrence.

(P043) Stereotactic Radiosurgery Following Resection of Brain Metastases: Optimizing Benefit and Minimizing Risk

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PURPOSE: Postoperative radiation consolidation following resection of a symptomatic brain metastasis has traditionally been administered as whole-brain radiation therapy (WBRT). Given the increasing survival in some cancer patients, an increasing number of centers are offering postoperative cavity consolidation in the form of stereotactic radiosurgery (SRS). While there are anecdotal reports of success using this approach, whether SRS to the resection cavity alone can control intraoperative spill of tumor cells is not well established. We sought to determine our institutional rates of local control at the surgical site, as well as the rates of leptomeningeal dissemination, in patients treated with postoperative SRS consolidation.

METHODS: We conducted a retrospective analysis of prospectively recorded data for all patients who underwent surgical resection of brain metastases, followed by consolidative SRS, at our institution between June 2007 and March 2013. All magnetic resonance (MR) imaging following SRS until death was reviewed for local recurrence and leptomeningeal disease (LMD). Patients without follow-up imaging were excluded. A univariate analysis was used to compare groups, and P < .05 was considered significant.

RESULTS: A total of 23 patients were treated with SRS after surgical resection and had MR imaging follow-up. Primary pathology was melanoma in nine patients, lung cancer in four, breast in three, prostate in two, and colorectal carcinoma in one, and four had other cancer types. Median overall survival was 7.5 months (range: 2–51 mo) from surgical resection, with SRS administered at a median of 14 days post-resection (range: 3–143 d). Median resection cavity treatment volume was 13.8 cc (range: 3.1–42.9 cc). In addition to the surgical lesion, 17 patients (74%) had additional intraparenchymal lesions treated at the time of SRS, with a mean of 5 additional lesions per patient (range: 1–37). Treatment doses to the cavity margin ranged from 15–22 Gy (median 18 Gy). There were no cases of local tumor recurrence; however, four patients developed LMD between 131–1193 days after craniotomy. Their primary pathologies were breast cancer in two patients, squamous cell carcinoma in one, and melanoma in one. Two of the four patients had posterior fossa resections, and all four patients were treated with WBRT at time of LMD diagnosis. The patients with LMD received SRS on average 47 days after their surgical resection, compared with an average of 22.7 days for those without LMD (P = .295).

CONCLUSIONS: LMD appears to occur as a result of systemic disease progression, as opposed to intracranial tumor spill at the time of resection, given the lengthy time interval between resection and LMD development in our sample. Given the 100% control rate of tumors in our resection cavities, we feel that SRS is a viable option for management of the postoperative resection bed. These findings will require further validation in a prospective trial.

(P044) Feasibility of Preoperative SBRT for Chondrosarcomas and Chordomas

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PURPOSE: To determine the outcomes of chordomas and chondrosarcomas treated with preoperative, postoperative, and definitive CyberKnife radiosurgery. The goals of preoperative radiosurgery are to improve disease-free survival (DFS) by achieving clean margins and to decrease morbidity by achieving a smaller resection volume.

MATERIALS AND METHODS: We identified 14 patients with chordomas and chondrosarcomas treated at our institution with radiosurgery using CyberKnife robotic radiosurgery and a stereotactic body radiation therapy (SBRT) system. Using original imaging at the time of diagnosis, preferably fat-saturated, T2-weighted sequences, clinical target volume (CTV) was defined as gross disease and, in the spine, the entire involved vertebral body or sacral segment. Any tissue felt to be at risk was included. For patients treated preoperatively, the entire tumor was targeted along with a 3–5-mm margin. In all cases, a planning target volume (PTV) was generated by expanding the target by 2–3 mm. All patients received 25–45 Gy in five fractions. All patients had follow-up magnetic resonance imaging (MRI) with T2-weighted sequences. Some patients with spine
or sacral tumors also had follow-up CT scans. Toxicity data were retrospectively collected by reviewing clinic notes.

**RESULTS:** The median age for these patients was 46 years (range: 15–76 yr). Eastern Cooperative Oncology Group (ECOG) performance status ranged from 0–1. Eight tumors were intracranial, three were in the spine, and three were in the sacrum. Four patients received prior external beam (three with photons, one with protons; range: 50.4–73.8 Gy) (all postoperative). Of the patients who had undergone surgery, six were gross total, three were near-total, and three were subtotal resections. The median gross tumor volume was 20.9 cc (mean 54.72; range: 3–309.4 cc). The corresponding original PTVs were 27.34, 97.63 (range: 11.16–418 cc). Median time between imaging diagnosis and CyberKnife was 7.78 months. Mean dose was 35 Gy (median 35 Gy; range: 25–40 Gy). Mean maximum dose to PTV was 55.23 Gy (median 57.21 Gy; range: 37.63–67.80 Gy). Median imaging follow-up after CyberKnife was 6.27 months. Median imaging follow-up after diagnosis was 17.57 months (range: 3.9–173.8 mo). The median follow-up after diagnosis was 17.67 months (range: 6.77–173.87 mo). Only one recurrence was noted after CyberKnife. The recurrence was 3.47 months after CyberKnife in a patient who had previously undergone surgery. No patients developed metastatic disease. One patient is deceased. There were no recurrences in the definitive or preoperative cohorts. There were five toxicities > grade 2. One patient treated with preoperative radiosurgery for a large sacral chondrosarcoma experienced a grade 3 postoperative wound infection and poor wound healing. There were too few patients and too few recurrences to determine whether a dose-response relationship was present. For the entire cohort, overall survival (OS) was 93% and locoregional control (LRC) was 86%. There was no difference in LRC, OS, or toxicity based on pre-, post-, or definitive CyberKnife radiosurgery (CKRS).

**CONCLUSION:** SBRT for definitive, preoperative, postoperative, or salvage treatment of chordomas and chondrosarcomas demonstrates a local control of 86%. In the future, we would seek to hypo-fractionate spine or sacral chordomas preoperatively and collect more data on the incidence of toxicities, especially wound healing and infection.

**Table P043  Patient Characteristics**

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>23</th>
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</thead>
<tbody>
<tr>
<td>Median age (yr) (range)</td>
<td>64 (30–83)</td>
</tr>
<tr>
<td>Sex</td>
<td>Male 11, Female 12</td>
</tr>
<tr>
<td>Region</td>
<td>Frontal 11, Temporal 2, Parietal 7, Occipital 4, Posterior Fossa 4</td>
</tr>
<tr>
<td>Primary pathology</td>
<td>Melanoma 9, Non–small-cell lung cancer 4, Breast 3, Prostate 2, Colorectal 1, Other 4</td>
</tr>
<tr>
<td>Mean target volume (cc) (range)</td>
<td>8.3 (0.4–31.3)</td>
</tr>
<tr>
<td>Mean prescription isodose volume (cc) (range)</td>
<td>13.8 (3.1–42.9)</td>
</tr>
<tr>
<td>Mean prescription isodose volume/target volume (range)</td>
<td>1.6 (1.25–2.25)</td>
</tr>
</tbody>
</table>

(P045) Involved-Nodal Radiation Therapy Leads to Lower Doses to Critical Organs at Risk Compared With Involved-Field Radiation Therapy

**BACKGROUND:** Involved-field radiotherapy (IFRT) after cytotoxic chemotherapy has become the standard of care in treating pediatric patients with Hodgkin disease. However, recent interest in shrinking the treatment volume to involved-node radiotherapy (INRT) may allow lower doses to critical organ structures. We dosimetrically compared IFRT and INRT treatment approaches.

**METHODS:** INRT treatment plans were retrospectively constructed from 18 pediatric patients identified with Hodgkin disease who had been treated with conventional IFRT. The radiation doses delivered to organs at risk (OARs) with virtual INRT treatment plans based on INRT field design were then compared with the original treatment plans. Metrics for comparison included mean doses to organs and volumes of organ receiving at least 50% of the original prescription dose (V50). A one-tailed, paired t-test was then performed to verify statistical significance at an alpha level of .025.

**RESULTS:** Three OARs that were compared in this investigation (thyroid, parotids, and lungs) had significantly lower doses of radiation with INRT when compared with IFRT (P < .025). Furthermore, the volume of breast receiving at least 50% of the initial prescription dose was statistically lower in the INRT plans. We did not find statistical improvements in dosimetrics for exposure to kidney and heart with INRT in our patients.

**CONCLUSIONS:** Utilizing the concept of INRT results in a reduction of radiation dose to critical organ structures in pediatric
patients with Hodgkin disease when compared with the more traditional method of IMRT.

(P046) Use of Intensity-Modulated Radiotherapy (IMRT) With Daily Image Guidance and Reduced Treatment Margins Is the Most Significant Predictor of Reduced Late Toxicity in Patients With Human Papillomavirus–Associated (HPV+) Oropharyngeal Cancer

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PURPOSE AND OBJECTIVES: We hypothesize that patients with oropharyngeal squamous cell carcinoma (OPSCC) treated with definitive chemoradiotherapy (CRT) with intensity-modulated radiotherapy (IMRT), daily image guidance, and reduced planning margins will have fewer significant late effects and improved functional outcomes than those treated with conventional techniques.

MATERIALS AND METHODS: Patients with stage III–IVb OPSCC and known tumor human papillomavirus (HPV) status treated with CRT between 2002 and 2012 and rendered disease-free were identified from an institutional review board (IRB)-approved registry. HPV+ disease included patients who tested positive for HPV DNA by in situ hybridization or had diffuse and strong (>75%) staining for p16 by immunohistochemistry. RT was administered once (79%) or twice daily (21%) to a total dose of 70–74.4 Gy. A 3-field approach (3D-RT) with standard margins and weekly ports was used in the earlier years of the study, while IMRT with daily cone-beam CT and 2–3-mm clinical target volume (CTV) and planning target volume (PTV) expansions, respectively, was used more recently. Most patients were treated with cisplatin and 5-fluorouracil (5-FU) (62%), while more recently, patients were treated with cisplatin (26%) or cetuximab (9%) at standard dosing. Toxicity was scored according to Common Terminology Criteria for Adverse Events version 4.0 (CTCAE v4.0). Significant late toxicity was defined as any grade 3 or any persistent grade 2 fibrosis, dysphagia, osteoradionecrosis, trismus, pain, hoarseness, or hearing loss that occurred > 3 months after the completion of treatment. Xerostomia and taste and skin changes were excluded from this combined endpoint. Logistic regression analysis was performed to identify patient-, tumor-, and treatment-related variables associated with significant late toxicity.

RESULTS: Of the 197 patients included in this study, the majority were Caucasian (95%) and male (91%), and 32% were never-smokers. The median age was 56 years, median Karnofsky performance score (KPS) was 90, and median follow-up was 39.4 months (range: 3.1–137.8 mo). A total of 129 patients (65%) were treated with 3D-RT, while 68 (35%) were treated with IMRT and image-guided radiation therapy (IGRT) with reduced treatment margins. At last follow-up, 91% of patients returned to a normal diet, while 6.5% had a limited oral diet and 2.5% were feeding tube–dependent. Of the 41 patients (20%) who required dilation for a stricture, 21 had their dysphagia resolve. The use of fluorouracil (5-FU)-based chemotherapy (76% vs 37%; P < .0001) and the use of 3D-RT (70% vs 44%; P = .0005) were independently associated with the need for a feeding tube. Similarly, 5-FU–based chemotherapy (43% vs 16%; P ≤ .0001) and 3D-RT (44% vs 13%; P < .0001) were associated with higher rates of significant late toxicity. In patients treated with once-daily IMRT and non–5-FU-based chemotherapy, the rate of significant late toxicity was 5.7%. On multivariate analysis, not using IMRT was associated with the highest risk of significant late toxicity (odds ratio [OR] = 3.4; P = .005), overshadowing smoking status, T stage, neck dissection, and chemotherapy type.

CONCLUSION: The use of IMRT with daily IGRT and reduced treatment margins dramatically reduces significant late effects for patients with HPV+ OPSCC. Nearly all patients treated with IMRT and non–5-FU-based chemotherapy have minimal significant late effects and excellent long-term function.

(P047) Dosimetric and Toxicity Analyses of Reirradiation for Recurrent Pediatric Brain Tumors

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BACKGROUND: Reirradiation is increasingly used to treat recurrent pediatric brain tumors, but data-driven dose-volume constraints for repeat radiation are lacking.

METHODS: Records of 12 pediatric patients treated with reirradiation for recurrent brain tumors between July 2009 and May 2013 at MD Anderson Cancer Center were retrospectively reviewed for toxicity and outcomes. To determine dosimetric parameters, Digital Imaging and Communications in Medicine (DICOM) data-sets of the initial and repeat radiation plans were deformed and merged to determine the maximum dose to 0.03 cc of the optic chiasm, optic nerves, spinal cord, brainstem, cochlea, pituitary, and normal brain and to 1 cc of the brainstem on the individual and composite plans.

RESULTS: Median follow-up was 3.5 years. Median age at initial radiation was 4.5 years and 6.7 years at repeat radiation. Patients had medulloblastoma (n = 4), primitive neuroectodermal tumor (PNET) (n = 2), anaplastic ependymoma (n = 2), or other tumors (n = 4). All patients initially received proton radiotherapy to a median dose of 55.8 cobalt grey equivalent (CGE). At recurrence, patients were treated with intensity-modulated radiation therapy (IMRT) (n = 6), proton (n = 5), or both (n = 1) to a median total dose of 42.5 CGE. All patients completed the planned second course of radiation. At last follow-up, four patients were alive with disease, five were dead, and three had no evidence of disease. No patient developed radiation necrosis. Two patients developed optic pathway defects, likely related to tumor progression. Four patients developed secondary hypothyroidism (median composite maximum dose of 36 CGE to pituitary), and one patient developed growth hormone deficiency (composite maximum dose of 39 CGE to pituitary).

CONCLUSION: Repeat radiation for recurrent brain tumors may be performed in the pediatric population with acceptable short- and long-term toxicity. Establishment of dose-volume guidelines will facilitate treatment planning for these challenging cases.
(P048) Quality Assurance Assessment of Diagnostic and Therapy Simulation Computed Tomography Image Registration for Head and Neck Radiotherapy: Anatomic Region of Interest-Based Comparison of Rigid and Deformable Algorithms

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BACKGROUND AND PURPOSE: Developing a framework to validate the performance of image registration algorithms is critical before application for tumor localization and therapeutic targeting. The purpose of this study was to develop a workflow process that enables quantitative assessment of different image registration techniques used for head and neck simulation CT (SimCT) to diagnostic CT (DxCT) coregistration.

MATERIALS AND METHODS: A total of 68 reference anatomic regions of interest (ROIs) were manually contoured on each of 11 paired SimCTs and DxCTs of head and neck patients treated with definitive intensity-modulated radiotherapy (IMRT). DxCT was registered to SimCT rigidly and through four different deformable image registration (DIR) algorithms: Atlas-based, b-spline, demons, and optical flow. The resultant deformed ROIs were compared with manually contoured reference ROIs using similarity coefficient metrics (ie, Dice similarity coefficient) and surface distance metrics (ie, 95% maximum Hausdorff distance).

RESULTS: All DIR algorithms showed improved performance over rigid registration for all used comparison metrics (Steel test: P < .008 after Bonferroni correction), excepting optical flow for surface distance metrics. The Atlas-based algorithm had the best DIR performance (mean Dice of 0.65 ± 0.15, mean false-negative Dice of 0.11 ± 0.18, mean false-positive Dice of 0.58 ± 0.26, and mean 95% maximum Hausdorff distance of 6.79 mm ± 7.6). The performance of different algorithms varied substantially for specific anatomic ROIs and subgroups. Overall, the performance of most algorithms was better in matching bony and cartilaginous ROIs than muscular, glandular, vascular, and other soft tissue ROIs.

CONCLUSIONS: Development of a formal ROI-based quality assurance workflow for registration assessment revealed improved performance with DIR techniques over rigid fusion and provided head and neck ROI-specific benchmarks for DxCT-SimCT coregistration for future efforts. After QA, DIR implementation should be the standard for head and neck DxCT-SimCT alignment.

(P049) Simultaneous Integrated Boost–Intensity-Modulated Radiation Treatment in Head and Neck Cancer: Outcomes From a Single-Institution Series

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BACKGROUND: Locoregional (LR) failures remain a major problem in locally advanced head and neck cancers following chemoradiation. Despite aggressive combined treatment modalities for advanced head and neck cancer during the last decade, LR recurrence rate remains suboptimal. Patients are generally treated with sequentially planned radiation treatment in which the same dose is delivered to shrinking tumor volumes. Accelerated hypofractionated schedules with the simultaneous integrated boost–intensity-modulated radiotherapy (SIB-IMRT) technique have gained interest in hopes of obviating accelerated repopulation. The main aim of this study is to assess the acute and late toxicity as well as clinical outcomes in patients with head and neck cancer treated with SIB-IMRT at a National Cancer Institute (NCI)-designated comprehensive cancer center.

MATERIALS AND METHODS: Between January 2005 and December 2012, 89 patients (67 males, mean age 61.4 y) with head and neck cancers were treated with definitive SIB-IMRT at the University of Pittsburgh Cancer Institute. Seventy patients (79%) received chemotherapy concurrent with radiation. The median Karnofsky performance score (KPS) at the time of treatment was 90 (range: 50–100). Kaplan-Meyer survival analyses were used to estimate local control (LC) and overall survival (OS) rates. The multivariate Cox regression method was used to model predictors of outcome.

RESULTS: The median follow-up from SIB-IMRT was 21 months (range: 12.0–24.0 mo); 22.2% of patients had stage I/II disease, while 21.2% and 56.5% of patients had stage III and IV disease, respectively. The majority of patients had oropharyngeal (35%) and laryngeal (30%) cancer, while the remaining had oral cavity, nasopharynx, hypopharynx, and salivary cancers. The median prescription dose was 70 Gy (range: 60.0–75.6 Gy) delivered in 32 (range: 28–36) fractions. The high-risk tumor volume received a median dose of 2.18 Gy (range: 2.0–2.5 Gy) per fraction, while the intermediate-risk and low-risk tumor volumes received a median dose of 2 Gy (range: 1.8–2.25 Gy) and 1.8 Gy (range: 1.64–2.0 Gy) per fraction, respectively. The 1- and 2-year LR control, OS, and distant metastases-free (DMF) survival rates were 72%/70%, 80.2%/71%, and 89%/83%, respectively. Twenty-seven patients (30%) had acute grade 3 toxicity, while none had grade 4 acute toxicity. Only two patients (3%) had grade 3 late toxicities, and no grade 4 late toxicities were noted. On univariate analysis, T-stage, and gross tumor volume (GTV) were significant predictors of local failure, while on multivariate analysis, only T-stage was a significant predictor of local failure. On univariate analysis, HPV, number of pack-years of smoking, and KPS were significant predictors of OS, while on multivariate analysis, only T-stage was a significant predictor of OS.

CONCLUSION: IMRT using SIB is an effective and safe technique in the treatment of patients with head and neck cancer, even with concurrent chemotherapy. Our results are comparable with those obtained with conventional RT. Given this, along with the inherent superior dose homogeneity and lower total number of fractions, SIB-IMRT can be offered as a standard treatment.

Acknowledgment: The project was funded by the Thomas H. Nimick, Jr. Competitive Research Fund.

(P050) Hypothyroidism After Definitive Radiation Therapy for Oropharyngeal Cancer

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Adam S. Garden, MD; UT MD Anderson Cancer Center

PURPOSE AND OBJECTIVE: We conducted a retrospective cohort study of oropharyngeal cancer patients to evaluate the incidence of hypothyroidism after definitive radiation therapy (RT).

MATERIALS AND METHODS: Follow-up records of 439 oropharyngeal cancer patients staged I–Ivb and treated with definitive RT between January 2000 and October 2008 were reviewed. The occurrence of hypothyroidism was defined as elevated levels of thyroid-stimulating hormone (TSH) above 5.50 mcU/mL. Patients with baseline hypothyroidism before treatment were excluded from the study. Cox proportional hazards analysis was used to compute hazard ratios (HRs) comparing patients with and without hypothyroidism.

RESULTS: A total of 408 out of 439 patients had follow-up data on TSH levels and were included in the analysis; 200 patients (49%) developed hypothyroidism after radiation. The median time to developing hypothyroidism was 12 months (range: 1–69 mo). Of the 200 patients with hypothyroidism, 13 (7%) did not take oral thyroid hormone replacement, and their median TSH was 5.84 mcU/mL (range: 5.53–8.38 mcU/mL). Further, 156 of the 200 patients had information on thyroid hormone replacement use, and their median TSH level was 7.4 mcU/mL (range: 5.55–119 mcU/mL). There was no difference in the occurrence of hypothyroidism between patients treated with 3D-conformal radiation vs intensity-modulated RT ([IMRT] 54% and 48%, respectively; chi-square P = .34). Patients who received ≥ 70 Gy of the prescribed radiation dose to the primary tumor had a higher risk of hypothyroidism compared with those whose prescription dose was < 70 Gy (55% and 44%, respectively; P = .04). In univariate Cox proportional hazards analysis, patients who were never-smokers had a higher risk of hypothyroidism compared with current smokers (HR = 1.6; P = .02). Age, sex, treatment technique (3D vs IMRT), clinical T category, clinical N category, and chemotherapy use were not significantly associated with hypothyroidism risk. Multivariate Cox proportional models demonstrated elevated risk of hypothyroidism among never-smokers (HR = 1.6; P = .02) and those who received a prescribed radiation dose of 70 Gy or more (HR = 1.2; P = .04) after adjusting for age, sex, treatment technique, and chemotherapy use.

CONCLUSION: Patients who received a radiation prescription dose of 70 Gy or more to the primary tumor and were never-smokers had an increased risk of hypothyroidism after definitive RT for oropharyngeal cancer.

(P051) Correlative Study of Thyroid DVH and Incidence of Subsequent Thyroid Dysfunction After Head and Neck Radiotherapy

Stella Ling, MD; Phuong Nguyen, MD, Yi Rong, PhD, Jennifer Sipos, MD; Ohio State University

MATERIALS AND METHODS: Using departmental databases, we were able to identify 65 patients who had head and neck radiotherapy from January 2008 to December 2009 as part of their overall treatment for head and neck cancer. Three patients were censored because of surgical intervention on the thyroid gland, leaving us with a study cohort of 62 patients. Treatment planning of all these patients had been done on Pinnacle treatment planning software.

RESULTS: We were able to retrospectively contour in the thyroid glands on these patients and assess the dose-volume histograms (DVHs) of the thyroid gland. In none of the patients was the thyroid gland considered an organ at risk (OAR). Twenty-four patients (38.7%) subsequently developed thyroid abnormalities, either clinical or subclinical, as expressed by changes in thyroid-stimulating hormone (TSH) and free T4 and clinical history. Further, 25% of the women and 42% of the men developed such abnormalities. The median time to developing abnormalities was 7.8 months after starting radiotherapy treatment, and the earliest abnormality was noted at 1.3 months after starting treatment. Ten of the abnormalities were within the first 6 months after starting radiotherapy. The median age of patients who developed thyroid abnormalities was 50 years, and was 57 years for those who did not develop abnormalities (difference not statistically significant). The correlation of thyroid DVH with subsequent abnormality trended toward significance at D50 with P < .117.

CONCLUSION: In this small cohort of patients, we were able to show increased incidence of thyroid abnormalities after radiotherapy as compared with the normal population. Males and patients less than 55 years of age may be at somewhat higher risk. Thyroid evaluation should be undertaken prior to starting head and neck radiation and again at subsequent follow-ups, even at the 1-month follow-up. Consideration should be given to including the thyroid gland as an OAR, with contouring being done at the time of treatment planning.

(P052) Evaluation of Pseudoprogression in Juvenile Pilocytic Astrocytomas Treated With Proton Beam Radiotherapy

Edward M. Manning, Jr., MD, MPH, MS, Greg Bartlett, CMD, Peter Johnstone, MD, Kevin P. McMullen, MD; Indiana University School of Medicine

INTRODUCTION: Pseudoprogression refers to post-treatment volume changes seen on magnetic resonance imaging (MRI) with or without clinical sequelae that subsequently regress without a change in therapy. Pseudoprogression is therefore distinguished from true tumor progression, and making this distinction has become an increasingly relevant topic in neuro-oncology as survivorship improves and assessment of follow-up MRI directs management. Patients treated with radiation therapy (RT) to the central nervous system (CNS) for low-grade gliomas represent a patient cohort at risk of pseudoprogression. The degree of response, tumor progression, or pseudoprogression in pediatric patients treated with proton therapy for pilocytic astrocytomas is evaluated here.

METHODS: Eight pediatric patients diagnosed with juvenile pilocytic astrocytoma by either biopsy or radiographic criteria are the subject of this report. From August 2005 through October 2007, these patients were treated to a median dose of 5,400 cGy using proton beam radiotherapy and subsequently followed with serial MRI every 3 months to assess response. MRIs were collected for 3 years following completion of RT, and the T1-contrasted series were imported into the Eclipse 11 treatment planning software. All contours of the T1 contrast-enhancing volumes, including cystic
structures, were performed by one clinical radiation oncologist (EMM). Volume in cm³ was calculated and plotted against time since completion of therapy to assess for changes from the baseline radiotherapy gross tumor volume (GTV). Demographics, prior therapies, and postradiation interventions were cataloged for each patient.

RESULTS: This is a retrospective review of eight pediatric patients with a mean age of 7.4 years (range: 4–12 yr), four of whom had biopsy-proven pilocytic astrocytomas. The mean number of follow-up MRIs collected was 9.4 (range: 4–12) per patient. One patient had prior radiation, and six (75%) patients had prior resections, all of which were R2; seven patients had cerebrospinal fluid (CSF) shunts in place prior to initiation of RT. All patients received at least a platinum agent and vincristine as part of their preradiation chemotherapeutic regimens. Seven (88%) patients remained alive at the time of this report, with one death due to tumor progression. Within the first year of follow-up, five (63.5%) patients declared themselves as responders (successive volumes less than pretreatment), and three (37.5%) patients declared themselves as nonresponders (successive volumes greater than pretreatment). Pseudoprogression was observed in two (40%) responders, with a maximum volume observed at 7.5 months. Following RT, three patients required shunt revisions, while one patient received hyperbaric oxygen for biopsy-proven radionecrosis, and another underwent stereotactic cyst aspiration. Volume changes ranged from an 83% reduction to an increase of 181% during the evaluation period.

CONCLUSIONS: Pediatric patients with pilocytic astrocytomas heavily pretreated with chemotherapy and status post-R2 resections can have extended survival following proton beam radiotherapy. Close observation for treatment sequelae, such as pseudoprogression, remains a challenge. This retrospective report illustrates that treatment responders declare within the first year, but vigilant surveillance is necessary due to risk of pseudoprogression during this time.

(P053) Proton Irradiation for Pediatric Central Nervous System Malignancies: Radiation Treatment Effect Risks in High-Risk Patients

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BACKGROUND: Recently reported studies have indicated low rates of radiation-induced central nervous system (CNS) toxicity following proton therapy in patients ≤ 18 years of age. However, subgroup analysis revealed potentially higher rates of toxicity in younger patients or those receiving methotrexate. We retrospectively evaluated rates of CNS toxicity following proton therapy in potentially high-risk patients in order to assess the incidence, clinical and dosimetric risk factors, and natural course of radiation treatment (RT) effects.

METHODS: Patients who were treated for brain tumors at the MD Anderson Proton Therapy Center from 2006–2013, ≤ 9 years of age at the time of radiation, and receiving local-field RT only with or without chemotherapy were included. Eighty patients, all of whom were treated as part of a prospective data collection protocol, were identified. Clinical records as well as serial magnetic resonance imaging (MRI) were reviewed, and dosimetric factors were recorded. Patients with less than 1 month of imaging follow-up were excluded.

RESULTS: A total of 60 patients met the follow-up criteria; 30 males and 30 females were included, with a median age of 2.6 years (range: 10 mo–9 yr). Location was posterior fossa in 39 patients and supratentorial in 21 patients. Ten patients were treated for recurrent disease but had not received prior irradiation. One patient received reirradiation. The most common histologies were anaplastic ependymoma (24), ependymoma (11), medulloblastoma (10), and atypical teratoid rhabdoid tumor (ATRT) (9). Forty-seven patients underwent a gross total resection prior to radiotherapy, with the remainder having subtotal of biopsy only. Patients had received chemotherapy before, during, and after radiation in 28, 6, and 17 cases, respectively. Fourteen patients received methotrexate. Median total dose and fraction size prescribed was 54 Gy at 1.8 Gy.

With a median imaging follow-up of 13.7 months (range: 1–80 mo), a total of seven patients (12%) developed RT effect consistent with radiation necrosis, as determined on serial MRI. Six of the seven (10%) were symptomatic from the treatment effect. Of the symptomatic patients, one had treatment effect in the supratentorial brain; the others developed treatment effect in the brainstem. The median time to development of was 3.9 months (range: 2.6–4.5 mo). The median age of those who developed radiation necrosis was 1.9 years vs 2.6 for those who did not (t-test P = .4). Two patients were treated with methotrexate before radiation for ATRT. Five of the seven patients were treated for ependymoma.

CONCLUSIONS: In this small retrospective series, proton radiation for pediatric brain malignancies was associated with a 12% crude risk of radiation-induced imaging changes and a 10% risk of symptomatic necrosis. The incidence of MRI changes was similar to reported photon series. The relatively high incidence of symptomatic necrosis likely reflects the young age at treatment and common use of chemotherapy in the patient population that is included. Changes tend to occur early within 3–5 months after completion of radiation. Due to the low incidence, no statistically significant predictive factors were found. However, further study that includes dosimetric modeling is warranted.

(P054) Stereotactic Body Radiation Therapy as Salvage for Intrathoracic Recurrence After Definitive Stereotactic Body Radiation Therapy for Early-Stage Non-Small-Cell Lung Cancer

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PURPOSE: Despite the success of stereotactic body radiotherapy (SBRT) as a treatment modality for early-stage non–small-cell lung cancer (NSCLC), some patients develop localized intrathoracic recurrences after treatment. Effective salvage therapy for these
Stereotactic Body radiation therapy (SBRT) has been demonstrated to be well tolerated and to offer high rates of local control in patients with biopsy-proven early-stage lung cancer. However, biopsy is not feasible in many SBRT candidates. Here, we review patient outcomes and toxicity data of unbiopsied positron emission tomography (PET)-positive pulmonary lesions treated with SBRT for presumed non–small-cell lung carcinoma (NSCLC).

METHODS: We performed a review of all patients treated between March 2008 and January 2013 who received SBRT for PET+ pulmonary tumors. Criteria for pulmonary tumor diagnosis by PET were defined by high radiographic suspicion of malignancy, based on a hypermetabolic or enlarging lung nodule. The median SBRT dose was 60 Gy delivered in a median of four fractions. Dose was prescribed to a nonuniform planning target volume (PTV), based on the internal target volume (ITV) constructed from a 4D CT scan, allowing for tumor motion and continued alignment of surrounding organs at risk. The treatment plans consisted of noncoplanar static aperture arcs and noncoplanar static fields. Treatments were delivered using 6-MV x-rays with image guidance. Follow-up with PET/CT occurred every 3 months. Toxicity was scored using Common Terminology Criteria for Adverse Events version 4.0 (CTCAE v4.0). The Kaplan-Meier product estimator was used to measure outcomes, such as overall survival (OS), local control (LC), and distant metastasis–free survival (DMFS). The Charlson Comorbidity Index (CCI) was used to assess pretreatment morbidity.

RESULTS: We identified 51 lesions in 51 patients who had a median follow-up of 10 months (range: 2–47 mo). The most common reasons for nonbiopsy included poor pulmonary status (n = 23) and patient refusal (n = 16). The median tumor size was 1.8 cm (range: 0.9–4.8 cm), with 73% located peripherally and 27% located centrally. There were 37 patients with T1 disease and 14 patients with T2 disease. The median age was 77 years (range: 53–90 yr), with a median CCI score of 6 and a median 2-year predicted survival based on CCI of 55%. Median pretreatment % predicted forced expiratory volume 1 (FEV1) and diffusion lung capacity for carbon monoxide (DLCO) were 63.5% and 59%, respectively. The initial median pretreatment standardized uptake value (SUV) was 4.40 and decreased to a median SUV of 1.9 at 10 months. The overall 4-year LC was 80%, and OS was 58%. The 4-year DMFS was 55%. Patients with stage I–IIA disease (n = 47) had an LC of 87% at 4 years. Only 8% of patients had a marginal failure, and 7% had an involved lobe recurrence. There was minimal toxicity, with 7.8% of patients with grade 2 dyspnea and 1.9% of patients with grade 3 fatigue. Serious toxicity, such as pneumothorax, pneumonitis, or bronchial airway obstruction, was not observed.

CONCLUSIONS: Our experience suggests that SBRT is a well-tolerated and effective treatment option for patients with PET+ pulmonary tumors who are not candidates for biopsy. Our cohort of medically inoperable patients demonstrated a high rate of LC combined with low toxicity, further supporting the rationale for a
prospective randomized controlled study of SBRT in patients who are unable to be biopsied.

**P056** VATS With HDR Intraoperative Brachytherapy for Chest Wall Tumors
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**PURPOSE:** To report on the Roswell Park Cancer Institute experience with iodine-192 high-dose-rate (HDR) intraoperative brachytherapy (IOBT) in minimally invasive, video-assisted thoracoscopic surgery (VATS) for localized pulmonary malignancies involving the chest wall.

**MATERIALS AND METHODS:** Five patients in 2012–2013 with node-negative thoracic malignancies involving the chest wall were chosen and consented for pulmonary resections with HDR-IOBT to their chest wall disease via VATS. After completion of the wedge resection, lobectomy, or pneumonectomy, a MicroSelectron HDR unit (model digital V3, Elekta Inc) was used for dose delivery in a specially designed, shielded operating room (OR). This unit uses a 10-Curie (Ci) miniaturized Ir-192 source 1 mm in diameter and around 5 mm in length. The actual treatment plans were generated on the Oncentra Treatment planning system within the OR itself, utilizing the standard geometry treatment plan library generated for various configurations for the Freiburg applicator. The number of catheters, active dwell position along each catheter, prescription depth, and dose prescription were customized based on clinical needs.

**RESULTS:** Four of the lesions treated were adenocarcinoma (T3N0–IIB), and the fifth was a sarcomatoid carcinoma. One of the patients, with non–small-cell lung cancer, required conversion to open thoracotomy; therefore, the remaining four cases are the focus of this report. All patients received and tolerated treatment without complications. However, the patient with sarcomatoid carcinoma died with brain metastasis within 1 month after the procedure. The patients with adenocarcinoma each received adjuvant chemotherapy, as tolerated, and remain in follow-up with no evidence of disease on surveillance imaging (median follow-up = 4 mo).

**CONCLUSIONS:** HDR-IOBT with Ir-192 via VATS is a technically feasible, well-tolerated procedure for intrathoracic disease involving the pleura and/or chest wall. Further follow-up and larger case population will speak to the efficacy and durability of this procedure, as well as indicate whether larger, analytic trials are appropriate. Laparoscopic images and media are provided.

**P057** Acute-Phase Response Before Treatment Predicts Radiation Esophagitis in Non–Small-Cell Lung Cancer
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**BACKGROUND AND PURPOSE:** Radiation esophagitis (RE) represents an inflammatory reaction to radiation therapy (RT). We hypothesized that aspects of the physiologic acute-phase response (APR), specifically increased platelet and decreased hemoglobin levels, predict RE.

**MATERIALS AND METHODS:** We retrospectively analyzed 285 patients with non–small-cell lung cancer treated with definitive radiation. The primary analysis was the association of pre-RT lab values with symptomatic (grade ≥ 2) RE. Univariate and stepwise multivariate odds ratios (ORs) were calculated to test associations of clinical and pretreatment lab values with RE. Optimal cutpoints for individual variables and multivariable RE risk stratification groupings were determined via recursive portioning analysis (RPA).

**RESULTS:** Pretreatment platelet counts were higher and hemoglobin levels were lower in patients who developed RE (P < .05), findings consistent with the APR. Based on these two pretreatment risk factors—high platelets and low hemoglobin—an APR score was defined as 0 (no risk factors), 1 (either risk factor), or 2 (both risk factors). A 1-point increase in APR score was significantly associated with RE in both univariate (OR = 2.3; P = .001) and multivariate (OR = 2.1; P = .002) analyses. Other variables identified on multivariate analysis to be significantly associated with RE include concurrent chemotherapy use (OR = 2.5; P = .008), in addition to mean (OR = 2.3; P = .0004) and max (OR = 2.4; P = .009) esophageal doses. RPA-based RE risk stratification produced three risk groups based on APR score, chemotherapy use, and dosimetric parameters.

**CONCLUSIONS:** Patients exhibiting aspects of the APR prior to RT initiation were more prone to RE development. The APR score may represent a novel metric to predict for RE. We propose a multivariate algorithm incorporating this score.

**P058** Stereotactic Body Radiotherapy for Non–Small-Cell Lung Cancer Patients With Central Lung Tumors: An Analysis of Outcomes and Toxicity
Benjamin Mou, MD, Kenneth W. Merrell, MD, Dawn A. Owen, MD, PhD, Katy Nelson, RN, Yolanda I. Garces, MD, Kenneth R. Olivier, MD; Mayo Clinic

**BACKGROUND:** Stereotactic body radiotherapy (SBRT) is increasingly used as the primary treatment for early-stage medically inoperable non–small-cell lung cancer (NSCLC). Although the role of SBRT is established in the treatment of peripheral lung tumors, the outcomes and toxicities of SBRT for central lung tumors are not well characterized. This study investigates our institutional experience with SBRT for central tumors in NSCLC patients.

**MATERIALS AND METHODS:** The Mayo Clinic SBRT database prospectively collects patient demographic and treatment-related data for all patients treated at our institution. We performed a retrospective chart review on NSCLC patients with primary and recurrent central lung tumors treated with SBRT between April 2008 and May 2013. The most frequently used dose fractionation regimens were 50 Gy in five fractions and 48 Gy in four fractions delivered over consecutive days. Local control (LC) and overall survival (OS) were measured using Kaplan–Meier estimates. Tumor response was scored using Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1). Toxicity was graded using the Radiation Therapy Oncology Group (RTOG) Common Toxicity Criteria.

**RESULTS:** A total of 85 central lung tumors from 80 patients were
included for analysis. Median age was 74 years (range: 40–91 yr), and median follow-up was 19.1 months (range: 3.3–61.0 mo). There were 54 primary tumors and 31 recurrent tumors. Median tumor size was 2.0 cm (range: 0.6–5.5 cm). There were three local failures, resulting in 2-year and 4-year LC rates of 96.6% and 87.8%, respectively. The median survival was 46.1 months. The 2-year and 4-year OS rates were 69.8% and 39.9%, respectively. Rates of complete response, partial response, and stable disease were 29% (n = 25), 53% (n = 45), and 18% (n = 15), respectively. There were 16 patients with grade III or higher pneumonitis, including one grade IV and one grade V toxicity. The patient with grade V toxicity had a 5.5-cm tumor and prior pneumonectomy. There were no grade III or higher acute toxicities. Toxicities were not associated with tumor size, radiation dose, or previous local therapy. Univariate analysis demonstrated no statistically significant differences in LC or OS between primary or recurrent tumors, histology, tumor size, or radiation dose.

CONCLUSIONS: SBRT provides excellent LC for central NSCLC tumors. Toxicity rates are acceptable; however, appropriate patient selection is imperative, as we await results from prospective trials of SBRT for central lung tumors.

(P059) Increased Rates of Radiation Pneumonitis in Patients Receiving Stereotactic Ablative Radiotherapy for Central Versus Peripheral Lung Tumors

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PURPOSE: Treatment of central lung tumors with stereotactic ablative radiotherapy (SABR) has been associated with higher rates of toxicities than in patients with peripheral tumors. Here, we report our institutions’ experience in treating central lung tumor patients with SABR, compared with patients treated for peripheral lung tumors.

METHODS: We retrospectively reviewed outcomes in 85 patients with a total of 99 primary or metastatic lung tumors treated by SABR. The cohort included 49 central and 50 peripheral tumors, and all were treated with 50 Gy in 4–5 fractions. Outcomes and radiation-associated toxicities were compared between the two groups, not including patients in whom central and peripheral tumors were concurrently treated (eight such patients). Dosimetric analysis was performed on patients with central tumors to determine the maximum point dose (MPD) and volumetric maximum dose (V(max)) to central structures.

RESULTS: Median follow-up time was 15 months (range: 1–59 mo). Actuarial local control rate was 84% and 91% (P = .15) at 1 year for central and peripheral lesions, respectively. Median overall survival was 34 and 40 months (P = .55) for patients with central and peripheral tumors, respectively. We observed no hematopoietic and no grade 5 toxicities. Rates of symptomatic toxicity were higher in patients with central tumors (grade 2+, 38% vs 11%; P = .004) but were similar for severe toxicity (grade 3+, 7.7% vs 5.3%; P = .66). The majority of toxicities was due to radiation pneumonitis, the incidence of which was significantly greater in patients with central tumors (grade 2+, 28% vs 2.6%; P = .001; grade 3+, 7.7% vs 0%; P = .88). Dosimetric analysis of 37 central tumor treatment plans revealed that 25 (68%) exceeded at least one of the dose constraints used in Radiation Therapy Oncology Group (RTOG) 0813, most commonly for central airway and/or great vessels. Toxicity rates were similar in patients receiving RTOG 0813 constraints compared with those meeting them (grade 2+, 32% vs 33%; P = .86).

CONCLUSION: Central lung tumor patients treated with SABR appear to have greater risk for radiation pneumonitis than patients with peripheral tumors. A subset of commonly used dosimetric constraints for lung SABR, particularly those for central airway and great vessels, may be more conservative than necessary.

(P060) Evaluation of 4D-CT Acquisition Methods Designed to Reduce Artifacts

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INTRODUCTION: Four-dimensional computed tomography (4D-CT) is used to account for respiratory motion in radiation treatment planning, but image artifacts resulting from the acquisition and postprocessing limit its accuracy.

METHODS: We investigated the efficacy of three experimental 4D-CT acquisition methods to reduce artifacts in a prospective institutional review board (IRB)-approved study. Eighteen thoracic patients scheduled to undergo radiation therapy (RT) received standard clinical 4D-CT scans, followed by each of the alternative 4D-CT acquisitions: (1) data oversampling, (2) beam gating with breathing irregularities, and (3) rescanning the clinical acquisition acquired during irregular breathing. Relative values of a validated correlation-based artifact metric (CM) determined the best acquisition method per patient. Each 4D-CT scan was processed two ways: by clinical standard phase sorting and by extended phase sorting by optimization of the quantitative artifact metric (CM sorting).

RESULTS: The CM-sorted oversampling acquisition achieved the lowest artifact presence among all acquisition and sorting combinations—a 38% reduction from the phase-sorted clinical acquisition. The CM-sorted oversampling and gating acquisitions both resulted in significant artifact reductions from the CM-sorted clinical (21% and 16%, respectively) and rescanning the clinical acquisition acquired during irregular breathing. Relative values of a validated correlation-based artifact metric (CM) determined the best acquisition method per patient. Each 4D-CT scan was processed two ways: by clinical standard phase sorting and by extended phase sorting by optimization of the quantitative artifact metric (CM sorting).

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CONCLUSIONS: CM-sorted oversampling acquisition reduced artifact presence from the clinical phase-sorted acquisition to the largest degree, although both the gating and oversampling acquisitions can significantly reduce artifact presence in 4D-CT image sets when alternative quantitative correlation-based sorting is applied.

(P061) Activity Verification and Localization Using PET-CT for Patients Treated With Radioembolization

Matthew E. Johnson, MD, Eugene Fourkal, PhD, Iavor Veltchev, PhD,
SBRT for early-stage NSCLC.

**BACKGROUND:** Radioembolization with yttrium-90 (Y-90) microspheres is a treatment option for primary and metastatic liver tumors. The activity of the microspheres is provided by the manufacturer with an uncertainty of +/- 10% and is verified by the institution prior to injection. While the amount of activity injected into the patient is known, the resultant activity and distribution within the liver remain relatively unknown. We have developed a positron emission tomography (PET)/CT-based method to identify the injected activity and distribution within the liver following radioembolization. We aim to demonstrate correlation between activity measured within the patient and the administered activity and to describe the distribution within the liver.

**METHODS:** Twelve patients were enrolled in institutional review board (IRB)-approved prospective studies and underwent Y-90 radioembolization for primary or metastatic liver tumor(s). As part of the protocols, each patient underwent a postinfusion PET/CT for quantification of activity, measuring pair production from Y-90 beta decay. Six patients also underwent pretreatment PET/CT for quantification of background noise. Contours were delineated on the postinfusion CT with a uniform 1-cm margin to account for PET resolution and motion. Structures that were delineated included liver, up to three liver tumors, liver lobe targeted (right or left), and left kidney. For this analysis, the left kidney mean activity density (Bq/mL) was used as background. Net activity density was determined by measuring liver + 1 cm mean activity density and subtracting background activity density. The resulting net density was then multiplied by the volume to obtain the total activity in the patient.

**RESULTS:** Six patients underwent treatment with SIR-Spheres, and six were treated with TheraSpheres. Measured activity was +/- 10% of the injected activity in 8 of 12 patients (67%). Three patients had measured activity 20% to 30% less than injected, and one patient had activity 40% less than injected. When localization of total liver activity was examined, a median of 98% (range: 87%–100%) was found within the targeted lobe, and a median of 40% of activity (range: 7%–99%) was localized to the contoured liver tumors.

**CONCLUSION:** In the majority of radioembolization cases examined, activity measured using this PET/CT method was able to account for the amount of injected activity with an error of +/- 10%. This method should be further studied to enable evaluation of radiation dose distribution within the liver and tumors following radioembolization.

**PREFERENCE:**

**SUV_{max} and Early Radiographic Changes as Prognosticators for Progression-Free Survival in Non–Small-Cell Lung Cancer Treated With Stereotactic Body Radiation Therapy**

**Zachary D. Horne, MD, Paul P. Koffer, MD, Albert Yuen, MD, Michael L. Haas, MD; Reading Hospital Medical Center**

**BACKGROUND:** In patients with non–small-cell lung cancer (NSCLC) treated with stereotactic body radiation therapy (SBRT), there are few established predictors of outcomes. Pretreatment maximum standardized uptake value (SUV_{max}) has recently been debated as a prognosticator of progression-free survival (PFS). Here, we present a retrospective series with up to 86 months follow-up evaluating potential prognosticators of outcomes.

**MATERIALS AND METHODS:** Patients with primary stage I NSCLC (n = 80; median age 78 years; T1a = 33, T1b = 28, and T2a = 19) (American Joint Committee on Cancer [AJCC] 7th ed) were treated with SBRT between 2006 and 2013 at a regional medical center. All patients underwent motion studies to determine need for respiratory gating and were treated over a median of 9 days (range: 4–21 d). Survival curves were estimated using the Kaplan–Meier method, with the log-rank test and Cox proportional hazards regression utilized for univariate and multivariate analyses. Chi-square test and Pearson’s correlation were utilized to establish correlations between variables.

**RESULTS:** The median follow-up was 21 months (range: 4.4–86.4 mo). Actuarial local (LC), regional (RC), and distant control (DC) at median follow-up was 96.3%, 92.5%, and 88.8%, respectively. Overall survival (OS) and progression-free survival (PFS) at median follow-up were 80% and 85%, respectively, with median OS of 43.5 months. Median PFS was not reached. Cancer-specific survival (CSS) at 2 and 5 years was 100% and 96.3%, respectively. Median time to initial follow-up CT scan was 1.8 months (range: 0.5–8.8 mo), with a median percent size reduction (PSR) of 22% (range: 36%–100%). On univariate Kaplan–Meier analysis, LC differed significantly by histology (P = .047). PFS was predicted to be worse by an SUV_{max} cutoff of 5.0 (P = .022) and, paradoxically, tumor reduction greater than the median percentage at first imaging (P = .025). As continuous variables, SUV_{max} and PSR at first follow-up remained significant for PFS on univariate Cox regression analysis (P = .008 and P = .049, respectively). Eleven percent of patients with < 22% tumor reduction progressed, while 36% of patients with > 22% tumor reduction progressed (P = .009), with the majority in the latter group being distant failures (P = .08). On multivariate analysis, SUV_{max} was the only significant predictor of improved PFS (P = .036), LC (P = .049), and DC (P = .032). SUV_{max} and PSR were found to be correlated by dichotomous comparison in two-sided chi-square (P = .026) and continuous comparison by one-tailed Pearson’s correlation (R = .224; P = .030).

**CONCLUSIONS:** SBRT is the standard of care in nonsurgical patients with early-stage NSCLC. Patients in this series with highly metabolic tumors experienced a greater degree of size reduction at first follow-up CT and appear to be at higher risk of progressive disease. Increased tumor reduction at first follow-up CT may serve as a trigger for closer observation or potential intervention. Higher pretreatment SUV_{max} may serve as a risk-stratifying variable in future studies evaluating the integration of systemic therapy with SBRT for early-stage NSCLC.

**PREFERENCE:**

**Multiple Course Stereotactic Ablative Body Radiotherapy for Non–Small-Cell Lung Cancer**

**O. Kenneth Macdonald, MD, David A. Schomas, MD; Therapeutics Radiologists, Inc**

**INTRODUCTION:** Historically, aggressive local therapy of early-stage non–small-cell lung cancer (NSCLC) in frail, elderly, or medically unresectable patients has been avoided. Technical advances...
in radiotherapy (RT), especially stereotactic ablative body radiotherapy (SABR), have allowed for many of those once considered untreatable to be eligible for locally effective therapies. Some patients will experience recurrence or will present with multiple lung primaries. We review the success and impact of SABR in patients who have undergone multiple course therapy.

**METHODS:** The records of 12 patients were identified and reviewed for clinical and treatment information. All patients received two or more courses of SABR for synchronous or metachronous primary NSCLC or for pulmonary recurrent NSCLC after previous SABR or conventional radiotherapy. The Kaplan-Meier method was used to calculate survival rates. Toxicity was evaluated and graded using Common Terminology Criteria for Adverse Events version 4.0 (CTCAE v4.0). The radiographic response was graded per Response Evaluation Criteria in Solid Tumors version 1.0 (RECIST v1.0).

**RESULTS:** The median age of those included was 72 years. Five patients were male. A total of 28 lesions (courses) were treated, 20 of which were biopsy-confirmed malignancy, with 18 considered to be primary NSCLC. Two patients underwent planned, synchronous SABR to two lesions within 1–2 months. Four patients were treated with a subsequent SABR course for regional or metastatic lung-limited disease at a median of 26 months following initial SABR. Six patients were treated with SABR for local recurrence following previous RT: two following SABR (median 12 months) and four following previous conventional RT (median 48 months). Twelve treatment courses were preceded by baseline symptoms (oxygen supplementation requirement, cough, pain), with four (33%) experiencing improvement of those baseline symptoms following completion of SABR. Seven patients received chemotherapy as a component of their oncologic therapy—three prior to SABR. The remainder received chemotherapy following SABR. Median follow-up was 1.3 years. The median delivered total dose was 5,000 cGy in four fractions. The rate of overall survival (OS) at 1 and 3 years was 79% and 61%, respectively. Complete response was achieved in 13 targets, and partial response and stable disease were achieved in 6 and 7 targets, respectively. Distant metastasis developed in seven patients during follow-up, at a median 13 months, to sites, including pulmonary, lymph node, liver, and adrenal gland. The 1- and 3-year rates of distant metastasis were 75% and 45%, respectively. Toxicity was mild, with grade 1 fatigue in nine with another five grade 1–2 acute toxicities (pneumonitis or esophagitis). Chronic toxicity was limited to four patients: two with grade 1 and one with grade 2 lung fibrosis, and one patient with grade 2 chest wall pain.

**CONCLUSIONS:** The delivery of multicourse SABR, synchronously or metachronously, in patients who otherwise would not be candidates for local therapy was safe and effective for this small cohort of patients at a community hospital. Subsequent course of SABR successfully controlled recurrent or metastatic disease with minimal added morbidity.

**CONCLUSIONS:** The delivery of multicourse SABR, synchronously or metachronously, in patients who otherwise would not be candidates for local therapy was safe and effective for this small cohort of patients at a community hospital. Subsequent course of SABR successfully controlled recurrent or metastatic disease with minimal added morbidity.

**METHODS:** The records of 12 patients were identified and reviewed for clinical and treatment information. All patients received two or more courses of SABR for synchronous or metachronous primary NSCLC or for pulmonary recurrent NSCLC after previous SABR or conventional radiotherapy. The Kaplan-Meier method was used to calculate survival rates. Toxicity was evaluated and graded using Common Terminology Criteria for Adverse Events version 4.0 (CTCAE v4.0). The radiographic response was graded per Response Evaluation Criteria in Solid Tumors version 1.0 (RECIST v1.0).

**RESULTS:** The median age of those included was 72 years. Five patients were male. A total of 28 lesions (courses) were treated, 20 of which were biopsy-confirmed malignancy, with 18 considered to be primary NSCLC. Two patients underwent planned, synchronous SABR to two lesions within 1–2 months. Four patients were treated with a subsequent SABR course for regional or metastatic lung-limited disease at a median of 26 months following initial SABR. Six patients were treated with SABR for local recurrence following previous RT: two following SABR (median 12 months) and four following previous conventional RT (median 48 months). Twelve treatment courses were preceded by baseline symptoms (oxygen supplementation requirement, cough, pain), with four (33%) experiencing improvement of those baseline symptoms following completion of SABR. Seven patients received chemotherapy as a component of their oncologic therapy—three prior to SABR. The remainder received chemotherapy following SABR. Median follow-up was 1.3 years. The median delivered total dose was 5,000 cGy in four fractions. The rate of overall survival (OS) at 1 and 3 years was 79% and 61%, respectively. Complete response was achieved in 13 targets, and partial response and stable disease were achieved in 6 and 7 targets, respectively. Distant metastasis developed in seven patients during follow-up, at a median 13 months, to sites, including pulmonary, lymph node, liver, and adrenal gland. The 1- and 3-year rates of distant metastasis were 75% and 45%, respectively. Toxicity was mild, with grade 1 fatigue in nine with another five grade 1–2 acute toxicities (pneumonitis or esophagitis). Chronic toxicity was limited to four patients: two with grade 1 and one with grade 2 lung fibrosis, and one patient with grade 2 chest wall pain.

**CONCLUSIONS:** The delivery of multicourse SABR, synchronously or metachronously, in patients who otherwise would not be candidates for local therapy was safe and effective for this small cohort of patients at a community hospital. Subsequent course of SABR successfully controlled recurrent or metastatic disease with minimal added morbidity.
chemoradiation and examined the effects of metformin treatment on toxicity. Both cohorts are known to exhibit improved outcome in patients taking metformin compared with other methods of glucose control.[1,2]

**METHODS:** The charts of diabetic patients treated with concurrent chemoradiation for either locally advanced esophageal adenocarcinoma (EC) \((n = 49)\) or non–small-cell lung cancer (NSCLC) \((n = 62)\) were retrospectively evaluated for chemoradiotherapy-associated toxicity. Toxicities were scored using the Common Terminology Criteria for Adverse Events version 4.0 (CTCAE v4.0). The following toxicities were included: acute esophagitis, acute and subacute pneumonitis, nonpneumonitis severe pulmonary complications grade 3 (pneumonia, pleural effusion, pneumothorax, atelectasis, and acute respiratory failure), and severe cardiac complications grade 3 in the subacute or chronic setting (arrhythmias, congestive heart failure, and myocardial infarction). Symptomatic esophagitis was defined as grade 2 requiring new or increased use of narcotics. Cohorts were compared using chi-square statistical analysis.

**RESULTS:** In NSCLC, no significant differences were observed in symptomatic pneumonitis or esophagitis between patients taking metformin (28% and 50%, respectively) and patients using other methods for glycemic control (23% and 53%; \(P = .68\) and \(P = .77\), respectively). In EC patients, only seven cases of symptomatic pneumonitis were observed. However, no significant differences were observed in symptomatic esophagitis between patients taking metformin (48.3%) and those using other methods of glycemic control (30%; \(P = .2\)). No association between metformin dose \((0–1,500 \text{ mg/d vs } 1,500 \text{ mg/d})\) and symptomatic esophagitis was observed \((P = .19)\). EC patients taking metformin had significantly fewer nonpneumonitis severe pulmonary complications (17.2% vs 50%; \(P = .014\)) and similar severe cardiac (13.8% vs 10%; \(P = .69\)) complications compared with diabetics not taking metformin.

**DISCUSSION:** Diabetic patients with NSCLC or EC taking metformin who were treated with concurrent chemoradiation therapy experienced similar pulmonary, esophageal, and cardiac toxicities compared with patients using alternate methods of glycemic control. Importantly, these data suggest that metformin may be safely used concurrently with chemoradiation treatment. This is encouraging, given that metformin is a radiosensitizer agent associated with improved rates of pathologic complete response. Indeed, a national trial is currently being considered that would incorporate metformin into standard multimodality treatment for NSCLC.

**References:**

(P066) The Role of PET/CT in Radiation Treatment Planning for Non–Small-Cell Lung Cancer: Results of a National Survey

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**PURPOSE AND OBJECTIVES:** Positron emission tomography (PET)/CT imaging is rapidly being embraced by the radiation oncology community as a tool to improve the accuracy of target volume delineation for treatment optimization in various malignancies, particularly for non–small-cell lung cancer (NSCLC). The purpose of this study was to determine the standard practice patterns of the use of PET/CT imaging in treatment planning by radiation oncologists nationwide.

**MATERIALS AND METHODS:** An array of questions regarding the use of PET/CT in treatment planning was developed using a web-based platform (SurveyMonkey.com). The initial questions focus on the general use of PET/CT in treatment planning, while the latter set of questions addresses the use and implications of PET/CT in treatment planning for NSCLC patients. A list of recipients was obtained from the American Society for Radiation Oncology (ASTRO) Membership Directory. An email with the link for the survey was sent to approximately 1,500 practitioners. The responses were then collected and analyzed.

**RESULTS:** A total of 212 practitioners (14%) responded to the survey. Approximately 78% of the respondents use PET/CT for tumor staging, while 70% routinely uses PET/CT for treatment planning purposes. The most common sites for which PET/CT is used in treatment planning are NSCLC, head and neck cancer, esophageal cancer, and lymphoma. The majority of radiation oncologists (87%) use PET/CT to delineate volumes by fusing the PET/CT to the CT simulation scan. The most commonly used technique to delineate a gross target volume on PET/CT is by the visual method (64%). In the treatment planning of NSCLC, approximately 55% of radiation oncologists indicate that the use of PET/CT results in an increase in the treatment volume by 10% to 30%, with the majority of the expanded treatment volumes resulting from fluorodeoxyglucose (FDG)-avid lymph node (LN) stations that were not readily identifiable by CT scan alone. If an LN is <1 cm in size but is FDG-avid, 72% of respondents indicate that it would be included in the target volume. About 50% of the respondents indicated that the use of PET/CT results in a decrease in treatment volume by 10% to 30%, due mostly to atelectatic lung. In monitoring response following radiation therapy, 80% of the respondents obtain a PET/CT 8 weeks after completion of treatment. A standardized uptake value (SUV) cutoff of 3.1–4 is used to identify persistent or recurrent disease by 47% of responders. Of note, approximately 69% of the responders work in a private practice setting, and 31% practices in an academic center; the majority of the responders (60%) treat 10–50 cases of NSCLC annually.

**CONCLUSIONS:** To our knowledge, this represents the largest national survey amongst radiation oncologists on the patterns of use of PET/CT in modern treatment planning. Our findings illustrate the need for continuous training and ongoing standardization in an effort to optimize the use of PET/CT in radiation treatment planning.

(P068) CTC Levels as a Preliminary Biomarker for Non–Small-Cell Lung Cancer Patients Undergoing Radiation Therapy

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BACKGROUND: Circulating tumor cell (CTC) assays have been shown to have prognostic utility in patients with various carcinomas, including non–small-cell lung cancer (NSCLC). However, more limited data exist assessing the relationship between CTC count and other prognostic biomarkers. Furthermore, little data exist using CTC assays that are independent of surface markers, such as epithelial cell adhesion molecule (EpCAM), and therefore impervious to downregulation and potentially more useful as a prognosticator. This study examined CTC counts as measured by a novel EpCAM-independent assay and compared CTC counts with multiple known patient and tumor prognostic factors to determine the utility of pretreatment CTC levels as a preliminary prognostic biomarker for patients undergoing definitive radiation therapy (RT) for NSCLC.

METHODS: Pretreatment blood specimens were obtained on this institutional review board (IRB)-approved prospective clinical trial from patients with NSCLC who underwent 18F-fluorodeoxyglucose (18F-FDG)-positron emission tomography (PET) scans prior to starting stereotactic body radiotherapy (stage I) or concurrent chemoradiotherapy (stage III). CTC levels were identified via an adenoviral vector expressing the human telomerase (hTERT) promoter to drive expression of green fluorescent protein only in the presence of elevated telomerase activity (characteristic of almost all cancer cells but not normal cells). Patient characteristic prognosticators assessed included gender, race, and marital status, and the tumor characteristic prognosticators that were analyzed included tumor (T) stage, tumor diameter, tumor volume, histology, nodal (N) stage, clinical stage grouping, and metabolic activity on pretreatment 18F-FDG-PET. Differences and correlations between these prognosticators and pretreatment CTC levels were assessed by parametric t-tests, with statistical significance defined as P < .05.

RESULTS: Patients had stage I (n = 9) or stage III (n = 7) NSCLC with adenocarcinoma (n = 7), squamous cell carcinoma (n = 5), or poorly differentiated not otherwise specified (n = 1) histologies, with three patients treated with empiric stereotactic body radiation therapy (SBRT) for nonhistologically confirmed, 18F-FDG PET–avid lung nodules clinically consistent with stage I NSCLC. The mean tumor volume for all patients was 73.2 cm³ (range: 1.5–377.4 cm³) and 4.3 cm³ and 161.6 cm³ for stage I and III patients, respectively. Patients had a mean maximum standardized uptake (SUV max) on FDG-PET scan of 8.3 (range: 1.6–16.8; stage I mean 5.8, stage III mean 12.1). CTCs were detected in all patients, with a cohort mean of 26.3 per mL of blood. Elevated CTC levels significantly correlated with advanced N stage (≥ N2 vs N0–1; P = .007) and larger primary tumor volume (≥ 73.2 cm³ [mean tumor volume] vs < 73.2 cm³; P < .0001), with a trend toward significance for stage III vs stage I disease (mean 36.1 vs 3.2; P = .10). No significant correlations were seen between CTC levels and histological subtype (P = .24), SUV max (P = .77), or demographic prognosticators, including patient gender, race, and marital status (all P > .05).

CONCLUSIONS: In this pilot study assessing CTC levels using a novel telomerase-based assay that is independent of surface markers, pretreatment CTCs were detectable in all NSCLC patients, regardless of disease extent. CTC levels strongly correlated with advanced nodal stage and tumor volume. Integration of CTC levels with other pretreatment characteristics could enhance our ability to predict clinical outcomes and, with additional studies, could potentially prove to guide treatment recommendations.

(P069) Stereotactic Body Radiotherapy for T1 Versus T2 Non–Small-Cell Lung Cancers

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INTRODUCTION AND PURPOSE: Stereotactic body radiation therapy (SBRT) has become the treatment of choice for early-stage non–small-cell lung cancers (NSCLCs) in nonoperative candidates. Large prospective and retrospective series have established excellent local control (LC) and minimal toxicity in peripheral tumors smaller than 3 cm in stage (T1). The outcomes for T2 tumors are less well established. The purpose of this study was to examine the efficacy and toxicity of SBRT for stage T2 NSCLC.

MATERIALS AND METHODS: Patients treated with SBRT for T1 or T2 NSCLC were identified in a prospectively maintained institutional database that includes outcomes, demographic, clinicopathologic, and radiation treatment information. Toxicity was scored using the National Institutes of Health Common Terminology Criteria for Adverse Events version 4.0 (CTCAE v4.0). An acute toxicity was defined as a treatment-related side effect within 90 days of the first fraction; a late toxicity occurred after this time. The Kaplan–Meier method was used to estimate local control (LC), distant control (DC), disease-free survival (DFS), and overall survival (OS). Subgroups were compared with the log-rank test. Univariate and multivariate analyses were performed with SPSS.

RESULTS: A total of 244 consecutive patients who received SBRT between October 2007 and October 2013 were included—192 had T1N0M0 lesions and 52 had T2N0M0 disease; median tumor diameter was 2.0 cm (range: 0.54–6.4 cm). The median follow-up was 25.2 months (range: 0.9–68.5 mo). Median dose was 54 Gy with a range of 25–60 Gy (in 2–5 fractions); median biologically effective dose (BED) was 151.2 Gy (range: 56–180 Gy) using the linear-quadratic method with α/β = 10. The 2-year OS for T1 vs T2 disease was 59% vs 40% (median OS 31.2 mo vs 17.6 mo; P = .016). Both univariate and multivariate Cox regression analyses demonstrated a significantly increased risk of death for patients with T2 vs T1 disease (hazard ratio [HR] = 1.65; P = .018). Replacing T-stage with size thresholds of 2 cm, 3 cm, and 4 cm yielded similar results. T-stage was not significantly associated with 2-year LC (90% vs 77%; P = .42), DC (84% vs 77%; P = .47), or DFS (62% vs 52%; P = .50). T-stage was not significantly associated with 3-month freedom from acute toxicity (73% vs 79%; P = .47) or 2-year freedom from late toxicity (77% vs 78%; P = .52) on univariate or multivariate analyses. Of note, one acute grade 4 toxicity (pneumonitis) occurred in a patient after synchronous treatment of T1 lesions, and two late grade 4 toxicities (aspergillosis, pneumonitis) occurred in another two T1 patients. One late grade 5 toxicity (hemorrhage) occurred after synchronous treatment of T2 lesions.

CONCLUSIONS: SBRT for T2-stage NSCLC is associated with worse OS compared with T1 disease. There was a nonsignificant trend toward worse LC, DC, and DFS in T2 lesions, although these
findings were not significant. Overall, SBRT for T2 NSCLC was accomplished with acceptable toxicity, which was not significantly worse than that of T1 tumors.

(P070) Quantitative Analysis of Stereotactic Body Radiation Therapy (SBRT)-Induced Lung Injuries
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PURPOSE: Radiographic lung density changes are observed in most patients after stereotactic body radiotherapy (SBRT) for lung cancer. In this study, we assessed the relationship between SBRT dose and our treatment technique. Follow-up CT density changes were used as a surrogate for lung injury from SBRT.

METHODS: Six patients with non–small-cell lung carcinoma (NSCLC) were retrospectively assessed. Patients’ 4D-CT scans were acquired, and the reconstructed phase images were imported into the Phillips Medical Systems Pinnacle treatment planning computer. The internal target volume (ITV) for each patient was contoured using 10 to 14 phase image datasets. The planning target volume (PTV) was generated by adding a 5-mm margin to the ITV in the lateral and anterior-posterior directions and by adding a 7.5-mm cranial-caudal margin. Radiation Therapy Oncology Group (RTOG) protocol 0618 was generally followed for PTV dose coverage. A total dose of 48–54 Gy (32.33 ± 2.66 Gy) in three to five (3.50 ± 0.84) fractions to the isocenter was prescribed. Further, seven to nine coplanar and nonopposing conformal beams (8.50 ± 0.84 beams) were placed. The convolution dose algorithm with heterogeneity correction was used for dose calculations. Treatments were delivered on alternate days under cone beam CT (CBCT) image guidance. A follow-up positron emission tomography (PET)/CT scan was acquired 6–14 months (8.50 ± 3.02 mo) after SBRT treatment completion. The follow-up scan was then fused with the original planning CT. The high radiographic density region was contoured to determine the net SBRT-induced volume of lung tissue injury. The minimum dose causing radiographic injury was then determined.

RESULTS: The average and standard deviation for ITV, PTV, radiographic injury, and total lung volumes were calculated to be 12.74 ± 14.70 cm³, 49.67 ± 45.40 cm³, 16.49 ± 13.57 cm³, and 3,452.00 ± 235.00 cm³, respectively. The average radiographic injury volume-to-PTV ratio was 32.27 ± 21.67% (range: 0%–62%). The threshold dose responsible for radiographic injury was 10.70 ± 0.84 Gy, based on the scan acquired at an average of 8.50 months post-SBRT. There is a linear relationship between the biological effective dose (BED) with the radiographic injury volume.

CONCLUSIONS: In this study, increased CT density changes, a surrogate for damage to the normal lung tissue, was associated with higher BED and increasing PTV size, with a threshold dose of 10.70 Gy. Therefore, to reduce SBRT-induced lung injury, at least nine conformal equally weighted beams should be used to distribute dose evenly in normal lung tissue. Further, the noncoplanar and nonopposing conformal beams should be used if possible to minimize the radiographic injury. A study of serial follow-up scans of patients, at regular intervals, is warranted to determine the early and late SBRT-induced lung injuries.

(P071) SBRT Treatment of Central Chest Lesions: Experience at the University of California, San Francisco
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INTRODUCTION: Early experiences with stereotactic body radiotherapy (SBRT) for treatment of intrathoracic lesions have demonstrated excellent local control rates, upwards of 90% for primary and metastatic lesions in the lung parenchyma. However, there exists concern over normal tissue toxicity of central lung structures with such hypofractionated regimens; several single-institution series have recently reported varying rates of toxicity; and results of the Radiation Therapy Oncology Group (RTOG) 0813 trial are pending. We describe our institutional experience with SBRT treatment of central lung lesions and patient outcomes.

MATERIALS AND METHODS: We conducted a retrospective review of all patients who underwent robotic SBRT to thoracic lesions at UCSF from 2004–2012 (n = 482). We identified 90 patients who were treated for central lung lesions, defined as within 2 cm of the proximal bronchial tree. We describe patient and disease characteristics as related to locoregional control on routine interval imaging, as well as toxicity, as graded by Common Terminology Criteria for Adverse Events version 4 (CTCAE v4).

RESULTS: Of the 90 patients treated for central lung lesions, 18 patients were treated for primary lung tumors and 72 had recurrent or metastatic disease. Fifty-six percent of all patients had prior thoracic surgery, and 28% of all patients had prior thoracic radiotherapy. Median age at treatment was 65 years (range: 13–83 yr). Median Karnofsky performance score (KPS) was 80 (range: 40–90). Average lesion size was 2.7 ± 1.3 cm maximum transverse diameter (range: 0.5–6.2 cm). Average biological effective dose (BED) to the planning target volume (PTV) was 83 ± 30, over one to six fractions (median five), with dose per fraction ranging from 4–20 Gy. Median BED was 100 due to a large number of patients being treated with 50 Gy in five fractions (range: 20–180). With a median follow-up of 8 months (range: 0–71 mo, 12 mo primary lung, 12 mo living patients), 63% of patients reported no acute or late toxicity. One patient experienced acute grade 3 toxicity, consisting of radiation pneumonitis. Three patients experienced late-grade 3 toxicity, which were of respiratory or cardiac etiology. BEDs were 72, 100, and 100. Of the two patients who experienced grade 3 pulmonary toxicity, both had prior thoracotomies. None had prior RT. One patient’s tumor was within the mainstem bronchus. The patient with cardiac toxicity had a prior history of arrhythmia and coronary artery disease. The Kaplan-Meier estimate of locoregional control for all patients was 69% at 1 year.

CONCLUSION: We demonstrated local control of nearly half of all treated lesions associated with minimal toxicity. To increase local control, in the future we will raise the BED to treated lesions. Three percent of patients experienced greater than grade 2 treatment-related toxicity, which may have been confounded by systemic disease progression or prior surgery.
(P072) Reducing Radiation Dose to the Breast in Female Patients Undergoing Stereotactic Body Radiotherapy for Lung Cancer

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PURPOSE AND OBJECTIVES: Stereotactic body radiotherapy (SBRT) is gaining prominence as an effective treatment for early-stage inoperable non–small-cell lung cancer (NSCLC). To date, little attention has been paid to the radiation dose delivered to the breast tissue in female patients.

MATERIALS AND METHODS: We retrospectively reviewed the treatment plans and dose–volume histograms of all female patients undergoing lung SBRT at our institution from July 2010 to October 2013. No dose constraints were placed on the breasts initially. Bilateral breasts were retrospectively contoured to determine the dose received. The 14 plans receiving the highest mean ipsilateral breast dose were replanned, taking into account the breasts as organs at risk (OARs) using the following published constraints developed to minimize contralateral breast dose during intensity-modulated radiation therapy (IMRT): breast cancer treatment: $D_{\text{mean}} < 2$ Gy; $V_5 < 15$%; and $V_2 < 50$%. Statistical analysis was performed using SPSS v19.

RESULTS: A total of 84 patients underwent lung SBRT at our institution during the study period, of whom 42 were female. Twelve were excluded from this analysis because of a history of previously treated breast cancer ($n = 7$) or previous thoracic radiation ($n = 5$). Of the remaining 30 patients, the median age was 79 years (range: 59–94 yr). The predominant histology was adenocarcinoma ($n = 24$). Tumor stage was as follows: $T_1a = 12$, $T_1b = 11$, and $T_2a = 7$. Twenty tumors were right-sided, eight were left-sided, and three patients presented with bilateral tumors. Median dose was 48 Gy in four fractions (range: 32.5–56 Gy). Median planning target volume (PTV) was 30.2 cc. The median $D_{\text{mean}}$, $V_5$, and $V_2$ received by the ipsilateral breast initially were 261 cGy, 19.5%, and 26.2%, respectively. PTV and breast volume were not significant predictors of any of the aforementioned dosimetric parameters. Isocenter location anterior to the carina did significantly correlate with the ipsilateral breast $D_{\text{mean}}$ and $V_5$ ($P < .05$ for both). Results of the 14 patients who were replanned are shown in Table 1. $D_{\text{mean}}$, $V_5$, and $V_2$ were significantly lowered after replanning ($P < .05$ for all). Replanning did not significantly increase the total lung V20, ipsilateral lung V20, chest wall V30, heart $D_{\text{max}}$, esophagus $D_{\text{max}}$, contralateral breast $D_{\text{mean}}$, or $V_2$. There was a nonsignificant increase in the ipsilateral breast $D_{\text{max}}$. The spinal cord $D_{\text{max}}$ and contralateral breast $V_5$ were significantly increased, though still within tolerance.

CONCLUSION: This study demonstrates that incorporating constraints that minimize breast dose in lung SBRT is feasible and does not result in excess dose to other critical structures. With increasing long-term survivorship after SBRT for early-stage NSCLC, there is a commensurate increasing likelihood of patients developing a metachronous primary breast cancer. Limiting the dose to the breast, especially for tumors anterior to the carina, may preserve the option of breast-conserving therapy in those patients, as well as lower the as-yet unquantified risk of radiation-related late toxicity in the breast.

(P073) Helical Tomotherapy-Based Stereotactic Radiotherapy Is Safe and Effective in the Treatment of Peripheral Thoracic Tumors

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BACKGROUND: Stereotactic body radiotherapy (SBRT) has been established as the standard of care in medically inoperable patients with peripherally located early-stage non–small-cell lung cancer (NSCLC). Our objective is to report outcomes, toxicity, and dose-volume histogram (DVH) data for patients receiving helical tomotherapy–based SBRT. We hypothesize that adverse effects and oncologic outcomes using a helical approach will be similar to those previously reported using nonhelical treatment platforms.

METHODS: A retrospective review was performed for all consecutive patients with peripheral, early-stage NSCLC, or oligometastatic lung lesions treated at our institution from 2008–2013. All patients were treated with helical tomotherapy-based SBRT, where treatment planning followed full-body immobilized 4-D simulation with or without abdominal compression. Demographic data, DVH data, local failure (LF) as defined by Response Evaluation Criteria in Solid Tumors (RECIST), toxicity using Common Terminology Criteria for Adverse Events version 4.0 (CTCAE v4.0), progression-free survival (PFS), and overall survival (OS) were analyzed. The Kaplan-Meier method was used to estimate survival functions, while Cox regression (for PFS and OS) and competing risks analysis (for LF) were used to analyze the survival endpoints. The Fisher’s exact test was used to analyze association of prior therapy with development of clinical radiation pneumonitis (CRP).

RESULTS: Seventy-six patients (85 lesions) meeting the criteria above were identified. Fifty-three patients (70%) met Radiation Therapy Oncology Group (RTOG) criteria for early-stage NSCLC (American Joint Committee on Cancer [AJCC] 7th ed $T_1–2aN0M0$), whereas 23 (30%) did not. Mean age was 71 years, with 37 (49%) male and 39 (51%) female patients. The most common SBRT fractionation scheme was 48 Gy administered in four fractions over 2 weeks (70%). Local failure rate for all patients at 1 year was 3.2%, and 2-year rate was 10.3%. Median PFS and OS for all patients were 1.42 years (95% confidence interval [CI], 0.95–1.71 and 2.04 years (95% CI, 1.71–NR [not reached]). For patients with early NSCLC, median PFS and OS were 1.35 years (95% CI, 0.95–2.95) and 1.89 years (95% CI, 1.42–NR), respectively. Median percent lung volume receiving minimum 5 Gy (V5) was 21% (95%–
SBRT appears to be a safe and effective treatment for high-risk prostate carcinoma. Our data suggest that SBRT alone, without pelvic radiotherapy or ADT, may be the optimal approach. Further follow-up and additional studies are required to corroborate our results.

(P076) Stereotactic Body Radiation Therapy (SBRT) for the Primary Treatment of Localized Prostate Cancer
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INTRODUCTION: The American Society of Radiation Oncology (ASTRO) model policy update, published April 17, 2013, acknowledges that stereotactic body radiation therapy (SBRT) is equivalent to standard radiation modalities used to treat prostate cancer, such as intensity-modulated radiation therapy (IMRT). Furthermore, ASTRO supports the treatment of low- and intermediate-risk prostate cancer with SBRT, where it has excellent biochemical control rates with correspondingly low rates of severe toxicity. However, only recently have 5-year data been published, with a limited sample size. We report an update of our previously published experience for primary treatment of prostate cancer with CyberKnife SBRT, assessing efficacy and toxicity.

METHODS: From 2007 to 2012, 143 localized prostate cancer patients were treated with primary SBRT using the CyberKnife system. Risk groups analyzed ranged from very low (20%) and low (24%) to intermediate (43%) and high (14%). Various dose levels were used over the years of treatment and, for the purpose of this study, have been categorized into low-dose (35 Gy, n = 5 or 36.25 Gy, n = 109) and high-dose (37.5 Gy, n = 30). All treatments were delivered in five fractions. Twenty-nine percent of the patients received androgen deprivation therapy, usually administered to intermediate- and high-risk patients.

RESULTS: At a median follow-up time of 33 months, the median PSA value was 0.30 ng/mL. The 5-year freedom from biochemical failure (FFBF) was 94.1%, 93.9%, and 82.5% for very low-/low-, intermediate-, and high-risk patients, respectively. A dose response was observed between the low-dose and high-dose groups for all patients, with FFBF of 79.8% vs 100.0% (P = .0396), respectively, and for the combined group of intermediate- and high-risk patients, with FFBF of 87.6% vs 100.0% (P = .1255), respectively. Severe genitourinary (GU) toxicities included 2% acute and 3% late toxicities. No severe gastrointestinal toxicities were observed. At last follow-up, 12% of hormone-naive patients lost the ability to achieve erections strong enough for penetration and required erectile dysfunction (ED) medication for intercourse. No hormone-naive patient who was potent before SBRT developed ED refractory to medical treatment.

CONCLUSION: Our experience with CyberKnife SBRT for localized prostate cancer demonstrates favorable efficacy with less toxicity compared with the outcome for IMRT as reported in the literature.

(P077) Evaluating the Face of Failure: A Model to Predict Prostate Cancer Recurrences Using PSA Trends Following Brachytherapy Implant
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METHODS: From 2007 to 2012, 143 localized prostate cancer patients were treated with primary SBRT using the CyberKnife system. Risk groups analyzed ranged from very low (20%) and low (24%) to intermediate (43%) and high (14%). Various dose levels were used over the years of treatment and, for the purpose of this study, have been categorized into low-dose (35 Gy, n = 5 or 36.25 Gy, n = 109) and high-dose (37.5 Gy, n = 30). All treatments were delivered in five fractions. Twenty-nine percent of the patients received androgen deprivation therapy, usually administered to intermediate- and high-risk patients.

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CONCLUSION: Our experience with CyberKnife SBRT for localized prostate cancer demonstrates favorable efficacy with less toxicity compared with the outcome for IMRT as reported in the literature.
Medical Center Utrecht; Prostate Cancer Center of Seattle

PURPOSE: Following a brachytherapy implant for the treatment of prostate cancer, serial prostate-specific antigen (PSA) measurements are an important indicator of treatment response and disease control. When PSA rises during follow-up, clinicians must formulate appropriate workup to evaluate for recurrences and avoid unnecessary management if possible. We sought to develop a model for predicting prostate cancer recurrence by evaluating post-treatment PSA kinetics in patients with clinical failures.

MATERIALS AND METHODS: Our current analysis includes 1,816 patients treated with brachytherapy for prostate cancer from three contributing institutions. Disease recurrence was strictly defined as a recurrence confirmed by rising PSA and either a biopsy or radiographic confirmation of local or systemic disease. PSA trajectories were analyzed based on regression fit using a multilevel model among three arms: (1) none, (2) local, and (3) distant recurrences. Furthermore, three components of PSA trajectory (rate of decline, nadir, and rate of rise) were compared among the three groups.

RESULTS: The median follow-up for these 1,816 patients was 4.75 years, with a median pretreatment PSA of 6.6 ng/mL. Among this large cohort, there were only 37 clinically proven recurrence events after excluding biochemical failures alone. Using a quadratic fit model, the overall PSA trajectory analysis showed clear divergence of the PSA values for local failures compared with distant. However, the divergence was not statistically significant until 2 years postimplant (Year 1 \( P = .888 \); Year 2 \( P = .026 \); Year 3 \( P = .0012 \); Year 4 \( P = .001 \)). Interestingly, prior to clinical failure, PSA doubling time for local failures remained relatively constant, while for distant failures, doubling time decreased with time. To further evaluate PSA trajectory, several key components were examined. The rate of PSA decline was analyzed using an ANOVA test and revealed a significant difference between the three groups at the 6-month (\( P = .037 \)), 12-month (\( P = .003 \)), and 18-month (\( P = .007 \)) time points. Additionally, PSA nadir was evaluated for nonrecurrent patients compared with those who recurred (locally or distantly); nadir was not significantly different until the 12-month time point (\( P = .04 \)). A cutpoint analysis between no failures and local failures identified that a nadir below 1.8 ng/mL at 24 months was predictive of no local recurrences (\( P = .003 \)) and below 0.6 ng/mL at 42 months was predictive (\( P < .001 \)). Finally, the rate of PSA increase was also evaluated at 6-month time intervals; once again, it did not reach significance among the three groups until the 12-month interval postimplant (\( P < .001 \)) and remained significant throughout all subsequent time intervals (18 mo \( P = .01 \); 24 mo \( P < .001 \); 30 mo \( P < .001 \); 36 mo \( P < .001 \); 42 mo \( P < .001 \); 48 mo \( P < .001 \)).

CONCLUSIONS: This preliminary analysis suggests that following permanent brachytherapy implant for prostate cancer, close observation of PSA trends may predict patients who will ultimately recur and that differentiating between local and distant recurrences may be possible. Currently, additional patients are being added to the model for a more robust analysis of PSA trends. Ultimately, this large, multi-institutional analysis may produce a model that can predict postbrachytherapy failures by incorporating PSA kinetics and evaluating the PSA trajectory.

(P078) Using a Deformable Bladder Planning Contour Reduces Repeat CBCTs During Prostate Image-Guided Intensity-Modulated Radiation Therapy

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PURPOSE: To determine if a deformable bladder planning contour (DBPC) can help minimize repeat cone beam computed tomography (CBCTs) during a course of prostate image-guided volumetric arc radiation therapy (IG-VMAT).

MATERIALS AND METHODS: Between September 24, 2013 and November 1, 2013, a total of 246 patients were consecutively treated for prostate cancer using image-guided intensity-modulated radiation therapy (IG-IMRT) with VMAT, either in the definitive or postprostatectomy setting. Daily kilovoltage (kV) CBCT scans provided image guidance for all patients with matches made to gold fiducial markers for those with intact prostates or to the prostate bed/bony anatomy for those postprostatectomy. A radiation therapist and a physician prospectively reviewed each CBCT on a daily basis, and the images were compared with the CT simulation images, which included the prostate or prostate bed, seminal vesicles, nodal region if applicable, planning target volume (PTV), rectum, and bladder. Patients were typically simulated with a full bladder. During treatment planning, our dosimetry team manually generated a DBPC as a structure typically smaller than the bladder at simulation but one that met our minimum bladder dose constraints: bladder D5, and D20, of 7,200 cGy and 4,000 cGy, respectively. These dose constraints were notably more stringent than the current bladder dose constraints utilized by the ongoing Radiation Therapy Oncology Group (RTOG) protocol 08-15 (D15, D25, D35, and D50 of 8,000, 7,500, 7,000, and 6,500 cGy, respectively). These comparisons and whether a repeat CBCT was performed due to a bladder issue were all recorded. Prior to a repeat CBCT for a bladder issue, the patients were taken off the table, typically to drink more water or rarely to void urine. The decision to repeat the CBCT was made at the discretion of the radiation oncologist.

RESULTS: A total of 4,509 CBCT scans on 246 consecutively treated prostate cancer patients were prospectively reviewed. Further, 429 (9.5%) CBCT scans were repeated. Of the repeat scans, 230 (54%) CBCTs were repeated because of a bladder issue. The bladder size on treatment was smaller than, larger than, or the same size as the DBPC in 352 (8.5%) cases, 2,920 (69.5%) cases, and 926 (22%) cases, respectively. When the bladder at treatment was smaller than the DBPC, a repeat CBCT was performed in 218 cases (62%). When the bladder at treatment was the same size or larger than the DBPC, a repeat CBCT was performed in 25 cases (0.6%).

CONCLUSIONS: An underfilled bladder volume is the most common reason for repeat CBCT scans in IG-VMAT for prostate cancer. The use of a simple dosimetric supplemental bladder structure known as DBPC can greatly reduce the number of repeat CBCT scans due to incompletely filled bladders on treatment without compromising the ability to meet bladder dose constraints. Using a smaller DBPC that meets RTOG criteria may further improve these results.
(P079) Linac-Based SBRT Delivered in Five Fractions for Definitive Prostate Cancer Treatment Using VMAT and Flattening Filter-Free Beams: The Phase II Lankenau Experience

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BACKGROUND: To evaluate the feasibility and toxicity of hypofractionated stereotactic body radiation therapy (SBRT) with volumetric modulated arc therapy (VMAT) and flattening filter-free (FFF) beams.

METHODS: A prospective National Cancer Institute (NCI)-designated phase II study was approved by our institutional review board (IRB) (started in October 2011). Inclusion criteria were histologically proven prostate adenocarcinoma, Gleason Score 6–7, clinical stage T1b–T2b, prostate-specific antigen (PSA) ≤ 20 ng/mL, prostate volume ≤ 100 cc, Eastern Cooperative Oncology Group (ECOG) performance status 0–1, no prior prostatectomy, cryotherapy, or radiotherapy to the prostate. SBRT was delivered at a prescribed planning target volume (PTV) dose of 36.25 Gy in five fractions using the TrueBeam STx. Patients self-reported on validated quality of life (QOL) measures, such as American Urological Association (AUA) Index, Sexual Health Inventory for Men (SHIM), Utilization of Sexual Medications/Devices (USMD), Expanded Prostate Cancer Index Composite Short Form (EPIC-26) with five components (urinary irritative, urinary incontinence, bowel, sexual, and hormonal), and Short Form-12 (SF-12) with two components (physical and mental). Patients were analyzed at predefined time intervals.

RESULTS: A total of 25 patients have been recruited to date. Mean age of the patients was 68 years (range: 52–80 yr). Mean Gleason score was 6.32 (range: 6–7). Mean PSA was 6.45 ng/mL (range: 0.63–18.7 ng/mL). All patients tolerated the treatment well with no acute adverse effects, as noted on their QOL questionnaires. Evaluating patients in a time period ranging from 6 to 24 months, the EPIC-26 showed a significant difference using the Kruskal-Wallis Test between average total score at pre-entry when compared with 1-month, 6-month, and 12-month evaluations. However, mean pre-entry score was not significantly different from mean score at 24 months, demonstrating a transient decline in the bowel-related QOL. Also patients’ perception of bowel urgency showed no impact on QOL on the EPIC-26.

CONCLUSION: Early findings indicate that SBRT with VMAT and FFF beams for low-intermediate-risk prostate cancer delivered in five fractions is feasible and tolerated well. Long-term follow-up is needed for assessment of late toxicity and outcomes.

(P080) After the Thaw: Prostate IGRT Effectively Treats Cryotherapy Failures

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PURPOSE: To retrospectively analyze the efficacy and toxicity of image-guided radiotherapy (IGRT) in the management of prostate cancer (PCA) recurrence after primary cryotherapy.

METHODS: Patients with organ-confined PCA who developed biochemical failure after cryotherapy were treated with definitive IGRT. Acute and late genitourinary (GU) and gastrointestinal (GI) side effects were scored every 4 months using the Common Terminology Criteria for Adverse Effects (CTCAE). PSA was measured at 4- to 6-month intervals after IGRT.

RESULTS: From 2011 through 2013, 16 patients (9 low-risk, 5 intermediate-risk, and 2 high-risk) who failed to respond to primary cryotherapy were treated with 7,920 cGy IGRT. Thirty-one percent received a short course of concurrent androgen suppression. The median age was 72 years (range: 47–80 yr); The median prerecruitment PSA was 4 ng/mL (range: 1.6–17 ng/mL); the median interval from cryotherapy to IGRT was 48 months (range: 12–84 mo); and the median pre-IGRT PSA was 3.4 ng/mL (range: 1.2–27 ng/mL). At a median follow-up of 18 months (range: 9–34 mo), biochemical control was achieved in all patients. Fifty-six percent of patients developed grade 2 GU toxicity requiring the use of an alpha-blocker or cholinergic receptor antagonist, and 12% developed grade 2 GI toxicity requiring the use of corticosteroid suppositories. These side effects resolved within 12 months. No grade 3 toxicity was encountered.

CONCLUSION: Prostate IGRT after cryotherapy failure is well tolerated and, early results show excellent PSA response.

(P081) An Analysis of Soft Tissue Anatomy and Tracking of the Prostate Using Transperineal Ultrasound

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PURPOSE AND OBJECTIVES: Transperineal ultrasound (TPUS) imaging is capable of providing low-cost, noninvasive, and accurate anatomic imaging of the male pelvis without the use of ionizing radiation. TPUS imaging can also be utilized during external beam radiation therapy (EBRT) to aid in treatment simulation to improve visualization of soft tissue anatomy. Furthermore, this modality may be used during daily treatment delivery to localize the prostate and organs at risk (OARs) within the pelvis using native anatomic structures. Thus, this procedure would allow clinicians to perform precise intrafraction prostate-tracking. Magnetic resonance imaging (MRI) is currently employed as an adjunct to CT for enhanced soft tissue imaging. However, this study requires image fusion with CT, which can be a source of uncertainty and can not be used during treatment. In contrast, TPUS is portable and functions via benign acoustic waves, which have not been shown to affect the treatment field. Apart from these inherent advantages, TPUS imaging is more cost-effective than MRI. Given these advantageous features, we demonstrate that TPUS can identify structures of the male pelvis similar to those images gathered from an MRI prior to simulation.

MATERIALS AND METHODS: In order to evaluate the effectiveness of TPUS imaging, we analyzed the data collected for seven patients as part of an institutional review board (IRB)-approved clinical trial.
imaging has the promise to enhance seed localization compared to standard ultrasound imaging. Photoacoustic imaging utilizes light transmitted into tissue; metallic seeds absorb the transmitted light, undergo thermoelastic expansion, and generate sound waves that are detected with a conventional transrectal ultrasound probe. Excellent seed contrast is expected in photoacoustic images, because the optical absorption of brachytherapy seeds is orders of magnitude larger than that of the surrounding tissue, and this difference is larger than the corresponding acoustic echo difference. We conducted an institutionally approved canine study to investigate the in vivo feasibility of intraoperative seed visualization with photoacoustic imaging.

**MATERIALS AND METHODS:** Brachytherapy seeds, coated with black ink, were transperineally inserted into a live canine prostate. A transperineal, interstitial, fiberoptic light delivery method, coupled to a 1064-nm Nd:Yag laser, was used to emit laser into the prostate containing the seeds. The resulting acoustic waves were detected with a conventional transrectal ultrasound probe (Ultrasonix, BPI9-S/55, Richmond, BC, Canada) connected to a clinical ultrasound scanner (Ultrasonix Sonixtouch). Raw pre-beam-formed photoacoustic data were collected with a Sonixdaq data acquisition unit that was connected to a probe port on the ultrasound scanner. Ultrasound and postoperative CT images of the implanted seeds were acquired and analyzed to confirm seed locations in the photoacoustic images.

**RESULTS:** Multiple brachytherapy seeds were visualized within the in vivo prostate within American National Standards Institute (ANSI) laser safety limits for human exposure (100 mJ/cm²). Seeds that were difficult to localize in standard ultrasound images were more visible in coregistered photoacoustic images. The average seed contrast in the photoacoustic images was 20–30 Db for energy densities ranging from 8–84 mJ/cm² when the short-lag spatial coherence beamformer was applied to the raw data. There was excellent agreement between photoacoustic, ultrasound, and CT images.

**CONCLUSION:** Photoacoustic imaging is a promising complement to ultrasound imaging for intraoperative brachytherapy seed visualization. Work is ongoing for eventual translation into human clinical trials.

**P084** Prostate Volume > 60 ml Increases Risk of Urinary Retention in Prostate Cancer Patients Undergoing High-Dose-Rate Brachytherapy Monotherapy

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**INTRODUCTION:** The American Brachytherapy Society consensus guidelines state that prostate volume > 50 mL is a relative contraindication to high-dose-rate (HDR) brachytherapy. We reviewed our experience with HDR brachytherapy to determine if prostate volume affected prostate target coverage or the risk of acute urinary toxicity.

**MATERIALS AND METHODS:** Between January 2011 and October 2013, a total of 92 patients with low-risk or favorable intermediate-risk prostate cancer were treated with HDR brachytherapy monotherapy to 2,700–2,800 cGy in two 1,350–1,400-cGy fractions separated by 2–3 weeks. Prostate volumes and dose distributions

**CONCLUSION:** Patients with prostate volume > 60 ml at the time of implantation were at greater risk of acute urinary retention postoperatively.
were calculated based on pretreatment planning computed tomography (CT) scans. No androgen deprivation therapy was administered. Acute urinary toxicities within 30 days of radiation completion were recorded according to the Common Terminology Criteria for Adverse Events version 4 (CTCAE v4).

RESULTS: Median prostate volume was 51 mL (range: 25–129 mL). Twenty-four patients (26%) had a prostate volume > 60 mL. A prostate volume > 60 mL did not significantly affect mean prostate D90 (105.4 ± 1.9 vs 105.0 ± 3.0; \(P = .43\)) or V100 (94.8 ± 2.1 vs 94.8 ± 2.8; \(P = .98\)). There was no difference in acute grade 2 or greater cystitis (3 of 21 [14%] vs 11 of 57 [19%]; \(P = .67\)). However, patients with a prostate size > 60 mL did have a significantly higher rate of acute grade 2 urinary retention (5 of 19 [26%] vs 4 of 64 [6%]; \(P = .03\)). On logistic regression multivariable analysis, when accounting for age, clinical T-stage, pretreatment PSA, Gleason score, and pretreatment International Prostate Symptom Score (IPSS), a prostate volume > 60 mL was the only variable significantly associated with grade 2 acute urinary retention (odds ratio [OR] = 4.2; 95% confidence interval [CI], 1.0–17.3; \(P = .046\)). No patients had acute grade ≥ 3 urinary toxicities.

CONCLUSIONS: A prostate volume > 60 mL did not affect coverage of the prostate, as measured by the D90 or V100. However, a prostate volume > 60 mL increased the relative risk of acute grade 2 urinary retention.

(P085) Exploiting Androgen-Induced DNA Double-Strand Breaks: Optimal Sequencing of Androgen Suppression and Radiation for Superior Tumor Control in the Treatment of Prostate Cancer

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PURPOSE: Androgen suppression (AS) combined with radiation therapy is currently a standard of care in the treatment of intermediate- and high-risk prostate cancer (PCA), and this combination compared with radiation alone has been shown to improve therapeutic outcomes. Historically, the optimal sequencing of the two modalities has not been thoroughly tested. It was recently discovered by our group that androgen stimulation of PCA cells can result in the formation of topoisomerase II beta (TOP2B)-mediated DNA double-strand breaks (DSBs). Here, aiming to exploit this finding, we investigated the extent and timing of TOP2B-mediated DSBs in vitro, as stimulated by androgens. In addition, we explored the combination of androgen stimulation with radiation and its effects on tumor growth in an animal model.

METHODS: Androgen-sensitive LAPC4 PCA cells were grown in androgen-free media for 3 days. Androgen (R1881) was added at a final concentration of 100 nM, and the formation of DSBs at various time points was monitored by visualization of γH2AX foci and by comet assay analysis. For in vivo xenografts, nude mice were castrated, and silastic implants containing androgen were implanted. Cells were injected in the mouse flank. When tumor volumes reached approximately 0.1 cm³, the implants were removed for 16 days prior to reimplantation. A total of 8 Gy of ionizing radiation was delivered 4 days prior to reimplantation (traditional group) or at 12 hours after reimplantation (experimental group). The control group did not receive radiation; tumors were measured every other day, and time to 4× initial tumor volume was determined.

RESULTS: Addition of androgen to LAPC4 cells resulted in a significant increase in the number of γH2AX foci per cell: untreated (11.6 ± 3.3), 2-hour treatment (19.3 ± 5.4), and 6-hour treatment (45.2 ± 8.1) (\(P < .01\)). Comet assay (tail moments) results were consistent with γH2AX findings: untreated (14.3 ± 6.4), 2-hour treatment (29.8 ± 7.4), and 6-hour treatment (39.4 ± 11.5) (\(P < .03\)). The time to 4× tumor growth was significantly delayed in the experimental group (63.0 d) compared with the traditional (31.5 d) and control groups (23.0 d) (\(P < .01\)).

CONCLUSIONS: We provide evidence that irradiating tumors at a time point when formation of androgen-induced DSBs is ongoing provides superior control when compared with radiation that is delivered when tumors are fully deprived of androgens. These results may have significant implications for altering current clinical management of intermediate- and high-risk prostate cancer treated with definitive radiotherapy. There are numerous approaches that could be utilized in leading to transient increases in testosterone in patients, along with AS cycling, that are currently being tested in animal models and being proposed for human trials. In light of the new details uncovered about the mechanisms of androgen receptor (AR) signaling and downstream affects at the level of DNA processing, taking advantage of the very mechanism by which prostate cancers may grow (AR pathway) and using this knowledge to further improve therapeutic ratios in the setting of definitive radiotherapy is an attractive approach.

(P086) The First National Experience of TraceIT™ Tissue Marker Placed Intravesically under Local Anesthesia for Imaging Visualization of Recurrent Muscle-Invasive Transitional Cell Carcinoma for Targeted Radiotherapy

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BACKGROUND: Radiation oncologists often combine, or fuse, magnetic resonance (MR) and CT images to improve dose planning and accuracy. However, most markers do not have equivalent visibility on both CT and MR, creating a permanent image artifact in areas of particular interest and limiting their usefulness for image fusion. The TraceIT Tissue Marker (Augmenix, Waltham, MA) is an injectable polyethylene glycol-based hydrogel marker designed to be visible under CT, cone beam CT (CBCT), MR, and ultrasound imaging for 3 months after implantation and then absorbed within 7 months.

METHODS: Two patients with muscle-invasive bladder tumor underwent endoscopic injections of TraceIT for tumor localization in preparation for radiotherapy. The first patient was an 80-year-
administration (FDA), Ra-223 injections consisted of one dose of
accordance with the recommended dosage by the Food and Drug
Ra-223 were collected from a large multidisciplinary group. In
improve an oncological outcome with minimal side effects.

costs, side effects, and hematologic profile of patients with
ated with Ra-223’s cytotoxic mechanism of action and excretion

introduction and objectives: The many advantages associ-
and a Gleason score (GS) of ≥ 8; (2) pT3bN0 disease; (3) T2–T3aN0
disease with a PSA doubling time of ≤ 10 months; or (4) T2–T3aN0
disease with a pre-RT PSA of ≥ 1.0 ng/mL. The postprostatectomy
trimodality treatment consisted of 6 months of hormone therapy
(Casodex [50 mg po daily] and Zoladex [10.8 mg sc q 3 mo × 2] or
Lupron [22.5 mg im q 3 mo × 2]), 3D-CRT to 66.0 Gy at 2.0 Gy/fx
once daily (50 Gy to the surgical bed followed by a 16-Gy boost at
2.0 Gy/fx using either 3D-CRT or intensity-modulated radiation
therapy (IMRT), usually began after 2 months of hormone thera-

results: This cohort comprised 19 Caucasian men of median age
74 years (range: 53–85 y). All had bone metastasis. At baseline,
13.3% graded the pain at 1 according to the WHO pain score. At
the first follow-up, 27 days (range: 19–35 d) after the first injection,
21.5% (2/19) noticed pain relief and 37.5% had a WHO score of 1.
At 22 days after the second injection (range: 21–22 d), 44.4% (8/18)
reduced pain symptoms and 37.5% had a WHO score of 1. At
the third follow-up, 35 days (range: 22–35 d) after the third injec-
tion, 50% (6/12) had pain relief and 50% had a WHO score of 1.
Also, for 10.5% (n = 2) of our cohort, pain symptoms worsened,
while 21% (n = 4) reached total pain remission by the third injec-
tion. Increased bowel movement frequency was observed in 10.5%
of our cohort, diarrhea in 31.6%, constipation in 5.3%, nausea in
26.3%, vomiting in 5.3%, bone pain flare response in 26.3%,
and lower limb edema in 10.5%.

conclusions: Our short-term results demonstrated promising
bone-pain-relieving effects of Ra-223 in 50% of our patients, even
after a maximum of only three injections. Encountered side effects
were mild, including mostly gastrointestinal symptoms, but a
21.3% platelet reduction was observed by the third injection.

(p088) feasibility and efficacy of trimodality therapy
in patients with high-risk pathologic t2–3 n0 m0 prostate cancer:
preliminary results of an ongoing phase i/ii trial
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md, xinglei shen, md, james coster, md, jacek pinski, md;
university of Kansas school of medicine; University of Southern
California keck School of medicine
purpose and objectives: The objective of this ongoing phase
I/II trial is to determine the safety, feasibility, and efficacy of post-
prostatectomy 3D conformal radiation therapy (CRT), hormone
therapy, and concurrent docetaxel in patients with high-risk patho-
logic T2–3N0M0 prostate cancer.

patients and methods: Postprostatectomy high-risk prostate
cancer was defined as clinically nonmetastatic disease with an
undetectable, persistent, or rising prostate-specific antigen (PSA)
with one or more of the following clinicopathologic features: (1)
pathologic (p) T2–T3aN0 disease, positive or negative margins,
and a Gleason score (GS) of ≥ 8; (2) pT3bN0 disease; (3) T2–T3aN0
disease with a PSA doubling time of ≤ 10 months; or (4) T2–T3aN0
disease with a pre-RT PSA of ≥ 1.0 ng/mL. The postprostatectomy
trimodality treatment consisted of 6 months of hormone therapy
(Casodex [50 mg po daily] and Zoladex [10.8 mg sc q 3 mo × 2] or
Lupron [22.5 mg im q 3 mo × 2]), 3D-CRT to 66.0 Gy at 2.0 Gy/fx
once daily (50 Gy to the surgical bed followed by a 16-Gy boost at
2.0 Gy/fx using either 3D-CRT or intensity-modulated radiation
therapy (IMRT), usually began after 2 months of hormone thera-

(p087) early experience of radium-223 treatment
for metastatic castration-resistant prostate cancer: a preliminary report
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md, deborah zehel, bsc, modar alom, md, david m. albala, md,
vladimir mouraviev, md, phd, john crawford, md; associated
medical professionals of ny; University of montreal
introduction and objectives: The advantages associated
with Ra-223’s cytotoxic mechanism of action and excretion
make it a stronger and less myelotoxic and nephrotoxic option than
its counterparts (Sm-153 and Sr-89). We report the short-term pain
resolution, side effects, and hematologic profile of patients with
metastatic castration-resistant prostate cancer (mCRPC) undergo-
ing Ra-223 treatment.

methods: Clinical data from 19 mCRPC patients treated with
Ra-223 were collected from a large multidisciplinary group. In
accordance with the recommended dosage by the Food and Drug
administration (FDA), Ra-223 injections consisted of one dose of
50 kBq/kg monthly for 6 months. Up to the third injection, the
World health organization (WHO) pain scale was assessed, and the pain patterns were evaluated and classified in
groups: no or minimal pain relief, worsening of pain, and improve-
ment of pain. Also, short-term incidence of side effects was report-
ed together with the hematologic parameters at each injection.
Data are expressed as a median (range).

results: Clinical data from 19 mCRPC patients treated with
Ra-223 were collected from a large multidisciplinary group. In
accordance with the recommended dosage by the Food and Drug
administration (FDA), Ra-223 injections consisted of one dose of

70
and concurrent weekly docetaxel at 20 mg/m² × 7.

RESULTS: Between October 2008 and October 2013, a total of 20 patients have been enrolled to this ongoing phase I/II clinical trial. The clinical and disease characteristics of these 20 patients are median age = 64 years (range: 56–73 yr); GS 3 + 4 = 7 in five patients, 4 + 3 = 7 in three patients, 3 + 5 = 8 in two patients, 4 + 4 = 8 in two patients, 4 + 5 = 9 in four patients, and 5 + 4 = 9 in three patients; resection margin negative in five patients, close in two, and positive in 13 patients; extracapsular extension absent in six patients and present in 14; seminal vesicle invasion present in 10 patients and absent in 10; and pathologic T-stage was pT1a in one patient, pT2c in three patients, pT1a in six patients, and pT3b in 10 patients. Thirteen of the 20 enrolled patients have completed their entire trime-dotherapy. Five of the remaining patients have completed their chemoradiation therapy and most of their hormone therapy, and the remaining two patients just started their hormone therapy recently. The feasibility rate among the 13 patients who have completed their entire trime-dotherapy was 100%. None of these 13 patients experienced any grade ≥ 3 gastrointestinal (GI) and/or laxative-related grade 3 diarrhea but no GU grade ≥ 3 acute toxicity; the other three patients completed their entire chemoradiation therapy and are still taking their hormone treatment, two experienced diet-and/or laxative-related grade 3 diarrhea but no GU grade ≥ 3 acute toxicity; the other three patients completed their entire chemoradiation therapy without any treatment-related grade ≥ 3 acute GI and/or GU toxicity. The remaining two patients on the trial just started their hormone therapy.

CONCLUSIONS: The preliminary results of our ongoing phase I/II clinical trial indicate that our postprostatectomy trime-dotherapy is well tolerated, with a 100% feasibility rate, in patients with high-risk pT2–3N0M0 prostate cancer. We will continue to accrue patients to this trial until ≥ 30 patients have been enrolled.

(P089) A Phase III Randomized Trial of MRI-Mapped Dose-Escalated Salvage Radiotherapy Postprostatectomy: The Maps Trial—An Initial Dosimetric Assessment

Amber Orman, MD; Alan Pollack, MD, PhD; Radka Stoyanova, PhD; Kelin Wang, PhD; Adrian Ishkanian, MD, Matthew Abramowitz, MD; University of Miami Miller School of Medicine

PURPOSE AND OBJECTIVES: Long-term salvage rates for men who undergo standard fraction radiation therapy (SFRT) due to biochemical failure after prostatectomy remain suboptimal. There is a poor understanding as to which patients are curable with standard salvage doses of radiation. Compared with definitive prostate treatment, dose to the prostate bed is limited by the absence of a clearly defined target and the need to treat a large area of potential contamination into which the bladder has been pulled. Multiparametric magnetic resonance imaging (MRI) has enabled us to identify small foci of residual or recurrent disease in approximately 40% of patients—foci of disease that are not identifiable on CT, ultrasound, or physical exam. As demonstrated in definitive prostate cancer irradiation, dose escalation to these foci may show a benefit. The MAPS trial is currently underway to evaluate whether a simultaneous incorporated hypofractionated boost (SIHB) to these areas compared with SFRT improves biochemical control. This trial evaluates 68 Gy in 34 fractions to the prostate bed, vs the same dose and volume with the addition of 2.25 Gy daily SIHB to the MRI-identified gross tumor volume (GTV) (biologically effective dose [BED] = 80 Gy, α/β = 1.5).

MATERIALS AND METHODS: Two plans were generated for 14 patients treated per the MAPS protocol, one for each arm. 3D volumes of the MRI-identified GTV were generated in the Varian Eclipse treatment planning system (version 11.0). Intensity-modulated arc therapy was utilized for all plans. The trial stipulates that no more than 35% and 55% of the rectum (R) should receive ≥ 65 Gy and ≥ 40 Gy, respectively, and no more than 50% and 70% of the bladder minus the prostate bed clinical target volume (B-CTV) should receive ≥ 65 Gy and ≥ 40 Gy, respectively. Doses to targets and normal tissues were compared.

RESULTS: Prostate bed GTV volumes ranged from 84.8 to 202.7 cc, with a mean (standard deviation [SD]) of 143.3 cc (39.2). GTV volumes ranged from 0.31 to 10.4 cc, with a mean (SD) of 2.34 cc (2.8). The table contains normal tissue criteria, which were achieved for all variables aside from bladder. Five plans had > 70% of the bladder receiving ≥ 40 Gy, and one plan had > 50% of the bladder receiving ≥ 65 Gy; these were considered secondary protocol variations and appeared to be due to suboptimal bladder filling. The PT coverage ranged from 95.0% to 97.9%. The GTV coverage ranged from 95.0% to 100%. In terms of dosimetric constraints, as well as PT coverage, there was no difference between the SIHB plans and SFRT plans per patient or overall.

CONCLUSIONS: This study demonstrates that even though most GTVs are located in close proximity to critical structures, the escalated dose scheme as described in the MAPS trial can be achieved without exceeding the toxicity tolerance specified for the rectum in all cases and the bladder in the majority, with

<p>| Table P089 |</p>
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<th>SFRT Min</th>
<th>Max</th>
<th>Mean</th>
<th>SD</th>
<th>SIHB Min</th>
<th>Max</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>V40(R)%</td>
<td>20</td>
<td>45.6</td>
<td>34.6</td>
<td>7.7</td>
<td>19.7</td>
<td>45.7</td>
<td>34.5</td>
</tr>
<tr>
<td>V65(R)%</td>
<td>8.4</td>
<td>22.0</td>
<td>14.1</td>
<td>3.6</td>
<td>8.2</td>
<td>22.9</td>
<td>14.4</td>
</tr>
<tr>
<td>Max(R)Gy</td>
<td>71.6</td>
<td>80.4</td>
<td>76.7</td>
<td>2.8</td>
<td>73.5</td>
<td>83.4</td>
<td>78.5</td>
</tr>
<tr>
<td>V40(B-CTV)%</td>
<td>32.1</td>
<td>97</td>
<td>63.1</td>
<td>23.3</td>
<td>35.5</td>
<td>99</td>
<td>64.3</td>
</tr>
<tr>
<td>V65(B-CTV)%</td>
<td>14.5</td>
<td>49.8</td>
<td>31.3</td>
<td>10.9</td>
<td>14.5</td>
<td>55.5</td>
<td>33.8</td>
</tr>
<tr>
<td>Max(B-CTV)%Gy</td>
<td>74.4</td>
<td>83.2</td>
<td>77.8</td>
<td>2.8</td>
<td>75</td>
<td>82.5</td>
<td>78.1</td>
</tr>
</tbody>
</table>

SD = standard deviation; SFRT = standard fraction radiation therapy; SIHB = simultaneous incorporated hypofractionated boost.
expected variations due to unavoidably small bladders being entirely in the CTV. Treating MRI-identified prostate bed lesions to definitive doses using a SIHB is possible without increased dose to critical structures. Long-term follow-up will determine the biochemical outcome.

(P090) Comparison of Intraoperatively Built Custom-Linked (IBCL) Seeds to Free Seeds for Permanent Prostate Brachytherapy

Simon Brown, BS, Samuel L. Cooper, MD, Michael Ashenafi, MS, Harry Clarke, MD, PhD, David T. Marshall, MD; Medical University of South Carolina

PURPOSE: Our prostate brachytherapy technique at the Medical University of South Carolina evolved from implanting free seeds using a Mick Applicator (MA) (Mick Radio-Nuclear Instruments, Inc) to using intraoperatively built custom-linked (IBCL) seeds constructed with the QuickLink device (C.R. Bard, Inc). In this work, we compare dosimetric and early clinical outcomes using free seeds and IBCL seeds.

MATERIALS AND METHODS: From April 2005 to July 2012, a total of 197 patients with clinically localized prostate cancer underwent brachytherapy using real-time ultrasound-guided seed placement and intraoperative dosimetry to optimize target coverage based on the approach of Stock and colleagues at the Mount Sinai School of Medicine in New York. From April 2005 through February 2007, free seeds were placed using an MA. Starting in March 2007, brachytherapy was performed with IBCL seeds constructed using the QuickLink device in the operating room as needed during the implant. Patients were grouped per National Comprehensive Cancer Network (NCCN) risk stratification. All patients underwent postoperative computed tomography (CT)-based dosimetric analysis. Biochemical disease-free survival (bDFS) was calculated using Kaplan-Meier estimates with prostate-specific antigen (PSA) relapse using the Phoenix definition. Postoperative dosimetry for the two methods was compared with the Wilcoxon rank-sum test. Specific endpoint analyses included bDFS, Common Terminology Criteria for Adverse Events version 4.03 (CTCAE v4.03) toxicity criteria grades 3 or greater, urinary retention requiring catheter placement, hematuria, and rectal bleeding.

RESULTS: A total of 197 patients with median follow-up of 3.1 years were identified. Median follow-up for patients implanted with free seeds was 6.3 years and 2.7 years for IBCL seed patients. Median age at diagnosis was 64 years, and 66% of the patients were white. Median PSA at diagnosis was 6.0 ng/mL. NCCN risk group: low 53%, intermediate 40%, and high 7%. In total, 117 patients received I-125 alone, and 79 patients received Pd-103 plus external beam radiotherapy (EBRT). One patient received Pd-103 alone. Median prostate V90 was 172.1 Gy for I-125 and 109.3 Gy for Pd-103. Median prostate V100, urethra D30, and rectal V100 were 93.6%, 132.3%, and 0.55 cc, respectively. IBCL had significantly higher V100 (P = .008) and D90 with I-125 (P = .008) than for free seeds. Five-year bDFS was 90.6% for intermediate/high-risk patients and 96% for low-risk patients. Five-year bDFS was significantly higher in the low-risk group with IBCL at 100% compared with free seeds at 90.2% (P = .031). The 5-year rates of grade 3 toxicity, urinary retention requiring catheterization, any hematuria, and any rectal bleeding were 3.4%, 4.7%, 10.4%, and 10.2%, respectively, with no significant difference between IBCL or free seeds. The rate of rectal bleeding with radiation therapy (RT) changes on colonoscopy was 1.8% at 5 years. All hematuria resolved on its own, with no RT changes on cystoscopy.

CONCLUSION: Prostate implants using free seeds or IBCL seeds provide low rates of early biochemical failure and toxicity in patients with clinically localized prostate cancer. IBCL was associated with a higher D90 in patients receiving I-125. Patients with low-risk disease had better bDFS with IBCL seeds compared with patients treated with free seeds, but longer follow-up is needed to confirm these findings.

(P091) The Clinical Significance of Overlap or Underlap of the Prescription Isodose Line and Prostate Contour in Brachytherapy for Low-Risk Prostate Adenocarcinoma

Jerry T. Liu, MD, Michael Buckstein, MD, PhD, Todd J. Carpenter, MD, Asher Mandel, Nelson N. Stone, MD, Richard G. Stock, MD; Icahn School of Medicine at Mount Sinai

OBJECTIVE: While biochemical progression-free survival (BPFS) for prostate cancer treated with brachytherapy is excellent, reported outcomes differ between groups. One hypothesis that has been proposed for improved biochemical outcomes is prescribing to a planning target volume (PTV) that extends substantially beyond the prostate. We tested this hypothesis by analyzing the effect of overlap vs underlap between prescription isodose lines and prostate contours on BPFS. We also assessed whether these spatial differences are correlated with increased acute toxicity.

METHODS: Patients with biopsy-proven prostate adenocarcinoma definitively treated with an 125I implant ± androgen deprivation therapy and minimum 3 years of follow-up were selected from our institutional database. Implants were prescribed, in general, to 160 Gy, and 30-day CT-based postimplant dosimetry was performed for all patients. For superior (1 cm below superior–most axial slice of prostate), middle (midpoint of superior–inferior extent), and inferior (1 cm above inferior–most axial slice) portions of the prostate, the difference between the 160-Gy isodose line and prostate contour was measured in four (anterior, posterior, right, and left) axial directions. The presence of overlap vs underlap at any of the anatomic points was analyzed for effects on BPFS, change in International Prostate Symptom Score (IPSS) (from pretreatment to first post-treatment 3-month follow-up score), urinary retention, hematuria, and proctitis. Toxicity ratings were based on Radiation Therapy Oncology Group/European Organisation for Research and Treatment of Cancer (RTOG/EORTC) long-term toxicity scale and Common Terminology Criteria for Adverse Events version 3.0 (CTCAE v3.0). Proctitis events were confirmed endoscopically.

RESULTS: With a median follow-up of 4.1 years, 546 patients met inclusion criteria. Actuarial 5-year BPFS was 97.5%. As summarized in the Table, there was a median overlap of the 160-Gy isodose line for all 12 anatomic locations. There were no significant differences in BPFS when comparing patients with overlap vs
underlap at any site or cumulative axial direction (eg, all anterior sites). In addition, there were no significant differences in BPFS when comparing patients with overlaps at any site that were above vs below the median overlap for each respective site. With regard to toxicities, overlap vs underlap affected change in IPSS at the mid-left gland ($P = .040$, two-sided), proctitis incidence at the inferior-left gland ($P = .003$, two-sided), and incidence of retention at the inferior-left gland ($P = .003$, two-sided). Overlap vs underlap was not found to affect toxicities at any of the other sites.

### Table P091

<table>
<thead>
<tr>
<th>Superior Prostate</th>
<th>Median Anterior Difference (cm)</th>
<th>Median Posterior Difference (cm)</th>
<th>Median Right Difference (cm)</th>
<th>Median Left Difference (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>+0.31 (-3.45–1.2)</td>
<td>+0.27 (-1.75–3.8)</td>
<td>+0.51 (-1.15–1.4)</td>
<td>+0.54 (-0.9–1.5)</td>
</tr>
<tr>
<td>Middle Prostate</td>
<td>+0.20 (-1.1–0.75)</td>
<td>+0.33 (-0.45–0.90)</td>
<td>+0.40 (-1.9–1.0)</td>
<td>+0.40 (-0.35–0.85)</td>
</tr>
<tr>
<td>Inferior Prostate</td>
<td>+0.01 (-1.6–1.05)</td>
<td>+0.10 (-1.0–0.95)</td>
<td>+0.35 (-0.75–1.15)</td>
<td>+0.33 (-0.80–1.0)</td>
</tr>
</tbody>
</table>

### CONCLUSION: While presence and degree of overlap of the prescription isodose line relative to the prostate gland did not appear to affect BPFS for low-risk patients, overlap at certain sites was found to be associated with increased GI and GU toxicity. These findings did not, however, have a clear anatomic correlate. Further study is needed with larger numbers in a higher-risk-group population to test the effect of overlap on BPFS and toxicity.

(P092) **Initial Clinical Results of Intraoperatively Built Custom-Linked (IBCL) Seeds for Permanent Prostate Brachytherapy**

**Samuel L. Cooper, MD, Simon Brown, BS, Michael Ashenafi, MS, Harry Clarke, MD, PhD, David T. Marshall, MD; Medical University of South Carolina**

**PURPOSE:** In 2007, in partnership with industry, we developed a novel technique of performing prostate brachytherapy using intraoperatively built custom-linked (IBCL) seeds by means of the QuickLink device (C.R. Bard, Inc). We were the first in the world to use this technology for this purpose. We report the initial prostate-specific antigen (PSA) control and toxicity profile of patients treated using IBCL seeds with the QuickLink device for permanent prostate brachytherapy.

**MATERIALS AND METHODS:** From March 2007 to July 2012, 148 patients with clinically localized prostate cancer underwent brachytherapy with IBCL seeds using real-time ultrasound-guided seed placement and intraoperative dosimetry to optimize target coverage. Real-time planning and seed placement were based on the approach of the Mount Sinai group reported by Stock and colleagues. All patients underwent postoperative CT-based dosimetric analysis. Patients were grouped per National Comprehensive Cancer Network (NCCN) risk stratification. Percent biochemical disease-free survival (bDFS) was calculated using Kaplan-Meier estimates with PSA relapse using the Phoenix definition as the event. Specific endpoint analyses were bDFS, Common Terminology Criteria for Adverse Events version 4.03 (CTCAE v4.03) toxicity grade 3 or greater, any urinary retention requiring catheter placement, any hematuria, and any rectal bleeding.

**RESULTS:** A total of 148 patients with a median follow-up of 2.7 years were identified. Median age at diagnosis was 64.4 years, and 65.5% were white. Median PSA at diagnosis was 5.73 ng/mL. NCCN risk groups were as follows: low-risk 45%, intermediate-risk 46%, and high-risk 9%. In total, 76 patients received I-125 alone, and 71 patients received Pd-103 plus external beam radiotherapy (EBRT). One patient received Pd-103 alone. Median prostate $D_{90}$ was 176.9 Gy for I-125 and 111.1 Gy for Pd-103. Median prostate V100, urethra D30, and rectal V100 were 94.2%, 133.5%, and 0.55 cc, respectively. Five-year bDFS was 88.1% for intermediate-/high-risk patients. There were no failures in the low-risk group. The 5-year rates of grade 3 toxicity, urinary retention requiring catheterization, any hematuria, and any rectal bleeding were 3.8%, 5.3%, 12.2%, and 13.7%, respectively. Only one patient with rectal bleeding had radiation therapy (RT) changes on colonoscopy. All hematuria resolved on its own, with no RT changes at cystoscopy. For patients with at least 2 years of follow-up, median American Urological Association (AUA) symptom score and urinary quality of life peaked within 6 months of brachytherapy and returned to baseline between 2 and 3 years.

**CONCLUSION:** With early follow-up, this novel approach for permanent prostate brachytherapy in patients with clinically localized prostate cancer is associated with low rates of biochemical failure and toxicity.

(P093) **Induction Chemotherapy Followed by Concurrent Full-Dose Gemcitabine and Intensity-Modulated Radiation Therapy for Borderline Resectable and Locally Advanced Pancreatic Adenocarcinoma**

**Shahed N. Badiyan, MD, Jeffrey R. Olsen, MD, Andrew Y. Lee, MD, Motoyo Yano, MD, PhD, Christine O. Menias, MD, Shariq Khwaja, MD, PhD, Andrea Wang-Gillam, MD, PhD, Steven M. Strasberg, MD, William G. Hawkins, MD, David C. Linehan, MD, Robert J. Myerson, MD, PhD, Parag J. Parikh, MD; Washington University**

**OBJECTIVE:** To evaluate outcomes and toxicity of concurrent full-dose gemcitabine and intensity-modulated radiation therapy (IMRT) for patients with borderline resectable and locally advanced pancreatic adenocarcinoma following induction chemotherapy.

**METHODS:** From 2009 to 2012, a total of 32 patients were treated with concurrent gemcitabine and IMRT for borderline resectable or locally advanced pancreatic adenocarcinoma. All patients received induction FOLFIRINOX (folinic acid, fluorouracil [5-FU], irinotecan, oxaliplatin) or gemcitabine-based chemotherapy prior to chemoradiation. The radiotherapy volume was limited to the primary tumor, and the median dose was 55 Gy in 25 fractions. Gemcitabine was administered weekly during radiotherapy on Days 1, 8, 22, and 29 at a median weekly dose of 800 mg/m². Freedom from local and distant progression and overall survival (OS) were calculated using the Kaplan-Meier method and com-
pared between groups using Kaplan-Meier log-rank statistics. Cox proportional hazards model was used for univariate and multivariate analysis.

**RESULTS:** Twenty-five patients had locally advanced disease, and seven had borderline resectable disease. Median follow-up time was 14.6 months. Median progression-free survival (PFS) and OS were 13.9 months and 23.1 months, respectively. A radiographic complete or partial response was achieved in 13 patients (41%), with 4 (13%) patients having complete radiographic responses. Surgical resection was performed in 10 patients (31%): 6 patients with locally advanced disease and 4 with borderline resectable disease. Grade 3/4 hematologic toxicity during and up to 6 weeks after chemoradiation occurred in 12 patients (38%); grade 3 nonhematologic toxicity occurred in 7 patients (22%), with no grade 4 or 5 toxicity. All patients completed their radiotherapy. There was a trend toward improved OS for patients receiving induction FOLFIRINOX compared with gemcitabine-based therapy (median not reached vs 22.1 mo; \( P = .08 \)). There was an improvement in OS in patients who were able to undergo a pancreatectomy compared with those who did not undergo a pancreatectomy (median not reached vs 19.9 mo; \( P = .001 \)). On univariate analysis, undergoing a pancreatectomy was the only treatment factor associated with OS (hazard ratio [HR] = 0.11; \( P < .05 \)). No other patient, disease, or treatment factors were identified to be associated with OS.

**CONCLUSION:** Concurrent full-dose gemcitabine and limited-field IMRT after induction chemotherapy for the treatment of borderline resectable and locally advanced pancreatic cancer is promising with acceptable toxicity rates.

**Table P094**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of Patients</th>
<th>MST (range)</th>
<th>TTLP (range)</th>
<th>TTLRP (range)</th>
<th>TTDP (range)</th>
<th>KPS (median)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>16</td>
<td>7 (6–10)(^{abc})</td>
<td>6 (4–10)(^{abc})</td>
<td>7 (4–10)(^{abc})</td>
<td>6 (3–8)</td>
<td>80</td>
</tr>
<tr>
<td>C-CRT</td>
<td>29</td>
<td>15 (8–24)(^{b})</td>
<td>11 (8–14)(^{b})</td>
<td>13 (9–22)(^{b})</td>
<td>9 (6–11)</td>
<td>90</td>
</tr>
<tr>
<td>C-CRT-C</td>
<td>9</td>
<td>17 (8–20)(^{a})</td>
<td>12 (4–18)(^{a})</td>
<td>14 (8–18)(^{a})</td>
<td>12 (4–18)</td>
<td>90</td>
</tr>
<tr>
<td>C-CRT-C</td>
<td>15</td>
<td>12 (7–18)(^{c})</td>
<td>12 (7–18)(^{c})</td>
<td>10 (6–12)</td>
<td>9 (5–12)</td>
<td>90</td>
</tr>
</tbody>
</table>

Statistical comparisons (all \( P < .05 \)): \( ^{a} \)C-CRT vs C; \( ^{b} \)C-CRT vs C; and \( ^{c} \)C-CRT-C vs C.

**CONCLUSIONS:** In this single-institution experience, chemoradiation therapy plus pre-CRT and/or post-CRT chemotherapy significantly improved MST, TTLP, and TTLRP compared with chemotherapy alone. However, given the limited number of patients, the various chemotherapy agents used, and the limitations of a retrospective review, further investigation is needed in determining the most appropriate treatment regimen in patients diagnosed with LAUPC.

**Table P095**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>No. of Patients</th>
<th>MST (range)</th>
<th>TTLP (range)</th>
<th>TTLRP (range)</th>
<th>TTDP (range)</th>
<th>KPS (median)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C</td>
<td>16</td>
<td>7 (6–10)(^{abc})</td>
<td>6 (4–10)(^{abc})</td>
<td>7 (4–10)(^{abc})</td>
<td>6 (3–8)</td>
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<tr>
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<td>15 (8–24)(^{b})</td>
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<td>13 (9–22)(^{b})</td>
<td>9 (6–11)</td>
<td>90</td>
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<tr>
<td>C-CRT-C</td>
<td>9</td>
<td>17 (8–20)(^{a})</td>
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<td>12 (4–18)</td>
<td>90</td>
</tr>
<tr>
<td>C-CRT-C</td>
<td>15</td>
<td>12 (7–18)(^{c})</td>
<td>12 (7–18)(^{c})</td>
<td>10 (6–12)</td>
<td>9 (5–12)</td>
<td>90</td>
</tr>
</tbody>
</table>

Statistical comparisons (all \( P < .05 \)): \( ^{a} \)C-CRT vs C; \( ^{b} \)C-CRT vs C; and \( ^{c} \)C-CRT-C vs C.

C = chemotherapy alone; C-CRT = concurrent chemoradiation therapy; C-CRT-C = induction C followed by concurrent chemoradiation; C-CRT-C = C-CRT followed by chemotherapy; C-CRT-C = C-CRT followed by C; KPS = Karnofsky performance score; MST = median survival time; TTDP = time to distant progression; TTLP = time to local progression; TTLRP = time to local regional progression.
PURPOSE: To compare toxicity and treatment outcomes in human immunodeficiency virus (HIV)-positive vs HIV-negative patients with squamous cell carcinoma of the anal canal who underwent definitive concurrent chemoradiation at a single institution.

MATERIALS AND METHODS: A total of 53 consecutive HIV-positive patients treated between 1987 and 2007 were compared with 205 consecutive HIV-negative patients treated between 2003 and 2007. All patients received radiotherapy at a single regional facility. Median radiation dose was 54 Gy (range: 28–60 Gy). Concurrent chemotherapy consisted of 2 cycles of 5-fluorouracil (5-FU) (1,000 mg/m²/day on Days 1–4 and 29–32), along with mitomycin C (10 mg/m²) given on Day 1 (+/– Day 29). After treatment, patients were closely followed with imaging studies, clinical examinations, and rigid proctoscopies. Outcomes assessed were toxicity rates, progression-free survival (PFS), colostomy-free survival (CFS), cancer-specific survival (CSS), and overall survival (OS).

RESULTS: Median follow-up was 34 months. Compared with HIV-negative patients, HIV-positive patients were younger (median age: 48 yr vs 62 yr) and predominantly male (98% of HIV-positive patients were male vs 22% of HIV-negative patients). Also, 37 (70%) HIV-positive patients were on highly active antiretroviral therapy (HAART), and 26 (65%) had an undetectable viral load at the time of treatment; 36 (72%) had a CD4 count > 200 (mean CD4 count: 455). There were no significant differences in acute or late nonhematologic or hematologic toxicity rates between the two groups. At 3 years, there was no significant difference between HIV-positive and HIV-negative patients in regard to PFS (75% vs 84%), CSS (85% vs 85%), or CFS (79% vs 88%; \( P = .36 \)), respectively. On univariate analysis, there was a trend toward worse OS in HIV-positive patients (72% vs 84% at 3 yr; \( P = .06 \)). On multivariate analysis, only male gender and stage were predictive of worse survival outcomes. HIV status was not associated with worse outcomes in Cox models.

CONCLUSIONS: In the HAART era, HIV-positive patients with anal cancer can undergo standard definitive chemoradiation and expect equivalent toxicity and survival outcomes compared with HIV-negative patients.

(P096) Preoperative Radiation Dose Escalation for Rectal Cancer Improves Tumor Downstaging Without Significant Increase in Toxicity: A Matched-Pair Analysis


PURPOSE: With large studies demonstrating improved sphincter preservation and local control following neoadjuvant chemoradiation therapy (NCRT) for rectal cancer, this approach has been established as standard in locally advanced or node-positive disease. While a tantalizing minority of patients enjoys pathologic complete response (pCR) at the time of surgery, ~50% of lesions fail to be downstaged by treatment. We sought to explore a potential dose-response relationship with tumor downstaging after NCRT. To this end, we conducted a case-control analysis of 152 patients treated preoperatively, with and without a concomitant boost.

METHODS: From 1995–2003, 76 patients were enrolled on an institutional review board (IRB)-approved phase II protocol examining the feasibility of adding a concomitant boost to NCRT. Patients received venous infusion 5-fluorouracil (5-FU) and 52.5 Gy in 5 weeks—42.5 Gy at 1.8 Gy per fraction daily, plus a concomitant boost of 1.5 Gy per day in the final week of treatment. Using a case-control approach, 76 additional patients were identified who received low-dose NCRT (5-FU plus 45 Gy in 1.8-Gy fractions), matching for type of surgery performed, tumor stage (T-stage), and clinical nodal metastases (N-stage). For all 152 patients, chart review was undertaken with respect to clinicopathologic parameters and treatment outcomes. Radiation toxicity and surgical complications were assessed in a subset of 63 pairs with complete toxicity data available. McNemar’s chi-square test and Kaplan-Meier analyses were used as appropriate.

RESULTS: The high-dose (HD) and low-dose (LD) cohorts were well matched; in addition to the selection criteria, there were no significant differences in gender (HD 64.5% male vs LD 65.8% male) or age (HD 57.1 yr vs LD 55.9 yr). For a subset of patients, information regarding circumferential involvement (50% of patients) and tumor length was available (65% of patients); there were no significant differences in these criteria. A statistically significant difference in distance from the anal verge was noted (HD 4.7 cm vs LD 5.7 cm; \( P < .03 \)).

The rate of tumor downstaging was substantially improved in the HD cohort, with 76% of patients found to have reduction in T-stage vs 51% in the LD arm (\( P < .01 \)). However, the rates of pCR did not differ significantly (HD 17.1% vs LD 15.8%). Toxicity data reveal that T-downstaging did not appear to come at a cost of substantially increased toxicity. While ~90% of patients experienced some radiation toxicity, the incidence of grade 3 or higher toxicities was low (HD 9% vs LD 3%), as was the rate of wound complication (HD 8% vs LD 7%), with no statistically significant differences between the cohorts.

CONCLUSIONS: Our results suggest that dose escalation in NCRT is feasible without significant increase in radiation toxicity or surgical complication. While pCR rates did not differ between HD and LD NCRT groups, the increased T-downstaging seen in the HD arm supports a dose-response relationship with tumor downstaging and suggests further exploration of dose escalation as a tool to improve sphincter preservation rates in appropriately selected patients.

(P098) Dose-Painting Technique in SBRt of Hepatocellular Carcinoma of Unfavorable Locations: Feasibility and Outcomes

Benjamin K. Hinton, MD, Craig Baden, MD, MPH, Sui Shen, PhD, Kimberly Dempsey, CMD, Nicole A. Safiano, BS, Rojymon Jacob, MD, University of Alabama at Birmingham

INTRODUCTION: Stereotactic body radiotherapy (SBRT) is increasingly utilized for the treatment of inoperable hepatocellular carcinoma (HCC) alone or in combination with other local treatment modalities. However, proximity to bowel often precludes the ability to deliver the full prescription dose to the planning target volume (PTV). In this study, we evaluate our experience using the technique of radiation therapy (RT)–dose-painting (DPRT) to decrease...
the dose received to critical structures with the PTV.

**MATERIALS AND METHODS:** Twenty-nine patients with inoperable HCC treated in our institution using SBRT between April 2009 and November 2012 were analyzed to determine acute toxicity, local control (LC), and feasibility of delivery of SBRT. All patients were simulated and planned for SBRT in a standard fashion. Gross tumor volume (GTV) encompassed all visible disease on contrasted computed tomography (CT) simulation. Clinical target volume (CTV) included an additional 4 mm; PTV was constructed by adding a 5-mm geometric uncertainty margin around the CTV. All but three patients were simulated and treated with respiratory gating, and all had cone beam CT for image guidance. In seven patients, the PTV extended into the small bowel, stomach, or esophagus. The gastrointestinal structures within the PTV were contoured with an additional 5-mm margin within the PTV to create the dose-painting PTV (DPTV). Twenty-two patients did not require any modification to the PTV. Prescription dose was 45 Gy or 60 Gy in three fractions to the PTV in all patients. Dose to the PTV was limited to < 21 Gy in three fractions. All patients were analyzed for LC and distant liver control (DLC). Statistical significance was tested with the Wilcoxon rank-sum test. Treatment plans of seven patients who were planned using DPTV were analyzed by comparing dose-volume parameters when planned with or without DPTV to illustrate the impact of the dose-painting strategy. The gastrointestinal data points that were analyzed were: V20-Gy (volume receiving 20 Gy), V22-Gy (volume receiving 22 Gy), and $D_{max}$ (maximum point dose).

**RESULTS:** Use of DPRT helped to restrict gastrointestinal doses to within tolerable limits. The acute toxicity rates were not statistically different between the groups of patients planned with or without DPRT (no grade 2 or higher toxicities). No differences were noted in outcomes between patients treated with or without DPRT. Disease-related outcomes for patients receiving DPRT ($n = 7$) vs full-dose RT ($n = 22$) were as follows: LC 100% vs 85.7% ($P = NS$) and DLC 62.5% vs 66.7% ($P = NS$). On average, DPRT reduced V20-Gy, V22-Gy, and $D_{max}$ by 9.7 cc (6.8%), 10.7 cc (6.0%), and 17.0 Gy, respectively.

**CONCLUSIONS:** DPRT allowed for significant reduction in gastrointestinal dose during SBRT planning. Utilization of DPRT to spare gastrointestinal structures did not adversely impact local tumor control.

**(P099) A Multidisciplinary Approach to the Management of Patients Diagnosed With Stage IV Anal Canal Cancer: A Multi-institutional Retrospective Study**

Lorraine Portelance, MD, Neil Kopek, MD, Peter Hosein, MD, Maria Restrepo, MD, Caio Rocha-Lima, MD, Joe Levi, MD, Omar Mahmoud, MD, Adrian Ishkanian, MD, Govindarajan Narayanan, MD, Ike Akunyili, MD; Sylvester Comprehensive Cancer Center, University of Miami; McGill University Health Center

**BACKGROUND:** While there is a large amount of literature published on the management of patients with stage IV colorectal cancer presenting with liver-predominant metastatic disease, there is a paucity of data on the management of patients with stage IV squamous cell carcinoma (SCC) of the anal canal who have the same pattern of presentation. This retrospective study presents the results of a multidisciplinary approach adopted in two cancer centers where patients diagnosed with stage IV SCC of the anal canal (liver-predominant disease) and a good performance status (Eastern Cooperative Oncology Group [ECOG] 0–2) were offered a full course of concomitant chemoradiation followed by cisplatin-based palliative chemotherapy. In addition, for the patients who achieved a complete local response in the pelvis, consideration was given to proceed with local treatment of the liver metastasis (either by surgery or radioablation).

**METHODS:** An institutional review board (IRB)-approved anal cancer database including two institutions was queried to identify patients who presented with liver-predominant metastasis at diagnosis. A detailed retrospective review of the medical records was performed to capture demographic and clinical characteristics, as well as treatment delivery, response, toxicity, and survival.

**RESULTS:** Between May 2009 and September 2013, a total of 11 patients were diagnosed with SCC of the anal canal and had liver-predominant metastatic disease at presentation. The median age was 53 years, and three patients were HIV-positive. The median follow-up was 23.6 months (range: 2–53 mo). Ten patients completed the full course of chemoradiation therapy with the Nigro protocol (mitomycin/flourouracil and 54 Gy of external beam radiotherapy). Patients went on to receive systemic chemotherapy with cisplatin/flourouracil. This was then followed by resection of residual liver metastases in seven patients and transarterial radioembolization with yttrium-90 microspheres in one patient. The 2-year overall survival (OS) and disease-free survival (DFS) rates were 87% and 27%, respectively. Complete response of the primary pelvic disease was documented during follow-up in 70% of the patients. These results were achieved with acceptable treatment-related toxicity. The most frequent acute toxicity encountered was reversible myelosuppression and radiation enteritis. No deaths were directly related to therapy.

**CONCLUSION:** Patients with anal canal SCC usually have significant pelvic symptoms at diagnosis from their primary disease. In our series, patients with liver-predominant stage IV disease had a high 2-year survival rate. Our experience suggests that upfront concomitant chemoradiation plays a significant role in controlling the pelvic symptoms in this population. Moreover, when an aggressive treatment approach was used, 27% was disease-free at 2 years, suggesting that the approach to patients with oligometastatic disease used in colorectal cancer may also be of benefit in patients with anal canal SCC.

**(P100) Radiation Therapy Is Associated With Improved Survival In Patients With Localized Pancreatic Cancer S/P Whipple Procedure Without Increased Morbidity: Results of a Study from the Surveillance, Epidemiology, and End Results (SEER) Registry Data**

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BACKGROUND: Patients with localized pancreatic cancer tend to receive chemotherapy after surgery. However, the role of radiation therapy (RT) in resectable pancreatic cancer is still debated. For the current study, we evaluated the effect of adjuvant RT on survival as well as treatment-related toxicity in patients with localized pancreatic cancer who underwent Whipple procedure (pancreaticoduodenectomy).

METHODS: The analysis included 3,721 patients reported to the Surveillance, Epidemiology, and End Results (SEER) registry of the National Cancer Institute from 2003 to 2010 who had localized pancreatic cancer and underwent a cancer-directed Whipple procedure (pancreaticoduodenectomy). Cause-specific survival (CSS) was evaluated by Kaplan-Meier survival analysis, and the log-rank test was used to compare CSS between treatment categories of interest. Multivariable Cox regression model analysis was used to elucidate the factors that contribute to pancreatic cancer death. Adjusted hazard ratios (AHRs) and 95% confidence intervals (95% CIs) were calculated for risk of pancreatic cancer-related death. Deaths due to RT were also studied.

RESULTS: Of the 3,721 patients, 1,520 (40.8%) received RT. Median follow-up time (based on survivors) was 17 months (range: 0.10–83.0 mo). CSS improved significantly in patients who received RT, with a median survival of 21.0 months (95% CI, 19.8–22.2 mo) compared with 17 months (95% CI, 15.8–18.2 mo) for patients who did not receive RT (P < .0001). On multivariable analysis, age > 65 years, T-stage, N-stage, and grade were associated with improved CSS compared with cancer-directed surgery alone without radiation in patients with localized pancreatic cancer. Old age, white race, higher T- and N-stage, and grade were associated with worse outcome. Morbidity was not increased with adjuvant RT.

CONCLUSIONS: Adjuvant RT following Whipple procedure was associated with improved CSS compared with cancer-directed surgery alone without radiation in patients with localized pancreatic cancer. Old age, white race, higher T- and N-stage, and grade were associated with worse outcome. Morbidity was not increased with adjuvant RT.

(P101) Impact of a Single-Day Multidisciplinary Clinic on the Management of Pancreatic Cancer: A 6-Year Update

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BACKGROUND: Multidisciplinary clinics (MDCs) are increasingly prevalent in the management of cancer patients. This practice model has been shown to improve the accuracy of staging in breast, ovarian, and pancreatic cancers. Pancreatic cancer provides an ideal practice model for MDCs, because management recommendations require crossdisciplinary input, treatment is often multimodal, and initiating therapy in a timely manner is known to have a positive impact on clinical outcomes. Herein, we report the 6-year update from the Johns Hopkins Pancreas Multidisciplinary Clinic (PMDC) and evaluate the impact of an MDC on the clinical care recommendations of patients with pancreatic cancer.

METHODS: The records of 1,040 consecutive patients evaluated by the weekly PMDC at our institution were prospectively collected from November 2006 to November 2012. Cross-sectional imaging, pathology, and medical history were evaluated by a panel of providers that included at least one medical oncologist, radiation oncologist, surgical oncologist, pathologist, diagnostic radiologist, palliative care specialist, and geneticist. Patient characteristics and changes in diagnosis and/or staging between the referring institution and the PMDC were recorded and compared.

RESULTS: The patient population consisted of 513 females and 527 males. The median age at diagnosis was 64 years (range: 28–94 y). Seventy-three percent of patients had pancreatic adenocarcinoma, 6% had intraductal papillary mucinous neoplasms (IPMNs); 2% had cholangiocarcinomas; and the remainder (19.2%) had other tumor types, including neuroendocrine tumors, cystadenomas, and insulinas.

Overall, 319 patients (30.7%) had a change in diagnosis based on imaging studies and/or review of pathology that led to changes in treatment recommendations. Review of histological slides by pathologists specializing in the pancreas resulted in a change in the pathologic diagnosis for 66 patients (6.3%). The majority of changes were based on review of imaging submitted outside and imaging studies performed at Hopkins, including a 3D reconstructed pancreas protocol CT scan. Nineteen percent of patients were upstaged, and 8% were downstaged. Of those upstaged, the majority (115 patients, or 11% of the total population) were found to have previously unrecognized metastatic disease. A total of 32 patients (3%) who were referred with locally advanced pancreatic cancer were determined to have resectable disease after PMDC evaluation. Overall, 20% of patients underwent surgical resection after being seen in the PMDC, and 95.7% of these patients had margin-negative resections.

Seven patients initially diagnosed with a presumed locally advanced malignancy were found to have benign disease after evaluation at PMDC. For example, a patient referred for a presumed unresectable malignant mass in the tail of the pancreas was determined to have clinical and imaging findings consistent with pancreatitis.

CONCLUSION: The single-day multidisciplinary pancreatic cancer clinic provided a comprehensive and coordinated evaluation of patients that led to a change in therapeutic recommendations in approximately one-third of the patients evaluated. These results highlight the value of an MDC in the management of patients with pancreatic cancer.

(P102) Effectiveness and Toxicity of Yttrium-90 Microsphere Brachytherapy

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INTRODUCTION: By exploiting the liver’s dual blood supply and the beta-emission of yttrium-90 (Y-90), microsphere brachytherapy enables treatment of primary or metastatic liver tumors with tumoricidal radiation doses while preferentially sparing normal...
liver parenchyma. Though utilization of Y-90 microsphere brachytherapy continues to increase, data regarding toxicity and effectiveness remain limited. Here, we report findings from a series of 82 Y-90 microsphere brachytherapy treatments.

PATIENTS AND METHODS: Between October 2010 and August 2013, a total of 59 patients underwent 82 treatments with Y-90 SIR-Spheres at our tertiary care academic medical center. Median patient age was 60 years (range: 33–82 yr), and median Karnofsky performance score (KPS) was 80% (range: 40%–90%). Seventy-two treatments were completed in patients with Child-Pugh class A disease and 10 in class B. Of the 82 treatments, 36 (43.9%) were to colorectal carcinoma metastases, 15 (18.3%) to neuroendocrine tumors, 11 (13.4%) to cholangiocarcinoma, 5 (6.1%) to hepatocellular carcinoma, 5 (6.1%) to breast carcinoma, and 10 (12.2%) to other tumor types. The majority of radioembolization treatments were preceded by other therapies, including systemic therapy in 87.8%, liver resection in 18.3%, transcatheter arterial chemoembolization (TACE) in 14.6%, and radiofrequency ablation in 4.9%. The median maximum radiographic lesion size was 49 mm (range: 12–200 mm). Median treated tumor volume was 90.7 mL (range: 5–3,096 mL), constituting a median of 9.1% (range: 1.1%–78.5%) of the treated lobe. Median activity of microspheres was 1.03 GBq (range: 0.2–2.1 GBq). Procedures were uncomplicated in 73.2% of cases, while 15.9% developed stasis and 9.8% developed reflux. We collected laboratory, imaging, and other clinical data from the pretreatment visit as well as at the 1-, 3-, and 6-month and subsequent follow-up visits in order to determine toxicity, effectiveness, and survival associated with treatment.

RESULTS: Acute toxicities of treatment were generally very mild and included fatigue (45.1%), anorexia (15.9%), weight loss (6.1%), abdominal discomfort (36.6%), nausea (24.4%), hepatic encephalopathy (12.2%), jaundice (3.7%), and ascites (3.7%). Grade 2 or higher laboratory toxicities included derangements of alkaline phosphatase (24.4%), albumin (23.2%), total bilirubin (19.5%), aspartate aminotransferase (AST) (12.2%), alanine aminotransferase (ALT) (3.7%), and international normalized ratio (INR) (3.7%). Radiographic response was measured at 3 and 6 months post-treatment. Of 48 treatments with available imaging after 3 months, 25.0% showed partial response, 29.2% stable disease, and 45.8% progression. Median change in the maximum lesion diameter after 3 months was +1 mm (range: -22 to 92 mm). Six-month imaging was available for 28 treatments, with 28.6% demonstrating partial response, 42.9% stable, and 28.6% progression. Median change after 6 months was +1 mm (range: -47 to 70 mm). At 3 months, only 22.2% of neuroendocrine tumors had progressed, whereas 72.2% of colorectal carcinoma had progressed (P = .04). Radiographic response was not significantly associated with tumor diameter, tumor volume, previous chemotherapy, TACE, or liver resection. Median survival from time of first treatment was 37.4 weeks (95% confidence interval [CI], 24.4–45.7). There were no significant differences in survival with respect to Child-Pugh class, tumor volume, tumor diameter, previous TACE, or previous systemic therapy.

CONCLUSION: Findings from this institutional series corroborate the safety of Y-90 microsphere radioembolization and demonstrate its effectiveness in treating a variety of unresectable primary and metastatic liver tumors.
Aim of our study was to identify if patients underwent radiation first vs surgery and if the treatment patterns changed with time. We examined differences between academic and community institutions and if concordance existed between clinical and pathological stage.

**METHODS:** A retrospective analysis was performed using the National Cancer Database (NCDB), looking at all patients who were diagnosed with rectal cancer from 1998 to 2011. We tested differences in rates of treatment and stage migration using chi-square tests and logistic regression models.

**RESULTS:** A total of 90,594 patients were identified having undergone both surgery and radiation for rectal cancer. In 1998, 42% of patients received radiation therapy (RT) prior to undergoing surgical resection. In 2000, 53% of patients were treated with neoadjuvant radiation. A steady increase in the use of induction radiation was observed during the study period, with 86% of patients treated with radiation prior to surgery in 2011, correlating with a 33% increase ($P \leq .001$). When comparing the type of institution, academic vs community, in 1998, 51% of patients seen in an academic institution received radiation prior to surgical resection, vs 39% in a community facility ($P \leq .001$). Although rates were consistently higher in academic institutions, both types demonstrated a consistent increase over the study period. In 2011, radiation was given first in 91% and 84% of patients in academic and community institutions, respectively ($P \leq .001$). In patients receiving radiation first, 27% did not have clinical staging available. Overall, 17% of patients were successfully downstaged, 8% was upstaged, and 24% had no changes in stage. An additional 25% had no recorded pathological stage, 21% had unknown clinical stage, and 5% had no clinical or pathological staging available. When comparing academic vs community centers, 20% was downstaged, 8% was upstaged, and 26% had no changes in the academic centers, vs 15%, 8%, and 23% in the community, respectively ($P \leq .001$). Staging was unknown in 46% in the academic institution and 54% of patients in the community ($P \leq .001$).

**CONCLUSION:** The use of neoadjuvant radiation for the treatment of rectal cancers has seen a steady increase from 1998 to 2011. Although academic centers seem to have higher rates of adoption, the overwhelming majority of centers in the United States now follow a radiation-first strategy in the treatment of rectal cancer.

**P105: Figure**

Definitive HDR alone, and eight were treated with definitive combined external beam radiation therapy (EBRT) plus HDR. Two of eight EBRT + HDR patients received concurrent cisplatin/5-fluorouracil (5-FU) at weeks 1 and 4 of EBRT. Kaplan-Meier analysis was used to determine disease-free survival (DFS), overall survival (OS), and LC. The dose-volume relationship for CTV and implant volume for the 1-tube vs 3-tube technique planned with V100 of 90% in our initial patient was completed. Dice’s coefficient (DC) was calculated in 11 patients who underwent 43 total HDR applications and 36 3-tube vs 7 1-tube procedures.

**RESULTS:** Of 13 medically unresectable patients, 11 were male and 2 were female, with a mean age of 72 years (range: 52–90 yr). Histology was adenocarcinoma in nine patients and squamous cell carcinoma in four patients. Tumor was located in the distal, middle, and proximal one-third of the esophagus in 10 patients, 2 patients, and 1 patient, respectively. Stage 0, 1A, 1B, 2A, 2B, 3A, and 4A occurred in one, one, six, one, two, and one of the patients, respectively. The HDR-alone dose was 25–30 Gy (mode 30 Gy) in 5–6 weekly fractions of 5 Gy/fx. The HDR dose after EBRT was 10–25 Gy (mode 15 Gy) in 2–5 weekly fractions. The EBRT dose was 50–64 Gy (mode 50 Gy). Of the five stage 0–1B HDR-alone patients, four are alive without disease (no evidence of disease [NED]); one is alive with distant failure (DF) in the lung/pleura. No local failures (LFs) occurred in five HDR-alone patients. Of the eight stage 1B–4A HDR + EBRT patients, five are alive with NED, one is alive with NED after cryotherapy for LF, and two are dead of distant failure in the liver. One of eight HDR + EBRT patients has LF but was salvaged with cryotherapy. Overall, 2 of 13 patients experienced LF after HDR +/- EBRT. At a median follow-up of 17.4 months, 18-month OS is 92.3%, 18-month DFS is 74%, and 18-month LC is 81%. No fistulas were seen. Two of 13 patients required dilatation for stricture. Eleven of 13 patients denied dysphagia, and 2 of 13 patients had grade 2 dysphagia, one requiring a stent.

The V100, V150, V200, and V300 were 90.0%, 66.7%, 41.5%, and 17.7%, for the 1-tube vs 3-tube technique, respectively. For the 3-tube technique, the implant volume was 50% smaller (V100: 42.7 cc vs 83.8 cc; V150: 22.2 cc vs 42.9 cc; V200: 13.1 cc vs 26.0 cc; V300: 5.6 cc vs 12.3 cc). The DC significantly improved to 0.38 from 0.30 for 3- vs 1-tube, respectively ($P < .058$).

**CONCLUSIONS:** A novel 3-tube endoesophageal HDR technique...
improved the dose homogeneity and DC in our initial 13 patients. Our initial OS and LC data suggest the potential for an improved therapeutic ratio using a novel 3-tube HDR technique as a component of definitive treatment for stage I-IVA esophageal cancer.

(P106) High Adherence to the NCCN Guidelines for Neoadjuvant Treatment of Stage II and III Rectal Cancer Patients at a Tertiary Cancer Center and Its Partnering Institutions

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INTRODUCTION: Standard treatment of patients with stage II and III rectal cancer consists of a multimodality approach, including the use of chemotherapy, radiation, and surgery. Current National Comprehensive Care Network (NCCN) guidelines recommend that patients with stage II and III rectal cancer receive neoadjuvant chemoradiotherapy to decrease local recurrence rates.

METHODS: We performed a retrospective chart review of patients treated for stage II and III rectal cancer at a tertiary referral cancer center and six of its community partner institutions from 2000–2011. We sought to evaluate the use of neoadjuvant and adjuvant chemotherapy and radiotherapy in these patients.

RESULTS: There were 769 stage II and III rectal cancer patients treated at the seven institutions. Of them, 513 were clinical stage II and III patients, with 253 being stage II and 260 being stage III. Among the 513 patients, 316 (61.6%) were male, while 197 (38.4%) were female, and the median age at diagnosis of rectal cancer was 64 years. There were 449 patients out of the 513 (87.5%) who received neoadjuvant therapy. For stage II patients, there were 215 out of 253 (85%) who received neoadjuvant therapy. There were 234 out of 260 (90%) stage III patients who received neoadjuvant therapy. Most patients, 438 out of 449 (97.6%), received both neoadjuvant chemotherapy and radiotherapy. Four patients (0.9%) received only neoadjuvant chemotherapy and radiotherapy, and seven (1.6%) received only neoadjuvant radiotherapy. Of the 64 patients who did not receive neoadjuvant therapy, 38 (59.4%) received adjuvant therapy and 26 (40.6%) did not receive any other therapy. When comparing the tertiary cancer center to the community partnering institutions, 191 out of 205 (93.2%) of the stage II and III patients received neoadjuvant therapy at the tertiary center, while 258 out of 308 (83.8%) received neoadjuvant treatment at the partnering institutions. The difference was statistically significant (P = .002).

DISCUSSION: Rectal cancer care across the US is provided at both community and academic centers. In general, academic centers tend to adopt practice changes sooner than community hospitals. At both our institution and partnering hospitals, there was a high rate of neoadjuvant therapy use in accordance with NCCN guidelines. However, patients at the tertiary center were more likely to receive neoadjuvant therapy, which may likely be due to the center being a part of early protocols that helped to establish the guidelines of neoadjuvant therapy use in rectal cancer. With the partnering relationship of community hospitals with tertiary centers like ours, which has an educational platform via tumor boards and regional symposiums, this can provide an opportunity for increased standardization of care across all hospitals so that rectal cancer patients are treated in accordance with current guidelines.

(P107) Duodenal Sparing Stereotactic Body Radiation Therapy for Locally Advanced Pancreatic Cancer: Technique, Toxicity, and Local Response

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PURPOSE AND OBJECTIVES: The proximity of the pancreas to the bowel presents a unique challenge for pancreatic cancer stereotactic body radiotherapy (SBRT). This study explores the safety and effectiveness of a novel approach optimizing pancreatic tumor coverage and duodenal sparing.

MATERIALS AND METHODS: From 2010 to 2013, a total of 30 patients with locally advanced pancreatic cancer (16 head, 13 body, and 1 tail) were treated with SBRT for their unresectable, borderline resectable, or recurrent disease. All underwent endoscopic ultrasound-guided fiducial placement in and around the tumor. The treatment planning CT scan with oral contrast. This CT was used in conjunction with endoscopic ultrasound (EUS) findings, positron emission tomography (PET), and biphase CT scans to identify the gross tumor volume (GTV) in the expiration phase. The planning target volume (PTV) was created by expanding the GTV by 2 mm. Volume–volume histogram (DVH) endpoints were constructed, keeping V7, V15, and V20 (stomach/duodenum volumes that received 7 Gy, 15 Gy, and 20 Gy) < 40%, < 25%, and < 15%, respectively; the dose to one-third of the duodenal circumference < 20 Gy; and duodenal point max dose < 23 Gy. Additional dose constraints included liver D50 < 5 Gy, ipsilateral kidney D25 < 5 Gy, and cord Dmax < 10 Gy. Three 10-Gy fractions, normalized to the 85% isodose, were delivered to the PTV on consecutive weekdays using fiducial-based respiratory motion tracking on a dedicated 6 MV linear accelerator (linac)-integrated stereotactic delivery system. The patients were offered systemic therapy for 6 months or until tolerance or disease progression. Follow-up occurred at 4 weeks, 12 weeks, and every 3 months.

RESULTS: All patients completed SBRT and a median of 5 total cycles of pre- and post-SBRT chemotherapy. Planning target volumes ranged from 14–197 cm3 (median 55 cm3). The 12-month survival and local control was 18% and 95%, respectively. One patient developed transient gastroparesis, two patients developed grade 2 abdominal pain, and one developed grade 2 hematologic toxicity. No late toxicity was observed.

CONCLUSIONS: Linac-delivered organ-sparing SBRT with chemotheraphy in locally advanced pancreatic cancer resulted in excellent local control and was also well tolerated acutely and subacutely. A phase I dose-escalation study is under way.
(P108) A Dosimetric Comparison of Endorectal Brachytherapy, Tomotherapy, Linac-Based Stereotactic Body Radiotherapy (SBRT), and Cyberknife for the Delivery of a Rectal Tumor Boost

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PURPOSE: Neoadjuvant chemoradiation or a short course of pelvic radiation therapy followed by surgery is the standard of care for patients diagnosed with locally advanced rectal cancer. For patients who are not surgical candidates, delivery of a tumor boost is frequently considered. The present analysis compares dosimetry of endorectal brachytherapy (ERBT) with three different image-guided radiation therapy (IGRT) techniques—namely tomotherapy, linear accelerator (linac)-based stereotactic body radiotherapy (SBRT), and CyberKnife (CK) SBRT.

MATERIALS AND METHODS: The planning CT scans of 10 patients who received ERBT were retrieved. These CT scans were acquired with an endorectal applicator in place, which distends the rectal wall and facilitates rectal immobilization and tumor localization. Using these planning CT scans, tomotherapy, seven-field linac-based SBRT, and CK dose distributions were generated for the same dose schedule that was used for the ERBT (26 Gy in four fractions, prescribed to the outermost tumor margin). All external beam plans were prescribed to an isodose envelope covering 95% of the target and ensuring 99% of the target receives a minimum of 90% of the prescribed dose. For this comparative dosimetric study, the planning target volume (PTV) was considered equal to the gross tumor volume (GTV) for all plans. One-way analysis of variance (ANOVA) testing was used to compare max and mean values observed for selected organs at risk.

RESULTS: All modalities achieved complete coverage over the target by the prescription dose. The target near maximum dose (D2%) was 175.9 Gy, 27.0 Gy, 29.1 Gy, and 31.96 Gy for ERBT, tomotherapy, linac-based SBRT, and CK, respectively. For the ERBT, tomotherapy, linac-based SBRT, and CK plans, the conformity index (prescription vol [cc]/target vol [cc]) was 4.1, 1.5, 1.5, and 1.2 (P = .01), respectively, and the homogeneity index ([D2%–D98%]/D50%) was 2.79, 0.03, 0.13, and 0.22 (P = .00), respectively.

CONCLUSIONS: All IGRT techniques (tomotherapy, linac-based SBRT, and CK) provided better target conformity and homogeneity compared with ERBT. The endocavitary brachytherapy plans were associated with significantly higher doses to the uninvolved rectal wall and adjacent anal canal. When considering the use of a tumor boost in the treatment of patients with unresectable rectal cancer, the IGRT techniques studied in this analysis offer better tissue sparing and CI than ERBT.

(P109) FDG-PET Feature and Texture Analysis as Potential Predictors of Pathologic Outcome Following Neoadjuvant Chemoradiotherapy for Locally Advanced Rectal Cancer

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BACKGROUND: Intriguing data suggest that clinical complete response following neoadjuvant chemoradiation (CRT) may obviate the need for definitive resection in patients with locally advanced rectal cancer. However, accurate radiographic assessment of clinical response remains challenging. Whereas prospective data suggest that positron emission tomography/computed tomography (PET/CT) scans do not have adequate value for predicting a pathologic complete response (pCR), minimal data are available on the value of PET/CT in predicting tumor regression grade (TRG)-based pathologic response. Herein, we investigate whether morphologic, textural, and quantitative features of PET/CT can be used to predict pathologic response in rectal cancer.

METHODS: With institutional review board (IRB) approval, we reviewed patients with locally advanced rectal cancer treated with neoadjuvant CRT from 2011–2013 who also underwent fluorodeoxyglucose (FDG)-PET/CT scans within 6 weeks pre-CRT and 6–8 weeks post-CRT. PET/CT images were deformably registered to the radiation therapy (RT) planning CT. Tumor volumes of interest were divided into 4.8-mm³ subvolumes, characterized by mean RT dose and comprehensive texture (energy, correlation, variance, sum

### Table P108

<table>
<thead>
<tr>
<th>Organ</th>
<th>ERBT Max/Min (Gy)</th>
<th>Tomotherapy Max/Min (Gy)</th>
<th>LBSBRT Max/Min (Gy)</th>
<th>CK Max/Min (Gy)</th>
<th>P Value</th>
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<tr>
<td>Uninvolved rectum</td>
<td>181.5/22.7</td>
<td>26.5/9.4</td>
<td>27.4/5.8</td>
<td>27.9/8.0</td>
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<td>Anal canal</td>
<td>14.3/4.3</td>
<td>4.9/1.5</td>
<td>3.2/0.6</td>
<td>5.9/1.9</td>
<td>&lt; .05</td>
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<tr>
<td>Bowel</td>
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<td>9.3/2.0</td>
<td>9.4/1.4</td>
<td>14.7/4.9</td>
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<tr>
<td>Bladder</td>
<td>23.4/5.2</td>
<td>15.2/4.2</td>
<td>14.5/3.6</td>
<td>16.0/5.6</td>
<td>NS</td>
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<td>5.8/3.0</td>
<td>8.4/2.4</td>
<td>5.0/2.8</td>
<td>NS</td>
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<tr>
<td>Right femoral head</td>
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<td>5.4/2.8</td>
<td>6.6/2.3</td>
<td>3.5/3.3</td>
<td>NS</td>
</tr>
</tbody>
</table>

CK = CyberKnife; ERBT = endorectal brachytherapy; LBSBRT = linear accelerator–based stereotactic body radiotherapy; NS = not significant.
mean, cluster tendency, inverse variance) and feature (pre/post-CRT maximum standardized uptake value [SUV\textsubscript{max}], mean SUV, coefficient of variation [CV], total lesion glycolysis [TLG], tumor size, MTV\textsubscript{40} [metabolic tumor volume 40%]) analysis. Mann-Whitney test and Cox modeling were used to identify predictors of complete/near-complete response (TRG 0–1) vs moderate/minimal/no response (TRG 2–3).

**RESULTS:** Fifteen patients with locally advanced rectal cancer were identified, all of whom received pre-CRT PET, while 9 of 15 also received post-CRT PET. Pathologic downstaging was noted in 60% of patients, and 13% had a PCR (ypT0N0). TRG of 0–1 and 2–3 was noted in 27% and 73% of patients, respectively. Pre-CRT tumor volume (\(P = .01\)), TLG (\(P = .04\)), and MTV\textsubscript{40} (\(P = .01\)) were found to be significant predictors of TRG, whereas no correlation was seen with SUV\textsubscript{max} (\(P = .38\)), mean (\(P = .29\)), or pre-/post-PET textural feature analysis between pathologic responders and nonresponders.

**CONCLUSIONS:** Parameters of metabolic response were generally not predictive of pathologic response or TRG in locally advanced rectal cancer, with the exception of pre-CRT tumor volume, TLG, and MTV\textsubscript{40}. Further research is warranted to further validate these predictors, given the potential clinical significance.

(P110) Breast Cancer Before Age 40: Current Patterns in Clinical Presentation and Local Management

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**BACKGROUND:** Although uncommon in women less than 40 years old, breast cancer in younger women may have unique biological and treatment implications. The purpose of this study was to evaluate treatment of breast cancer in young women with respect to previously established clinical predictors of local therapy choice.

**METHODS:** The design of the study was a case-control analysis. Using the National Cancer Institute (NCI)-Surveillance, Epidemiology, and End Results (SEER) database, breast cancer cases from 2010 were queried and limited to women between the ages of 20–39 years (cases) and 60–64 years (controls), lobular/ductal histology, nonmetastatic disease, and treatment with surgery. Controls were established based on the median age of women diagnosed with breast cancer. First, we tested for associations between young age (ages 20–39 y) and tumor/demographic variables by calculating the odds ratio (OR) and computing Pearson’s chi-square value. Second, we tested for associations between young age and surgical procedure (breast-conserving surgery [BCS], simple mastectomy, modified radical mastectomy, and bilateral mastectomy). Third, in mastectomy patients, we tested for associations between young age and postmastectomy radiation therapy (PMRT). Finally, we constructed separate multiple logistic regression models for treatment choice (ie, surgery type and PMRT), adjusting for significant \((P < .05)\) univariate relationships with young age (first analysis).

**RESULTS:** A total of 7,115 patients were analyzed, with 1,518 (21.3%) representing women between the ages of 20–39. Compared with older women (ages 60–64), young women (ages 20–39) with breast cancer were more likely to have large, node-positive, estrogen receptor (ER)-negative tumors with ducal histology and be of minority race in multivariate analysis. Further, 63.2% of older women underwent BCS, whereas only 40.5% of younger women underwent BCS. The OR of simple mastectomy was 1.30 (95% confidence interval [CI], 1.08–1.56), 2.07 for modified radical mastectomy (95% CI, 1.77–2.41), and 6.42 for bilateral prophylactic mastectomy (95% CI, 5.43–7.58) and significantly associated with young age relative to BCS. However, in multivariate analysis, only bilateral prophylactic mastectomy was significantly associated with young age (OR = 5.10; 95% CI, 4.24–6.13, \(P < .001\)). Finally, postmastectomy RT was more prevalent in young women (40.7%) compared with older women (23.1%), which retained significance in multivariate analysis (OR = 1.74; 95% CI, 1.42–2.14, \(P < .001\)).

**CONCLUSIONS:** In 2010, younger women with breast cancer were more likely to present with locally advanced, biologically aggressive malignancies. BCS was less common among young women, but this trend appears to be closely related to the tumor characteristics associated with young age and the prevalence of bilateral prophylactic mastectomy among young women. Postmastectomy RT was more frequently administered in young patients after adjustment for tumor and demographic variables.

(P111) Accelerated Partial-Breast Irradiation With Multicatheter High-Dose-Rate Brachytherapy; Feasibility and Results in a Private Practice Cohort

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**PURPOSE:** To report results and outcomes of use of multicatheter interstitial high-dose-rate (HDR) brachytherapy (BT) to deliver accelerated partial-breast irradiation (APBI) in a large cohort of women treated in a three-physician private practice setting over 10 years and 9 months.

**MATERIALS AND METHODS:** A total of 241 selected patients with Tis-2 N0-1mic breast cancer without an extensive intraductal component and with negative surgical margins were treated after breast-conserving surgery (BCS) with APBI using HDR BT. Three physicians performed the procedures as part of a comprehensive radiation oncology practice. Median patient age was 61 years. Dosage regimen was initially 34 Gy in 10 fractions over 4 elapsed days; subsequently, 32 Gy in 8 fractions over 3–4 elapsed days was used. Target volume was the surgical resection bed with a 1.5–2.0-cm margin. Ultrasound guidance was used in 231 cases, and mammographic stereotactic guidance was used in 10 cases. Overall median follow-up was 67.8 months and 67.4 months in surviving patients. Local breast and regional control, cancer-specific survival (CSS), disease-free survival (DFS), overall survival (OS), late effects, and cosmesis were evaluated.

**RESULTS:** Four (1.54%) local recurrences were observed. Four (1.54%) “elsewhere” breast failures (different quadrant) were observed. All local and elsewhere failures recurred 18 to 42 months after treatment. Twenty patients died of intercurrent disease, five died of breast cancer, and one is alive with metastatic breast cancer. OS and CSS rates were 89.6% and 97.9%, respectively, with a median follow-up of 67.4 months. Cosmesis was excellent or good in 96.7% of cases. Fat necrosis requiring surgical intervention
occurred in 28 patients (10.8%). Median V200 in patients who developed necrosis was 13.6 cc; median V200 in those without development of necrosis was 12.0 cc. Five (2.1%) patients developed telangiectasia > 1 cm². Three (1.25%) patients developed breast abscess requiring surgical intervention.

CONCLUSIONS: APBI using HDR multicatheter interstitial implants is feasible in small private practice with dedicated brachytherapists, yielding excellent long-term results comparable with large academic institutional series and clinical trials and also comparing favorably with the more common external beam regimens.

(P112) Single-Institution Experience With Intrabeam IORT for Treatment of Early-Stage Breast Cancer

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PURPOSE: Report preoperative and postoperative patient and tumor characteristics for breast cancer patients treated at New York Presbyterian Hospital, Weill Cornell Medical College with Intrabeam intraoperative radiation therapy (IORT).

METHODS: Records of all 61 patients treated with Intrabeam IORT from 2012–2013 were retrospectively reviewed.

RESULTS: The median follow-up time was 6.0 months (range: 0.0–18.1 mo), and no patients have developed a local recurrence. The average age was 71.1 ± 8.9 years (range: 53–89 yr). Left-sided breast cancer accounted for 50.8% of the patients. The median applicator size was 3.5 cm (range: 3–5 cm). The median tumor size was 1.0 cm (range: 0.1–2.5 cm). The histology of the tumors was 70.5% invasive ductal carcinoma (IDC), 19.7% invasive lobular carcinoma (ILC), and 9.8% ductal carcinoma in situ (DCIS). Only one patient with ILC was under the age of 65 years. With respect to grade, 26.2% of tumors were high-grade, 50.8% of tumors were intermediate-grade, and 23.0% of tumors were low-grade. Node positivity was seen in five patients (8.2%), and lymphovascular invasion was seen in six patients (9.8%), of whom only three patients were not recommended to undergo external beam RT (EBRT). With respect to receptor status, 91.8% were estrogen receptor (ER)-positive, 77.0% were progesterone receptor (PR)-positive, and 3.3% were human epidermal growth factor receptor 2 (HER2)-positive. All patients underwent same-day surgery, and there were no perioperative or postoperative complications.

CONCLUSION: Patients treated with Intrabeam IORT at our institution were a more favorable group of patients compared with the TARGIT trial, as they were elderly women with small, hormone receptor-positive, and node-negative tumors. Treatment was well tolerated, with high patient satisfaction.

(P113) Age and Marital Status Are Associated With Choice of Mastectomy in Patients Eligible for Breast Conservation Therapy

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PURPOSE AND OBJECTIVES: To evaluate clinical factors associated with the choice of mastectomy in patients eligible for breast conservation therapy (BCT).

MATERIALS AND METHODS: Between July 2009 and December 2011, a total of 208 women with invasive or noninvasive breast cancers were evaluated in a multidisciplinary breast cancer program at the University of Maryland and underwent surgery. Patients with lobular carcinoma in situ (LCIS) and atypical histologies (ie, lymphoma, sarcoma, and phyllodes) were excluded. A total of 131 who were eligible for BCT were analyzed for factors that predicted patient choice of surgery. We used Fisher’s exact test and likelihood ratio to examine whether choice of surgery (mastectomy vs BCT) differed by clinical characteristics (eg, age [< 60 vs ≥ 60 y], race [white vs black vs other], family history [yes vs no], marital status [married vs unmarried], clinical T-stage [Tis vs T1 vs T2], N-stage [N1–2 vs N0], group stage [stage 0–1 vs stage 2–3], histology [DCIS vs invasive ductal cancer (IDC) vs invasive lobular cancer (ILC)], bilateral disease [yes vs no], and previous breast cancer [yes vs no]).

RESULTS: Among the 208 patients who had mastectomy (n = 106), after advanced disease (T3/T4; n = 32), patient choice was the second most commonly cited reason for undergoing mastectomy (n = 29). Other reasons included poor expected cosmesis (n = 23), multicentric disease (n = 15), prior radiation (n = 5), and persistently positive margins (n = 2). Eleven patients who were initially deemed eligible for breast conservation were rendered ineligible after magnetic resonance imaging (MRI) findings showed multicentricity or tumor size > 5 cm. Twenty-nine of 131 patients were deemed eligible for BCT by their multidisciplinary team; yet, 29 chose mastectomy. Results of the Fisher’s exact and likelihood ratio tests showed that choice of surgery differed significantly by age and marital status. Specifically, patients were more likely to choose mastectomy if they were younger (< 60 years of age; 30% vs 13%; P = .02) or married (31% vs 17%; P = .04). Choice of surgery did not differ significantly by other clinical characteristics (P values > .16). Among younger patients (< 60 years), those who were married were more likely to choose mastectomy over BCT (37% vs 18%; P = .04), while those who were not married were equally likely to choose mastectomy or BCT (25% vs 21%; P = .65).

Within the group of 29 patients who chose mastectomy, 55% underwent breast reconstruction and 40% underwent prophylactic contralateral mastectomy. Postmastectomy radiation was recommended in 21% of these patients, based on pathologic findings at the time of surgery.

CONCLUSIONS: Of the patients who were eligible for BCT, younger age and being married were associated with choosing mastectomy. MRI findings alone resulted in 7% of patients initially eligible for breast conservation no longer being eligible for breast conservation. Also, 21% of patients who chose mastectomy required adjuvant radiation therapy.
(P115) Breast Cancer Laterality Does Not Influence Overall Survival in a Large Modern Cohort: Implications for Radiation-Related Cardiac Mortality

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OBJECTIVES: Radiotherapy for left-sided breast cancer has historically been associated with an elevated risk of cardiac mortality, based upon studies in the era predating computed tomography (CT)-based treatment planning. This study assessed the impact of tumor laterality on overall survival (OS) in a large cohort treated with modern techniques to determine if left-sided treatment is still associated with a heightened risk of cardiac mortality.

METHODS: Patients treated for breast cancer with breast-conserving surgery and adjuvant external beam radiotherapy were identified in the National Cancer Database (NCDB), a prospectively maintained nationwide database. Overall survival (OS) was compared based upon tumor laterality using Kaplan-Meier analysis. Separate analyses were performed for patients with noninvasive and invasive carcinoma, as well as patients treated with breast-only radiotherapy and breast plus regional nodal radiotherapy. Multivariate Cox regression analysis of OS was performed with age, estrogen receptor status, American Joint Committee on Cancer (AJCC) stage group, tumor grade, Charlson/Deyo comorbidity score, adjuvant chemotherapy or endocrine therapy receipt, and tumor laterality as covariates.

RESULTS: We identified 344,831 patients treated between 1998 and 2006 for noninvasive (12.1%) and invasive carcinoma (87.9%), with a median follow-up of 72.5 months (range: 0–170 mo) in the overall cohort. Clinical, tumor, and treatment characteristics of patients with left-sided cancers (50.7%) closely matched those of patients with right-sided cancers. Regional nodal radiation was employed in 14.2% of patients treated for invasive cancer. No difference in OS was noted when comparing patients by tumor laterality for patients treated with breast-only radiotherapy (hazard ratio [HR] = 0.984; 95% confidence interval [CI], 0.965–1.005; P = .132), as well as for invasive carcinoma treated with breast and regional nodal radiotherapy (HR = 1.001; 95% CI, 0.959–1.045; P = .957). In multivariate analysis including potential confounders of a potential OS-by-laterality effect, OS was identical between left- and right-sided cancers (Figure; HR = 1.002; 95% CI, 0.973–1.032; P = .874). When analyzing patients with at least 10 years of follow-up (n = 27,725), it remained that there was no significant difference in OS by laterality, both in patients treated with breast-only (HR = 0.955; 95% CI, 0.863–1.056; P = .368) and breast plus regional nodal radiotherapy (HR = 0.859; 95% CI, 0.668–1.080; P = .155).

CONCLUSIONS: Treatment of left-sided invasive and noninvasive breast cancer with radiotherapy does not appear to increase the risk of death in this large prospective national database relative to right-sided tumors. Consequently, radiotherapy delivered in a modern fashion using CT planning may not increase the risk of cardiac mortality.

(P116) Bilateral Immediate DIEP Reconstruction and Postmastectomy Radiotherapy: Experience at a Tertiary Care Institution

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PURPOSE: Although autologous and immediate reconstruction has potential advantages when compared with delayed and implant-based reconstruction for patients with breast cancer (BCA), concerns exist for potential increased complications and technical difficulty in the delivery of postmastectomy radiotherapy (PMRT). Bilateral immediate reconstruction (BIR) with a deep inferior epigastric perforator (DIEP) flap offers several distinct advantages for patients with BCA: it produces a chest wall reconstruction with a robust vascular supply, eliminates the need for subsequent reconstructive surgery, and potentially decreases the overall time needed to complete cancer therapy. The purpose of this study was to report the outcomes for patients treated with bilateral mastectomy (BLM), BIR with DIEP, and PMRT at our institution.

METHODS: We performed a retrospective review of patients with BCA who underwent BLM, BIR with DIEP, and PMRT at Yale–New Haven Hospital. A minimum of 6 months of follow-up since completion of PMRT was required.

RESULTS: A total of 17 patients were identified. Median age at the time of surgery was 53 years (range: 26–60 yr). Median follow-up from completion of PMRT was 26.4 months (range: 6.3–67.2 mo). All surgeries were performed by a single surgical team (SF and JS). Three patients received neoadjuvant chemotherapy (NAC), and 14 received adjuvant chemotherapy. The stage distribution for patients who received adjuvant chemotherapy was: stage IIA (3 patients), stage IIB (3 patients), stage IIIA (6 patients), and stage IIIC (2 patients). PMRT was delivered to the ipsilateral chest wall...
(all patients), supraclavicular fossa (16 patients), and axilla (5 patients). No patient had internal mammary nodal radiation. Prior to PMRT, five patients required additional chest wall surgery. One of these patients had total flap loss (due to necrotizing cellulitis), and two patients had partial flap loss. No patient had flap loss after PMRT. A total of 33/34 DIEP reconstructions were maintained at the time of last follow-up. Lung dose-volume histogram information was calculated for all patients. Median ipsilateral lung (IL) V20 was 22.7% (range: 6.7%–33.5%), median bilateral lung V20 was 11.7% (range: 3%–16.8%), and median mean IL dose was 13.3 Gy (range: 5.7–15.7 Gy). There were no reported cases of radiation pneumonitis and no isolated locoregional failures. Median time from surgery to completion of RT was 7.9 months (range: 2.4–10.4 mo) for all patients and 2.8 months (range: 2.4–4.1 mo) for patients undergoing NAC (reconstruction of the nipple-areola complex).

CONCLUSIONS: Our institutional review of 17 patients who had BLM, BIR with DIEP, and PMRT demonstrates that this approach was well tolerated. Using standard PMRT treatment techniques, the IL V20, total lung V20, and mean lung dose values were within acceptable limits. Furthermore, for patients who underwent NAC, median total time from surgery to completion of RT was 2.8 months—significantly shorter than that observed in the setting of delayed reconstruction with expanders. In our experience, BIR with DIEP can be performed prior to PMRT with a relatively low incidence of surgical complications, high rate of DIEP viability at 26.4 months, no pulmonary complications, and no compromise in standard lung DVH parameters. Longer follow-up will be needed to assess delayed complication rates and disease-free and overall survival.

(P117) Anatomical Variations and Radiation Technique for Breast Cancer

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PURPOSE: To compare conventional radiotherapy (RT) with proton-based RT in a series of patients with right- or left-sided breast cancer and anatomical variations resulting in technically challenging radiation plans.

METHODS: Eight women had conventional (photon and/or electron) and proton-based (proton only or combined photon-proton) radiation plans developed. Four were treated with the conventional plan, and four were treated with the proton-based plan. Cardiac V5, V20, and V50; mean heart dose; and ipsilateral lung V5 and V20 were documented for each plan, along with D95 to the breast or chest wall and regional lymphatics (supraclavicular, level I–III axilla, and internal mammary chain [IMC]). All plans were optimized to achieve adequate target coverage.

RESULTS: Dose-volume constraints were difficult to meet with conventional radiation in three patients with right-sided breast cancer because of significant breast ptosis (n = 2) or bilateral implants (n = 1). For two of the three patients, IMC irradiation was omitted in order to meet the lung V20 constraint. In these three patients, ipsilateral lung V20 with a conventional plan treating the IMC ranged from 44.7% to 47.5%. The lung V20 was decreased by adding a proton component to the plan, with lung V20 ranging from 14.4% to 26.1%. The mean heart dose ranged from 1.7–4.3 Gy for the conventional plans compared with 0.6–0.8 Gy for the proton-based plans. In the five patients with left-sided disease, constraints were difficult to meet in the two postmastectomy patients with a chest wall too thick or too variable in depth for electrons only, in one patient with large breasts and significant ptosis, in one patient with a heart-shaped thorax, and in one patient with severe arthritis limiting upper-extremity extension. In these five patients, the mean heart dose ranged from 6–19 Gy for the conventional plans compared with 0.8–2.9 Gy for the proton-based plans. In the conventional plans, ipsilateral lung V20 ranged from 40% to 46% compared with 9.8% to 31.6% with the proton-based plans. Cardiac V5 and lung V5 were reduced for both right- and left-sided disease treated with proton-based RT (mean cardiac V5 right: 15% vs 1.3%; mean lung V5 right: 75% vs 40%; mean cardiac V5 left: 29% vs 5%; mean lung V5 left: 58% vs 32% for conventional vs proton radiotherapy, respectively). In addition, for left-sided breast cancers, a decrease in cardiac V20 and V50 was seen with the proton-based plans (mean cardiac V20: 18% vs 2% and mean cardiac V50: 5.5% vs 1.5% for conventional vs proton radiotherapy, respectively).

CONCLUSION: Proton-based RT decreases the heart and lung doses
for both left- and right-sided breast cancer patients with unfavorable anatomy, such as implants, large breasts, a heart-shaped thorax, and limited upper-extremity range of motion. In these cases, proton-based RT allows adequate target coverage and goal organ-at-risk constraints to be achieved simultaneously.

(P118) Metadherin Overexpression Is Associated With Improved Locoregional Control After Mastectomy

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BACKGROUND: Breast cancer patients who develop a recurrence in the chest wall after mastectomy represent a high-risk subgroup that may benefit from early identification and more aggressive treatment. Traditional clinicopathologic factors have been proven useful for prognosis, but there remains a need to identify molecular markers with prognostic significance. Metadherin (MTDH) is an onco-gene that is overexpressed in all cancers studied so far. It has been linked to multiple pathways, including PI3K/Akt, NFkB, and Wnt/β-catenin, and is a key mediator of proliferation, metastasis, and chemoresistance. MTDH, while normally absent from human breast tissue, is overexpressed in 44% of primary breast tumors. The purpose of this study is to evaluate the association between MTDH expression and locoregional recurrence in a cohort of breast cancer patients treated with mastectomy.

PATIENTS AND METHODS: We retrospectively identified 22 patients who developed a locoregional recurrence as the first or only site of failure after mastectomy and had paraffin-embedded tissue blocks from the primary tumor available. These patients were case control–matched to 28 patients who were disease-free at last follow-up. They were matched with respect to age (± 3 yr) and follow-up duration (< 5 or ≥ 5 yr). All patients initially presented with 0–3 positive nodes, and none received postmastectomy RT. Tumor blocks were assembled into a tissue microarray, and MTDH expression was analyzed by immunohistochemical methods and then quantified electronically based on the intensity of staining. Conditional logistic regression was used to test the relationship between each variable and the risk of locoregional recurrence.

RESULTS: Immunohistochemical analysis revealed primarily cytoplasmic expression of MTDH, and 26 of 49 (53.1%) patients were positive for MTDH overexpression. Higher levels of MTDH expression were significantly associated with lower Ki67 expression (P = .006). Lower MTDH expression was linked to the triple-negative phenotype (P = .0027). In a univariate conditional logistic regression, lower MTDH expression was strongly linked to higher odds of locoregional recurrence (odds ratio [OR] = 0.80–0.96). However, in the DID model, the interaction term between increasing vs stable unemployment and year was not statistically significant, indicating that increasing unemployment was not associated with an additional negative impact beyond other unmeasured variables that also changed from 2004 through 2008 (OR = 0.93; 95% CI, 0.78–1.11). In the adjusted model, being Medicare-age-eligible was associated with higher likelihood of PLRT receipt, while black race and estrogen receptor–negative status were associated with lower receipt of PLRT.

CONCLUSION: The impact of increasing vs stable unemployment rate in patients’ residence areas was not significantly associated with lower PLRT receipt. This indicates that the lower rate of PLRT
receipt in 2008 in comparison with 2004 was due to multiple factors not completely encompassed by increasing unemployment alone.

(P120) Immediate Versus Delayed Reconstruction After Mastectomy in the United States Medicare Breast Cancer Patient

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BACKGROUND: Although recent data have been published regarding trends surrounding mastectomy with reconstruction for breast cancer, little data exist about predictors of immediate vs delayed reconstruction and the prevalence of reconstruction where it is traditionally contraindicated, such as inflammatory breast cancer and stage IV disease.

METHODS: Surveillance, Epidemiology, and End Results (SEER)-Medicare data were reviewed for women ≥66 years old and diagnosed between 1992 and 2005 with stage 0 through IV breast cancer. Immediate reconstruction was defined by claims dated the same day as their mastectomy, while delayed reconstruction was defined as reconstruction performed up to 36 months after that date. Postmastectomy radiotherapy was reviewed by searching for radiotherapy claims up to 1 year after mastectomy.

RESULTS: Of the 50,843 women who underwent mastectomy, 5.8% had reconstruction, increasing from 3.2% to 7.3% (P < .0001) during the study period, with a maximum patient age of 99 years. There were 4.3% of the 783 having inflammatory breast cancer and 2.9% of the 1,241 patients with metastatic disease who underwent reconstruction. Implants, autologous tissue flaps (ATFs), the combination, and unspecified reconstruction types occurred in 57.2%, 20.4%, 17.0%, and 5.2%, respectively, with radiotherapy performed in 14.9%, 37.3%, 14.6%, and 51.0% of those respective groups. Postmastectomy radiotherapy was also performed in 23% of immediate and 14.9% of delayed reconstruction cases. Among all patients having reconstruction, 79% underwent immediate reconstruction and 21% had delayed reconstruction, with a median delay of 8.5 months. From 1998 to 2005, immediate reconstruction increased from 2.6% to 5.8%, while delayed reconstruction plateaued at ~1.4% in this period. The likelihood of having any reconstruction declined with increasing comorbidities (trend P < .0001). Delayed-reconstruction patients had greater comorbidities than those who had immediate reconstruction (trend P = .04). ATF patients had greater comorbidities than implant patients (P = .0003). Variables associated with delayed reconstruction (vs immediate) were SEER region (P < .0001), higher stage (P < .0001), postoperative radiotherapy (P < .0001), diagnosis year (P < .037), and comorbidity index (P = .037). Age, marital status, race, and histology were not predictive.

CONCLUSION: A small minority of patients have reconstruction when it is traditionally considered contraindicated. Radiotherapy was used more frequently in patients having immediate than delayed reconstruction, with ATF reconstruction used to a greater degree than implants in both immediate and delayed reconstruction groups. Although immediate reconstruction is on the rise, its use in Medicare patients remains low. Further efforts to educate clinicians and patients about eligibility for immediate reconstruction, even in those over 65 years of age, may be worthwhile.


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BACKGROUND: Significant effort has been expended over the past decade to reduce racial disparities in breast cancer care. Whether disparities in receipt of appropriate radiotherapy care for breast cancer persisted despite these efforts is unknown, as is the impact of being eligible for Medicare. We therefore investigated trends in racial differences by age in post–breast lumpectomy radiation therapy (PLRT) from 2004–2009.

METHODS: We analyzed the Surveillance, Epidemiology, and End Results (SEER) registry database for women aged 40–85 years who underwent lumpectomy for stage I breast cancer and were eligible for PLRT. We examined variables potentially associated with the receipt of PLRT, including year of diagnosis and race, and examined women separately by age group.

RESULTS: Among 67,124 women aged 40–85 years undergoing lumpectomy, receipt of PLRT decreased from 80.7% in 2004 to 76.8% by 2009 (P < .001). There remained a persistent disparity in PLRT among African-American women (in 2004, 80.6% white vs 78.9% African Americans and in 2009, 77.5% white vs 72.0% African Americans). In multivariable logistic regression, African-American race (odds ratio [OR] = 0.82; 95% confidence interval [CI], 0.76–0.89) and being diagnosed more recently were associated with lower odds of PLRT (OR for 2009 vs 2004 = 0.74; 95% CI, 0.69–0.79), while older women typically covered by public health insurance (age 65–69) were more likely to receive PLRT (OR = 1.09; 95% CI, 1.02–1.15).

CONCLUSION: PLRT decreased by a significant percentage of 3.9% among all women in recent years, and racial disparities in PLRT receipt have persisted. Medicare eligibility increased the likelihood of PLRT receipt.

(P122) Streamlining Referring Physicians Orders With ‘Reflex Testing’ Significantly Decreases Time to Resolution for Abnormal Screening Mammograms

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INTRODUCTION: Patients with abnormal screening mammogram (abSM) often experience prolonged wait times for additional testing to resolve the cause of the abnormality. The purpose of this study was to initiate an intervention, termed ‘reflex testing’ (RefT), and analyze pre- and post-RefT timelines to determine if, where, and in whom RefT resulted in significant decreases in timelines for resolution of abSM of patients undergoing routine screening in an accredited community hospital-based breast center.

METHODS: All patients with abSM (Breast Imaging Reporting and
Data System [BIRADS] 0, IV, and V) from the diagnostic sites of our breast center program were eligible for analysis. The two cohorts consisted of women with abSM from January to June 2009 (preintervention) and January to June 2012 (postintervention), with timelines created for each patient from the date of abSM to date of: additional diagnostic tests (mammogram, ultrasound, magnetic resonance imaging [MRI]), upgrade to higher BIRADS score, biopsy, or resolution (BIRADS I/II). Based on analysis of the timelines, RefT was implemented to streamline physicians’ written orders as follows: All of the medical staff/referring physicians were notified that, as part of the initial written order, every abSM order would automatically result in additional diagnostic testing and/or biopsy reflexively (as deemed appropriate by the reading radiologist); thus, additional diagnostic test/biopsy-specific written orders would not be required by the referring physicians. Each abSM patient was contacted within 24 hours following the abnormal reading by the breast nurse navigation team to facilitate scheduling for additional testing. Data were collected from the hospital’s Meditech/PenRad electronic medical records. SPSS V.19 and Excel were utilized for statistical analysis.

RESULTS: Analysis of the preintervention abSM timelines revealed that significant delays (defined as > 1 month) occurred only in patients starting with a BIRADS 0 assignment, and thus, the two cohorts that were analyzed consisted of 1,523 patients initially designated BIRADS 0 (npre-RefT = 647; npost-RefT = 876). Comparison of the two cohorts demonstrated that the overall mean interval from abSM to return for additional testing decreased from 23.5 days pre-RefT (median 20, standard deviation [SD]: 6.987, range: 0–99 d) to 8.2 days post-RefT (median 7, SD: 6.987, range: 0–99 d) (P < .001). For patients not requiring a biopsy (n = 1,190), the RefT decreased the mean time from abSM to first diagnostic test/resolution from 29.7 days to 10.77 days (P < .001). For the 333 patients requiring biopsy (n = 1,190), the RefT decreased the mean time from abSM to first diagnostic test/resolution from 31.4 days to 7.77 days (P < .001) and the interval from first diagnostic test to biopsy from 21 days to 17 days (P < .013). There was no difference in the median number of days from biopsy to pathology report (2.44 vs 2.30; P > .05) for pre- vs post-Ref.

CONCLUSIONS: Reflex testing streamlines the resolution of abSM by allowing for supplementary diagnostic testing and/or biopsy reflexively (by the reading radiologist) without additional written orders from referring physicians. We have demonstrated that this simple initiative significantly decreases patient timelines to resolution of abSM and benefits both subsets of patients not requiring and those requiring biopsies. Implementation of this intervention should be considered in breast center programs wishing to further decrease scheduling times for resolution of abSMs.

(P123) National Trends in the Local Management of Early-Stage Paget Disease of the Breast
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PURPOSE AND OBJECTIVES: Paget disease (PD) of the breast is a condition characterized by infiltration of the epidermis of the nipple with neoplastic cells with or without an underlying malignancy of the breast parenchyma. Due to the rarity of PD, the role of breast conserving surgery (BCS) and radiation therapy (RT) is not fully defined. The specific aims of this analysis are to study national patterns of care in the local management of PD and to determine breast cancer–specific survival (BCSS) by type of treatment in a large population-based cohort.

MATERIALS AND METHODS: The Surveillance, Epidemiology, and End Results (SEER) database was queried for women ≥ 20 years of age diagnosed with Tis–T2 N0 M0 mammary PD who underwent definitive surgery +/- RT from 1998–2010, with minimum follow-up of 6 months. The cohort was stratified by type of treatment into four groups: BCS, BCS + RT, mastectomy (M), or M + RT. Clinical covariates were compared between the groups using the chi-square test. Cox multivariable regression analyses were performed to determine predictors of BCSS. Survival curves were calculated using the Kaplan-Meier method and compared using the log-rank test.

RESULTS: The median follow-up time was 5 years (range: 0.5–12.9 yr). The study cohort comprised 1,509 women, most of whom were ≥ 50 years (79%). The distribution of underlying histologic subtypes was as follows: PD with infiltrating ductal carcinoma (IDC, 43%), PD with ductal carcinoma in situ (DCIS, 46%), and PD with no underlying tumor (11%). High-grade histology was identified in 48% of patients, with estrogen receptor and progesterone receptor positivity in 27% and 18% of patients, respectively. Allocation to treatment groups was as follows: BCS (n = 200), BCS + RT (n = 216), M (n = 1,046), and M + RT (n = 47). Mastectomy rates were highest among patients with PD-IDC (87%). Rates of mastectomy were 74% in the early study period (1998–2004) vs 71% in the latter study period (2005–2010) (P = .12). Overall, lymph node sampling or dissection was performed in 72% of patients: 92% of those with PD-IDC, 61% of those with PD-DCIS, and 44% of those with PD and no demonstrable tumor. BCSS at 5 and 8 years was 93% and 91% for PD-IDC, 98% and 96% for PD-DCIS, and 95% and 95% for PD without underlying tumor, respectively. BCSS was higher among patients in the BCS + RT group (94% at 8 years) compared with those who received BCS alone (91% at 8 years) (P = .54). No difference in BCSS was noted between the BCS + RT and M-alone groups (94% at 8 years) (P = .98). After adjusting for patient and tumor characteristics, no differences were observed in BCSS based on type of surgery (P = .61). Patients who required postmastectomy RT had poorer pretreatment tumor characteristics and inferior BCSS (83% at 8 years).

CONCLUSIONS: This population-based analysis shows that mastectomy with lymph node assessment is the most commonly employed approach for local disease management in early-stage PD. Rates of mastectomy have remained relatively constant throughout the study era. Despite conferring comparable rates of BCSS to mastectomy, BCS + RT appears to be underutilized in the management of PD of the breast.

(P124) Effect of Inhomogeneity on Cardiac and Lung Dose in Partial-Breast Irradiation Using HDR Brachytherapy
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INTRODUCTION: Recent expert consensus statements have endorsed use of accelerated partial-breast irradiation (APBI) in select groups of low-risk women with early-stage breast cancer. APBI in the form of balloon brachytherapy is increasingly selected as a method of radiation treatment (RT). In APBI, accurate dose distribution representation is essential when considering organs at risk (OARs). The presence of inhomogeneities, like air pockets and contrast material in the bone, creates challenges for accurate dose estimation. Current treatment planning systems are based on the TG-43 dose calculation formalism, which assumes full scatter conditions and does not correct for inhomogeneities. Recent advances in dose calculation software have made estimation of the dose that is corrected for inhomogeneities possible. The aim of the current study is to examine the effect of inhomogeneity effects on cardiac and lung dose calculation as estimated by the Acuros BV (Varian) dose calculation algorithm, compared with uncorrected TG-43 doses. Accurate heart and lung dose calculation may be important to minimize long-term toxicity.

MATERIALS AND METHODS: This study looked at 29 MammoSite balloon brachytherapy patients treated with a single central dwell position to 3,400 cGy in 10 bid fractions. Balloon density was over-written to water in the treatment planning system so as to isolate the tissue inhomogeneity effect. Doses were calculated using both TG-43 and Acuros. Maximum and mean heart dose and lung V20 were recorded. A linear fit was used to characterize the relationship between Acuros and TG-43 calculations of these parameters.

RESULTS: Maximum cardiac doses calculated using TG-43 doses ranged from 232 to 4,422 cGy. Maximum cardiac doses as calculated by Acuros were proportional to TG-43 doses. For these patients, a linear fit shows Acuros dose = 0.97 * TG-43 dose ($R^2 = 0.999$). The 95% confidence interval (CI) for the proportionality constant was 0.963–0.978. For any individual patient, the proportional relationship agreed with the actual Acuros dose to $\pm 2\%$. When examining lung doses, the Acuros lung V20 is about 80% of TG-43 ($R^2 = 0.962$).

DISCUSSION: In this small cohort of partial-breast balloon brachytherapy patients, we found that differences in cardiac dose between TG-43 and Acuros (~3%) were less than those reported in previous studies on other critical structures, such as ribs (4%–5%) and skin (7%–8%). Compared with these other structures, we hypothesize that the low-density lung between the balloon and heart may be counterbalancing dose decrease due to lack of full scatter, but further study is warranted. As with ribs and skin, Acuros maximum point dose calculation for heart showed a proportional relationship to TG-43. However, the dose-volume parameter, lung V20, displayed larger variance from proportionality, as shown by the lower $R^2$ value. With evolving technology, it is important to elucidate accurate normal structure dosages to deliver high-quality care in this important patient population. Further study with a larger number of patients is needed to make any definitive recommendations. Our current results appear to be reassuring, that in Acuros-based heart and lung doses are lower than or comparable with TG-43-based calculations.

DISCUSSION: In breast cancer, the primary site residual burden of disease (PRBD) after neoadjuvant chemotherapy has been shown to correlate with poor prognostic outcomes. Currently, there is no established standard of care to offer patients with residual disease, in terms of adjuvant systemic treatment after full-dose neoadjuvant chemotherapy.

MATERIALS AND METHODS: We retrospectively analyzed data from patients treated on an institutional review board (IRB)-approved institutional protocol of neoadjuvant chemotherapy followed by surgery to determine whether patients with intermediate-or high-grade breast cancer, with T2 disease or greater, and with a PRDB greater than 0.5 cm demonstrate worse outcomes without further adjuvant systemic treatment.

RESULTS: The review included 11 patients with breast cancer treated between 2007–2011 with neoadjuvant chemotherapy followed by mastectomy or lumpectomy and followed by adjuvant radiation treatment (RT). A total of five patients with PRBD greater than 0.5 mm received an additional 3–4 cycles of anthracycline-based chemotherapy after surgery, followed by RT. Six patients with PRBD greater than 0.5 mm had radiation alone after surgery with no additional chemotherapy. Four of the five patients receiving additional systemic treatment for PRBD and all patients treated with RT alone had triple-negative or human epidermal growth factor receptor 2 (HER2)-positive status. On preliminary analysis in a median follow-up of 31 months (range: 18–47 mo) for patients receiving chemotherapy and a median follow-up of 45 months (range: 18–68 mo) for patients receiving RT alone, there was no evidence of disease recurrence (local or distant), based on imaging or clinical examination in any of the 11 patients.

CONCLUSIONS: Although limited, these preliminary data may provide a basis for future studies to correlate disease outcomes and pathological data, including initial nodal disease burden and pathological response to treatment.

INTRODUCTION: The World Health Organization predicts that 26.4 million new cancer cases will be reported in 2030 alone. Between 2010 and 2020, the number of patients receiving radiotherapy will increase by 22%. Assuming that the current graduation rate of 140 residents/year remains constant, the number of full-time equivalent radiation oncologists is expected to increase only 2%. The number of residents would have to increase to 280/year for the years 2014–2019 to equal expected demand. For these reasons,
it is necessary to establish an effective mentoring paradigm in radiological science, not just for medical students (MS) but also for high school (HS) and college undergraduate (UG) students, to promote a greater general awareness of the study of oncology as well as its therapeutic implementation.

**METHODS:** Research experience in the Department of Radiation Medicine provides full-time summer and/or year-round research educational experience to HS, UG, and MS interns. Interns are paired in a “near-peer” fashion—that is, a junior or less experienced student matched with a senior or more experienced student. Each pair is subsequently matched with an experienced faculty preceptor. All interns spend a minimum of 10–12 weeks working full time in the preceptor’s laboratory. Preceptors are encouraged to involve interns as much as possible in all facets of the research process, such as reading relevant literature and participating in regularly scheduled lab meetings and journal clubs, research seminars, and multidisciplinary tumor boards. Didactic sessions on how to conduct scientific research and program evaluation from learners will be a core of the program.

**RESULTS:** From 2007–2013, the department has mentored and sponsored a total of 50 students (excluding graduate, postdoctoral, and/or international students). A proud feature of the department’s mentorship program is that HS interns, like their UG and MS counterparts, are active participants who contribute significantly in the preparation of scientific abstracts for national/international conferences, as well as in the drafting of scientific manuscripts. While most HS interns typically start on short-term projects, they understand that research questions may not necessarily be answered in a limited time period. Nine of our HS students have coauthored at least one scientific abstract and/or peer-reviewed manuscript; three HS students successfully competed in regional and/or national science fairs, one UG intern was a laureate of the American Association of Physicists in Medicine (AAPM) Summer Research Fellowship, three UG interns have successfully earned college credits for their research, six MS have successfully secured competitive Research Medical Student Grant awards from the Radiological Society of North America (RSNA), and one MS was a Tartar Trust Fellow.

**CONCLUSION:** Based on the success of our current program, we will submit an R25 that will specifically meet the goals for the National Cancer Institute (NCI) Cancer Education Grant Programs initiatives through the following specific aims: *Aim 1:* To increase the number of students with an interest in cancer and radiation research by identifying and selecting HS and UG students and MS with strong interests in cancer and emphasize recruitment of women and underrepresented minorities into the program. *Aim 2:* Create and implement a structured mentored research and educational experience with emphasis on radiological sciences, near-peer mentorship, and dyadic mentorship.

**BACKGROUND:** There are over 3.0 million cases of nonmelanoma skin cancer (NMSC) diagnosed each year in the United States. Multiple treatment options exist for the treatment of these patients, including excisional surgery, curettage, Mohs micrographic surgery, cryotherapy, topical chemotherapy, and radiotherapy. We describe the outcomes of patients treated at a large private dermatology practice with electronic brachytherapy (eBrx) who had a minimum follow-up duration of 1 year.

**METHODS:** A retrospective review of patients with NMSC treated with eBrx in a large dermatology practice between January 2012 and September 2012 was performed. All patients had a biopsy to confirm the diagnosis of NMSC prior to treatment. Patients received between 40 Gy and 45 Gy in 3-Gy to 4-Gy fractions, delivered three times per week. The treatment was delivered with a Soft Axxent controller (50-kV source). Photographs were taken to document treatment outcomes at all follow-up visits.

**RESULTS:** A total of 58 patients with 74 lesions were identified. The median age was 76 years. There were 53 (72%) facial lesions, 18 (24%) lower extremity lesions, 2 (2.7%) upper extremity lesions, and 1 (1.3%) truncal lesion. There were 40 T1 lesions, 32 T2 lesions, and 2 T3 lesions. Follow-up ranged from 12 to 19 months with a median follow-up of 16 months. Local control was 98.6% in this patient population. Delayed wound healing (>3 months post-treatment) occurred in four (5.4%) lesions, all lower-extremity tumors. Cosmesis was rated as good to excellent at all treated sites except for two (2.7%) who developed hypopigmentation. These two patients were treated to a dose of 40 Gy in 10 fractions.

**CONCLUSIONS:** Early experience at a large dermatology practice treating NMSC in the office setting with eBrx shows excellent local control and acceptable cosmetic outcomes. Patients with lower-extremity lesions are at higher risk of developing delayed wound healing. Careful patient selection and dose selection should be considered in these patients. eBrx is an effective treatment in NMSC and offers patients an effective nonsurgical option.

**P128** Bi-Institutional Cosmetic Outcome of Radiotherapy for Benign Lymphoepithelial Cysts of Parotid Glands in HIV Patients

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**AIM:** To report the long-term outcomes of radiation therapy (RT) in patients infected with human immunodeficiency virus (HIV) who have benign lymphoepithelial cysts (BLECs) of the parotid glands.

**METHODS:** This is a bi-institutional retrospective study of HIV-associated BLECs of the parotids. The medical records of 67 HIV-positive patients treated with RT between 1987 and 2012 were reviewed. Patients were stratified into two groups: Group A consisted of 15 patients (22%) who received a total dose of ≤18 Gy with a median dose 10 Gy (range: 8–18 Gy), and Group B consisted of 52 patients (78%) who received a total dose >18 Gy with a median dose 25 Gy (range: 19–35 Gy).

**RESULTS:** In patients infected with human immunodeficiency virus (HIV) and treated with radiation therapy, 100% of patients had complete resolution of symptoms. There were no instances of recurrence. One (1.3%) patient in Group A developed hypopigmentation of the forehead and one (1.3%) patient in Group B developed hypopigmentation of the lower extremities.

**CONCLUSIONS:** Radiation therapy is an effective treatment for HIV-associated BLECs of the parotid glands.
of 52 patients (78%) who received a total dose of 24 Gy. Bilateral parotids were treated with RT. The median age at RT, HIV diagnosis, and duration of HIV seropositivity was 42 years (range: 7–70 yr), 38 years (range: 23–53 yr), and 11 years (range: 6–35 yr), respectively.

**RESULTS:** After a median follow-up of 38 months (range: 12–141 mo) for the entire cohort, the overall response (OrVr) was 66%. Specifically, complete response (CR) and partial response (PR) were 55% and 11%, respectively. Fourteen of 15 patients (93%) in Group A (≤ 18 Gy) eventually experienced local failure (LF) with the re-emergence of parotid hypertrophy. Among the patients in Group B (24 Gy), 69%, 14%, and 17% experienced CR, PR, and LF, respectively. Median times to failure in Groups A and B were 7 and 20 months, respectively (P < .0001). Similarly, logistic regression analysis revealed the higher dose to be associated with better response rate (ie, CR or PR) (P < .0001), which was also statistically significant (P = .03) after adjusting for confounding variables (age, race, gender, highly active antiretroviral therapy [HAART] use, and fractionation). No patients in either group experienced Radiation Therapy Oncology Group (RTOG) toxicities ≥ grade 2. Specifically, patients experienced mucositis (48%), xerostomia (45%), skin erythema (41%), and altered taste (14%).

**CONCLUSION:** Our data show that 24 Gy is a well-tolerated radiation dose for sustainable cosmetic control of BLECs of the parotid glands in HIV patients.

**(P129) Electronic Brachytherapy for Nonmelanomatous Skin Cancer: Report of First 565 Lesions**

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**PURPOSE:** Electronic brachytherapy for skin cancer is now available without the need for room shielding. Advances in radiobiology and radiotechnology permit the treatment course to be given in eight fractions over 4 weeks. This report describes the experience with our first 565 treated lesions.

**MATERIALS AND METHODS:** A miniaturized 50-keV x-ray tube and delivery system (Xoft Inc, Fremont, California) are FDA-approved for nonmelanotic skin cancers (NMS). The device is operated in a standard unshielded examination room.

**RESULTS:** Fifteen months following introduction of the system, a total of 565 NMS have been treated. There have been two recurrences, and cosmesis has been excellent.

**CONCLUSIONS:** Radiation therapy for NMS can now be given in an office setting as an alternative to Mohs surgery. Results are comparable to or better than those of surgery. Patients are pleased with the outcome and convenience of the short course of therapy given in the office.

**(P130) Implication of Treatment Approach Based on Histology of Thymic Tumors**

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**BACKGROUND:** Thymic tumors are a rare disease and have been treated in a similar manner without convincing data. We present our institutional results of outcomes between invasive thymoma and thymic carcinoma.

**MATERIALS AND METHODS:** Between 1964 and 2009, 125 patients with thymoma (85) or thymic carcinoma (40) were treated at UT MD Anderson Cancer Center. Treatments were as follows: 50 patients (induction chemotherapy + surgery + postoperative XRT), 49 patients (surgery + radiation therapy), 16 patients (radiation only), and 10 patients (chemotherapy + XRT). The data were analyzed using Kaplan-Meier survival function. The log-rank test was used to assess survival function. Cox regression analysis was used for univariate and multivariate analysis.

**RESULTS:** The median follow-up for invasive thymoma and thymic carcinoma was 79 and 46 months, respectively. Age, ethnicity, smoking history, clinical staging, Karnofsky performance score (KPS), and total dose of radiotherapy were not significantly different between the two groups. All clinical stage I or II patients, except for one inoperable patient, were found to have Masaoka stage III disease and received combined treatment. Five-year and 10-year survival rates were significantly better for the thymoma group compared with the thymic carcinoma group. Overall survival (OS) was 86% vs 60% and 59% vs 47%, respectively (P = .04). Disease-free survival (DFS) was 76% vs 58% and 72% vs 53%, respectively (P = .0326). Distant metastasis-free survival (DMFS) was 81% vs 62% and 75% vs 50%, respectively (P = .0141). Multivariate analysis showed that histology, clinical stage, and KPS were significant prognostic factors for predicting OS. Histology, ethnicity, and age were significantly correlated with DM.

**CONCLUSIONS:** Thymic carcinoma patients showed significantly poor OS, DFS, and DMFS compared with thymoma patients. We need to investigate more adequate systemic chemotherapy for thymic carcinoma rather than standard chemotherapy used for invasive thymoma.

**(P131) The Role of Radiation Therapy in the Management of Neurogenic Heterotopic Ossification**

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**BACKGROUND:** Patients who sustain brain and spinal cord injuries are at risk for developing neurogenic heterotopic ossification (NHO), the formation of bone in extraskeletal soft tissue. The pathogenesis of NHO is unclear but may be a combination of local inflammation, prostaglandins, and growth factors stimulating the differentiation of soft tissue mesenchymal progenitor cells into osteoblasts. NHO most commonly affects the hip and elbow joints and ranges from asymptomatic to clinically significant restriction in range of motion resulting in functional deficits. Prevention and management of NHO includes pharmacologic interventions, surgical resection, and radiation therapy (RT). Radiation for NHO is controversial, and the effectiveness of a single 700-cGy fraction, as used in heterotopic ossification (HO) prophylaxis, has been questioned. The purpose of this study was to review the experience and to report the outcome of eight consecutively irradiated joints in four patients with NHO at the Minneapolis Veterans Affairs
Medical Center between July and September 2013.

**MATERIALS AND METHODS:** The management of eight consecutively treated joints in patients with clinically significant NHO was reviewed. One patient had an anoxic brain injury, and the remaining patients had thoracic spinal cord injury (SCI) ranging from T4–T8. Patients were irradiated with 800 cGy in a single fraction to the area of visible ossification. Patients were followed with physical examination and imaging to determine efficacy of therapy. Toxicity was evaluated and reported according to Common Terminology Criteria for Adverse Events version 4.0 (CTCAE v4.0).

**RESULTS:** Sites irradiated included six hips and two elbows. The mean age was 34 years, and median follow-up was 11 weeks. Three hip joints were treated with surgical resection followed by RT and indomethacin at 25 mg tid for 6 weeks. One hip joint, previously treated with surgical resection and RT, had NHO recurrence within 2 months of therapy and was retreated. Radiation was delivered between 24 and 60 hours of surgery. All three patients with treated hip joints achieved improvement in joint range of motion and functionality. Three hip joints and two elbow joints were treated with RT and etidronate without surgical resection. All joints initially demonstrated improvement in range of motion after RT. One
patient subsequently experienced progression, clinically and radiographically, 2 months following treatment. Overall treatment efficacy was 87.5%. Acute toxicity was minimal and limited to grade 2 dermatitis in a single patient.

CONCLUSION: While this cohort of patients is small, outcomes suggest that a single fraction of 800 cGy, in addition to pharmacologic prophylaxis, may be a reasonable regimen to study in patients with NHO. Follow-up is short, and long-term efficacy and toxicity are unknown. The risk of secondary malignancy is small, as reported by others.

(P132) Stereotactic Radiosurgery to Five or More Brain Metastases in Melanoma Patients

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PURPOSE AND OBJECTIVES: Linear accelerator–based stereotactic radiosurgery (SRS) is a treatment option for melanoma patients who have developed brain metastases. Few data are available on treatment of patients with ≥ 5 lesions. We sought to determine the effectiveness of SRS in patients with ≥ 5 melanoma brain metastases.

MATERIALS AND METHODS: An analysis of patients with metastatic melanoma treated with SRS to ≥ 5 lesions in one treatment session was performed. Magnetic resonance imaging (MRI) scans were reviewed post-SRS to evaluate local control (LC). Disease progression by imaging was defined by the 2009 Response Evaluation Criteria in Solid Tumors (RECIST) criteria. Survival curves were calculated according to the Kaplan-Meier (KM) method from the date of brain metastases diagnosis or date of SRS. Univariate (UVA) and multivariate analysis (MVA) was performed by the Cox proportional hazards model.

RESULTS: We identified 149 metastatic brain lesions treated in 28 patients. The median age of patients was 60.5 (range: 38–83 yr), and the majority (n = 24, 85.7%) had extracranial metastases. Four patients (14.3%) received previous whole-brain radiation therapy (WBRT), and 11 patients (39.3%) received previous SRS. The median planning target volume (PTV) was 0.34 cm³ (range: 0.01–12.5 cm³). Median follow-up was 6.3 months (range: 1–46 mo). At the time of treatment, 7% of patients were recursive partitioning analysis (RPA) class I, 89% was RPA class II, and 4% was RPA class III. The rate of local failure was 11.4%. KM local control estimates at 6 and 12 months were 91.3% and 82.2%, respectively. PTV volume ≥ 0.34 cm³ was a significant predictor of local failure on UVA (hazard ratio [HR] = 16.1; 95% confidence interval [CI], 3.2–292.6; P < .001) and MVA (HR = 14.8; 95% CI, 3.0–268.5; P < .001). Sixteen (57.4%) patients were noted to undergo distant failure in the brain, with a median time to failure of 3 months (range: 1–15 mo). Nine patients with distant brain failures received WBRT, and seven patients received additional SRS. Median overall survival (OS) was 9.4 and 7.6 months from the date of brain metastases diagnosis and date of SRS, respectively. The KM OS estimates at 6 and 12 months were 57.8% and 28.2%, respectively, from the time of SRS treatment. RPA class was a significant predictor of KM OS estimates from date of treatment (P = .02). Patients who did not receive WBRT after SRS treatment had decreased OS on MVA (HR = 3.5; 95% CI, 1.1–12.0; P = .03), and patients who did not receive WBRT prior to SRS had improved OS (HR = 0.11; 95% CI, 0.02–0.53; P = .007).

CONCLUSIONS: SRS to ≥ 5 lesions appears to be effective for selected patients with metastatic melanoma, offering excellent local control. This is particularly important for patients, as new targeted systemic agents are improving outcomes but still have limited efficacy within the central nervous system.

(P133) Variation in Insurance Status by Patient Demographics and Tumor Site Among the Top Twenty-Five Causes of Cancer

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BACKGROUND: In the United States, an estimated 48 million individuals live without health insurance. The purpose of this study is to explore differences in key factors associated with insurance status among non-Medicare-aged adults diagnosed with the top 25 incident cancers using the Surveillance, Epidemiology, and End Results (SEER) public-use database.

METHODS: A total of 688,794 patients aged 18-64 years diagnosed with 1 of the top 25 incident cancers (representing 95% of all cancer diagnoses) between 2007 and 2010 in the SEER database were analyzed. Patient characteristics included age, race, gender, marital status, rural residence, and tumor stage. County-level demographics included percent poverty level. Insurance status was defined as insured, Medicaid, or uninsured. A multivariate logistic regression model was used to determine factors associated with lack of insurance.

RESULTS: Of the 688,794 eligible patients, 536,297 (77.9%) had insurance, 76,516 (11.1%) had Medicaid, and 33,798 (4.9%) did not have insurance. On univariate analysis, the following demographic characteristics were associated with lack of insurance: younger age, male gender, nonwhite race, being unmarried, rural residence, and residing in a county with a higher percent below poverty (all P < .0001). The cancer types with the highest rates of insurance coverage were prostate cancer (92.3%), melanoma of the skin (92.5%), and thyroid cancer (89.5%). The lowest rates of insurance were seen among patients with cancer of the cervix (64.2%), liver (67.9%), and stomach (70.9%). Among those uninsured, the top three causes of cancer were lung cancer (14.9%), colorectal cancer (12.1%), and breast cancer (10.2%). Among those with Medicaid, the top three causes of cancer were breast cancer (21.3%), lung cancer (15.7%), and colorectal cancer (9.2%). Males were more likely to be uninsured (5.8% vs 4.7%), and females were more likely to have Medicaid (13.3% vs 10.2%) (P < .0001). Insurance rates increased with age and ranged from 73.6% for 18–29-year-olds to 85.8% for 60–64-year-olds (P < .0001). Nonwhite individuals represented 45.5% of the uninsured vs only 26.9% of the insured (P < .0001). The rate of insurance decreased from 84.1% in 2007 to 81.5% in 2010 (P < .0001). In a multivariate logistic regression, younger age, female gender, nonwhite race, being unmarried, rural residence, and residence in a county with a higher percent below poverty were
associated with the lack of insurance.

**CONCLUSIONS:** Large disparities exist in the rates of insurance by cancer type. Younger age, female gender, nonwhite race, being unmarried, rural residence, and residence in a county with a higher percent below poverty were associated with lack of insurance. The expansion of private insurance would be expected to disproportionately benefit certain populations and cancer types.

**P134** Can a Radiation Oncology Social Media Website Be Used to Convey Reliable Radiation Oncology Information?

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**INTRODUCTION:** As the volume of radiation oncology information increases, the ability to gather and critically appraise high-quality information in order to answer clinical questions becomes increasingly challenging for radiation oncologists. Additionally, emerging technologies and new information lead to increasing variations in practice. Sharing knowledge about new information and practice variations is instrumental to high-quality radiation oncology practice. Sharing knowledge about new information and practice variations is instrumental to high-quality radiation oncology practice. The content of a radiation oncology–specific social media website may be a useful tool to share knowledge and practice patterns. Further research will be necessary to determine whether a social media format could provide reliable, data-driven radiation oncology information.

**METHODS:** All answers posted in a soft-launch period between December 2012 and September 2013 were evaluated. In the prelaunch phase, membership to the site was by invitation only. In September 2013, the site was opened to all radiation oncologists and radiation oncology residents. Answers were evaluated for quality based on whether they cited published data, personal experience, guidelines, or current and future clinical trials.

**RESULTS:** Between December 2012 and November 2013, there were 68 answers posted to 54 questions. The highest number of answers was related to breast cancer (12), followed by gastrointestinal cancers (10 each), palliation (7), gynecologic cancers (7), thoracic malignancies (6), mentorship/career development (4), head and neck cancers (3), lymphoma (3), central nervous system tumors (3), soft tissue tumors (1), protons (1), and global health (1). Of the 54 answered questions, the majority had one answer, while 12 had two or more answers. Academic radiation oncologists posted 54 answers, while community physicians and residents posted 4 and 5 answers, respectively. Fourteen answers were related to advanced technology (intensity-modulated radiation therapy [IMRT], proton therapy, intraoperative radiotherapy, stereotactic treatments, or advanced imaging). Thirty-three answers cited a total of 54 publications, while 11 referred to data without specifically citing a publication. Fifty-nine answers referred to personal experience, and 27 cited both data and personal experience. Additionally, 11 answers referred to current or future clinical trials.

**CONCLUSIONS:** In the initial launch of a question-and-answer social media website for radiation oncologists, the majority of content was found to refer to personal practices, followed by the published literature. Social media may be a useful tool to share knowledge and practice patterns. Further research will be necessary to determine if this form of knowledge-sharing can be used to improve the quality of patient care.

**P135** Dose Escalation Using Conventional Versus IMRT Planning for Hypofractionated Palliative Radiation of Lumbosacral Bony Metastases

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**PURPOSE:** The standard approach for palliation of bone metastasis (BM) is conventionally planned radiation (CRT). Randomized studies have shown the equivalence of hypofractionated vs conventionally fractionated regimens; yet, reported pain control is poor with either approach, resulting in some degree of pain relief in only 50% to 80% of cases and complete response in 15% to 60% of cases. We performed a dosimetric comparison of CRT vs intensity-modulated radiation therapy (IMRT) using standardized dose constraints to investigate if IMRT allowed hypofractionated dose escalation to bony targets in the pelvis and lumbosacral spine, based on the hypothesis that dose escalation will result in superior pain control if it can be delivered within acceptable dose limits to normal tissues.

**MATERIALS AND METHODS:** We retrospectively replanned 10 patients with IMRT who were initially treated with palliative CRT for BM involving the pelvis and/or lumbar spine at our institution, using standardized dose constraints for five- fraction regimens, as published in American Association of Physicists in Medicine (AAPM) Task Group (TG) 101. We defined the planning target volume (PTV) as all bony structures contained within the 50% isodose line based on original conventional plans. For IMRT plans, optimization was performed to achieve 95% PTV coverage with the prescription dose while meeting published dose constraints for five-fraction regimens, including spinal cord maximum 30 Gy, cauda equina maximum 32 Gy, and bowel maximum 35 Gy. IMRT plans were optimized for a prescription of 30 Gy in five fractions, and dosimetric characteristics were extracted for five-fraction regimens starting at 20 Gy and escalating by 1 Gy per fraction to 35 Gy.

**RESULTS:** IMRT allowed dose escalation to 30 Gy in five fractions using AAPM TG 101 constraints, with a mean maximum spinal cord dose of 29.6 Gy, mean maximum cauda equina dose of 31.5 Gy, and mean maximum bowel dose of 27.9 Gy. For the same targets, CRT five-fraction plans only allowed a dose of 25 Gy: the mean maximum spinal cord dose for a 25-Gy prescription was 29.3 Gy (within constraint) but 35.2 Gy for 30 Gy (above constraint); the mean maximum cauda equina dose for a 25-Gy prescription was 30.4 Gy (within constraint) but 36.4 Gy for 30 Gy (above constraint); and the mean maximum bowel dose was 28 Gy for a 25-Gy prescription and 33.6 Gy for 30 Gy (both within constraints). The bowel V20 was extremely low for five-fraction regimens using IMRT, with a mean V20 of 2 cc for IMRT plans, and much higher, 39.5 cc, for CRT plans.

**CONCLUSIONS:** IMRT resulted in the ability to dose-escalate to bony targets in the pelvis and/or lumbosacral spine while meeting standardized dose constraints to the spinal cord/cauda equina and...
bowel. IMRT allowed a dose of 30 Gy using a five-fraction regimen, while CRT allowed a dose of only 25 Gy using AAPM TG101 constraints. Prospective study is warranted to determine if the achieved dose escalation using IMRT results in clinically meaningful improvements in pain control and acceptable toxicity.

(P136) Uniting Publication Database Functions Across Three Existing Complex Organizations
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NRG Oncology is a member of the National Cancer Institute (NCI) National Clinical Trials Network program and was created by the integration of three adult cooperative groups: the National Surgical Adjuvant Breast and Bowel Project (NSABB), the Radiation Therapy Oncology Group (RTOG), and the Gynecologic Oncology Group (GOG). These legacy groups each have a rich history of conducting meaningful, scientifically valid clinical trials. The harmonization of similar yet different procedures is a daunting task. To provide a focused approach to the evaluation of individual approaches and retention/Modification of best practices, specific working groups were formed in a diverse number of different administrative and clinical areas. One group, the Publications Working Group, has begun the amalgamation of three publications databases into one to track progress in manuscript development and to provide access to a comprehensive bibliography that incorporates the past/current research of all three legacy groups.

NRG Oncology stresses the importance of timely and accurate publication of results of clinical trials, and each of the legacy groups has an excellent track record. Cumulatively, we have published over 5,000 abstracts and manuscripts in peer-reviewed journals spanning 5+ decades. As NRG Oncology moves forward, it is critical that results of past/current research be available to all members. Also, the groups have experienced continued growth in the number and complexity of publications in development, requiring sophisticated administrative oversight to ensure that NCI and NRG Oncology deadlines are efficiently assigned, monitored, enforced, and ultimately met. The adoption of a common database is vital to these objectives.

Existing legacy group publications databases were assessed during webinar/conference calls. Once a potential “best database” was identified, information technology (IT) resources were made available. To provide a hands-on opportunity to evaluate the proposed system, an electronic “sandbox” was created, allowing the working group access to a trial version of the database via website. IT staff created the sandbox within an isolated portion of the Statistical and Data Center private cloud, running VMware vSphere version 5.1–5.5. Within 24 hours, the server was deployed with the necessary software and configuration, the IT staff fully tested all processes, and user accounts were created. The underlying software is written in Microsoft .Net/C#, reports are generated by Crystal Reports, and access to a relational database management system is via ADO.NET. This sandbox allowed participants to gain experience utilizing the various features and provide feedback for desired modifications. As a result, the NRG Oncology Publications Database was endorsed within 1 month of initial discussion.

The combining of data from the original three legacy group publications databases is now under way. The IT architecture provides a comprehensive bibliographic format and methodology to download data from legacy group bibliographies; a search engine to seek publication information by selected criteria, including publication type, protocol number, author, year, disease site, keyword or phrase, date range, or publication ID; electronic links to PubMed and/or journals; and a publications management tool that tracks deadlines and completion for various stages of manuscript development. Details of the database and examples of its use will be presented.

(P137) Midlevel Providers in Radiation Oncology and Their Role in Brachytherapy
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BACKGROUND: With the increasing patient population in the oncology world and advancing technologies in radiation oncology in particular, there is an increasing need for assistance in providing high-quality care. In the setting of radiation oncology, brachytherapy has broadened its scope over the last decade, and assistance with procedure-based aspects of implementing brachytherapy has increased in demand. The implementation of nonphysician practitioner roles, such as midlevel providers and physician assistants, can provide an improvement in the workflow of brachytherapy procedures. Physician assistants can perform procedures under a license agreement with their attending physician, once well trained and experienced, as part of the delegation with the Board of Physicians. This allows midlevel providers to set patients up for brachytherapy procedures, construct equipment devices, insert appropriate devices, assess applicator localization images, and assess treatment fields, all prior to the physician being present to initiate treatment. Physician assistants also have the ability to charge for brachytherapy services while freeing up physician time to focus on treatment planning and target delineation, as well as other clinic demands.

METHODS: Review of literature of midlevel provider roles in radiation oncology, personal experience, and investigation of billing reimbursement for brachytherapy procedures for midlevel providers.

RESULTS: Physician assistant billing allows for 85% to 100% of the physician fee schedule, depending on the payer. Midlevel providers qualify to bill for Current Procedural Terminology (CPT) codes, including catheter placement and device placement for brachytherapy procedures. These advanced duties, performed under the supervision of a radiation oncologist, can be incorporated into delegation agreements with procedure logs for brachytherapy procedures, including vaginal/gynecological, endorectal, skin, interoperative, prostate, and bile duct sites. At our institution, we use midlevel providers for the GI group, which consists of intraoperative, endorectal, skin, and bile duct procedures, which includes simulation and treatment setup. Quite frequently, these procedures can take considerable time, therefore freeing up the physician during certain time points of the brachytherapy process.
CONCLUSION: The emergent role of midlevel providers has been increasing in awareness and utilization and is promising to assist in improving patient treatment flow, provider workflow, and overall patient care and patient experience. Integrating physician assistants with onsite training experience into brachytherapy procedures can be cost- and time-effective for radiation oncology departments. There is now more of a demand for experienced providers for brachytherapy procedures, and midlevel providers, such as physician assistants, can be well trained, experienced, and specialized to help fill the deficit. In an academic setting, establishing the role of physician assistants in brachytherapy technology is not meant to minimize the experience of the resident but to act as an additional enhancement to the teaching, allowing more time for the procedure-based aspect while the physicians will remain the integral part of the prescribing of treatment.

(P138) Yttrium-90 Radioembolization for Liver Metastasis From Neuroendocrine Cancer: A Single-Institution Retrospective Review

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PURPOSE: Many publications can be found on the use of yttrium-90 (Y-90) transarterial radioembolization (TARE) for the treatment of primary liver cancer or liver metastasis from colorectal adenocarcinoma. It is important to study the results that could be achieved when TARE is being used to treat liver metastasis of other origin. This retrospective analysis concentrates on our institutional experience with TARE for the treatment of liver metastasis from neuroendocrine cancer.

MATERIALS AND METHODS: Our institutional review board (IRB)-approved Y-90 databank was reviewed to identify patients with neuroendocrine cancer who received Y-90 TARE for liver metastasis from February 2011 to September 2013. Information on patient demographics, performance status, disease-related characteristics (liver panel, complete blood count [CBC], chromogranin A, and gross tumor volume [GTV] measured in cc on the most recent study pre-TARE), treatment-related parameters (Y-90 dose delivered), and treatment outcome (treatment toxicity, overall survival [OS]) were captured for this analysis.

RESULTS: Between February 2011 and September 2013, a total of 16 patients with metastatic neuroendocrine (liver-predominant disease) received Y-90 TARE in our institution. Eight of these patients received treatment to both liver lobes, for a total of 24 procedures. All patients had an Eastern Cooperative Oncology Group (ECOG) performance status between 0 and 2 prior to treatment. In addition, all patients had a bilirubin level below 2.0 and an albumin level above 3.0 prior to treatment. The median GTV per lobe was 299 cc (range: 27–670 cc). With a median follow-up of 16.5 months (range: 2–26 mo), the 1-year OS was 75%. There was no relationship between OS and GTV volume. Two patients with severe endocrine disorders that required repeated hospitalization (one patient with severe hypoglycemia and a second patient with hypertensive crisis) responded well to TARE, with marked improvement in their medical condition and no need for further admission postprocedure. In terms of treatment toxicity, one patient was diagnosed with a radiation-induced liver disease and died 13 months post-treatment. One patient developed a pancytopenia that was potentially related to treatment.

CONCLUSION: The use of Y-90 TARE for patients with liver metastasis from neuroendocrine carcinoma is a treatment option that should be assessed in a prospective multicentric study. In this series, Y-90 TARE was associated with a high 1-year survival rate. However, patients need to be monitored closely postprocedure, since serious treatment-related toxicity could develop.

(P140) Comparison of Split-Field IMRT With Whole-Field VMAT and IMRT for Locally Advanced Head and Neck Cancer

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BACKGROUND: Advances in intensity-modulated radiation therapy (IMRT) head and neck target delineation and treatment planning have led to improved sparing of organs at risk (OARs). The selection of an optimal IMRT technique is an ongoing debate. Split-field IMRT (HB-IMRT) and whole-field IMRT (WF-IMRT) represent two common techniques employed for the treatment of oropharyngeal cancers. The advent of volumetric modulated arc therapy (VMAT) offers the potential for fewer monitor units and shorter delivery time. It is unclear whether dose to normal critical structures, particularly organs involved in swallow function, are affected with VMAT compared with HB-IMRT and WF-IMRT. In this study, we compare three IMRT techniques for the treatment of common cases of oropharyngeal squamous cell carcinoma.

METHODS: CT of 10 patients with locally advanced oropharynx cancer treated at MD Anderson Cancer Center using HB-IMRT were replanned with WF-IMRT and VMAT. They included five base of tongue and five tonsil squamous cell carcinoma patients. The treatment plans were reviewed by a panel of radiation oncologists, and planning was performed by physicists with head and neck expertise. For each case, the planning target volume (PTV) and critical OARs were compared among the three techniques. In addition, target delineation of the pharyngeal constrictors was included. OARs were delineated according to Radiation Therapy Oncology Group (RTOG) 1016 guidelines. The larynx volume was divided into two subvolumes (supra and infra), separated at the base of the superior horn of the thyroid. For patients treated with the HB-IMRT technique, the isocenter was placed 3 mm above the arytenoids. The paired t-test was used to assess for significant differences of means.

RESULTS: For the 10 bilateral plans, the mean dose (Gy) to the larynx was 23.2 for VMAT (range: 18.9–26.4 Gy), 22.1 for WF-IMRT (range: 17.5–28.2 Gy), and 25.4 for HB-IMRT (range: 15.4–30.8 Gy). The mean supralarynx dose (Gy) was 40.7 (range: 27.7–63.7 Gy), 41.3 (range: 27.9–64.2 Gy), and 53.7 (range: 30.2–68.0 Gy) for whole VMAT, IMRT, and split-IMRT, respectively. The mean infralarynx dose (Gy) was 17.7 (range: 11.9–23.9 Gy) for VMAT, 16.0 (range: 9.7–22.4 Gy) for IMRT, and 15.9 (range: 7.6–25.8 Gy) for HB-IMRT. The upper pharyngeal constrictors received...
a mean dose (Gy) of 60.1 (range: 53.1–69.7 Gy), 60.1 (range: 54.5–69.2 Gy), and 62.2 (range: 55.6–70.0 Gy), for whole VMAT, IMRT, and HB-IMRT, respectively. The middle pharyngeal constrictors received a mean dose (Gy) of 46.4 (range: 20.3–70.1 Gy) for VMAT, 47.7 (range: 20.1–70.3 Gy) for IMRT, and 57.9 (range: 31.2–70.3 Gy) for HB-IMRT. The PTV receiving > 110% of the volume was 0% for all three techniques. In all comparisons, no statistical differences were observed.

CONCLUSIONS: These preliminary data suggest that similar sparing of critical swallow structures may be achieved with VMAT as compared with traditional IMRT techniques. Further analysis is ongoing, as well as recruitment of additional patients to validate these findings and assess whether there is significant compromise of tumor coverage, dose homogeneity, or non-laryngeal critical structures.

(P141) Dosimetric Comparison of Volumetric-Modulated Arc Therapy With Step-and-Shoot Intensity-Modulated Radiation Therapy for Prostate Cancer

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PURPOSE: Step-and-shoot intensity-modulated radiation therapy (IMRT) and variable-dose-rate volumetric modulated arc therapy (VMAT) are two common treatment techniques for the definitive treatment of prostate cancer. While VMAT is generally understood to be more rapidly delivered, minimizing intrafraction prostate motion, there is disagreement about whether VMAT produces more favorable planning target volume (PTV) coverage while delivering lower doses to bladder, rectum, and femoral heads. The disagreement may be partially explained by the inclusion of a wide variety of PTVs in prior studies, such as prostate ± seminal vesicles ± pelvic lymph nodes, as well as various prescribed doses and technical details of early precommercial implementations. In order to compare these two techniques in modern practice, we analyzed two cohorts of patients treated at our institution who were matched for PTV, prescribed dose, and patient characteristics.

METHODS: We studied 32 patients who received 8,100 cGy in 45 daily fractions to the prostate and proximal 1 cm of the seminal vesicles using VMAT (n = 22) or seven-field, step-and-shoot IMRT (n = 10) for intermediate-risk or high-risk prostate cancer between July 2010 and April 2013. Image guidance utilized daily pretreatment kV imaging of 3–4 gold fiducials. Treatment planning was by the Philips Pinnacle system. In 20/22 (91%) patients, VMAT was delivered with two 356-degree arcs on Varian Trilogy or TrueBeam linear accelerators. Acute toxicity was assessed using Common Terminology Criteria for Adverse Events version 3 (CTCAE v3) criteria.

RESULTS: VMAT reduced median radiation delivery time from 4.5 to 2.5 minutes (P = .02). There was no significant difference in PTV volumes between the VMAT and IMRT groups (P = .76). VMAT plans were more conformal, based on a conformity index (P = .04), and PTV coverage was more homogenous (ie, fewer hot and cold spots), based on a homogeneity index (P < .001). There was a slight improvement in the amount of rectum receiving 60 Gy or more (VMAT 18 cc vs IMRT 24 cc; P = .046). However, there was no difference between the two groups with regard to rectal V65, V70, and V75; bladder V65, V70, V75, and V80; or femoral heads V33. No grade 2 or higher acute diarrhea was observed in either group. No grade 3 or higher cystitis was observed in either group, and rates of grade 2 cystitis were not statistically different (VMAT 32% vs IMRT 60%; P = .13).

CONCLUSIONS: Two-arc VMAT resulted in shorter treatment times, as well as more conformal and more homogeneous treatment plans than seven-field, step-and-shoot IMRT for prostate cancer. Decreased treatment time results in less of an opportunity for intrafraction prostate motion during radiation delivery, thereby reducing the likelihood of a geographic miss.

(P142) Complementary and Alternative Medicine in Radiation Oncology Training: From a Resident’s Perspective

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BACKGROUND: Today’s health care system is evolving in its approach to the management of an ethnically diverse population, as it continues to struggle with the imperative of providing cost-effective care. Up to 90% of patients report utilizing some form of complementary and alternative medicine (CAM), such as supplements, acupuncture, or meditation, during their cancer journey. Integrative medicine (IM) is a field of study seeking to combine these nonconventional approaches with conventional methods to patient care by focusing on the least invasive, least toxic, and least costly methods to facilitate overall health. Despite the ubiquity of CAM, such teachings are not adequately covered in radiation oncology training programs. The glaring deficiency in education adversely affects both patients, as they seek optimal holistic care, and clinicians, as they begin their independent careers. This study attempts to assess the level of knowledge and interest current residents have in CAM teachings, with the goal of eventually incorporating such evidence-based study into training curriculum.

METHODS: A seven-question survey was developed, and study design was approved by the UCLA institutional review board (IRB). The questionnaire was electronically delivered through a free portal to radiation oncology chief residents across the country, with a request to disseminate the same amongst their colleagues. All trainees in the discipline were requested to participate. The aim of the study and the fact that participation was voluntary and that responses would be kept anonymous were explicited in the introduction. Aggregate data were downloaded and compiled.

RESULTS: Completed surveys from 145 of 577 total trainees were received, representing 51 of 87 accredited residency programs. Half of all respondents felt that their patients did not feel comfortable seeking their advice on the subject, and 70% did not consider themselves adequately informed on CAM for their professional work. Overall, 85% residents harbor an interest in IM, and about 75% wish to learn more during residency training.

DISCUSSION: To our knowledge, this study provides the first national assessment of trainee attitudes toward CAM, as previous
studies have focused more broadly on medical students or practicing health care providers. As a substantial percentage of participants are interested in but not sufficiently educated on this subject, there is a need for formal training to be incorporated in our curriculum. Limitations of this study include the small number of total participants, with the question of whether or not this group is representative of the entire specialty. Additionally, findings regarding educational activities are inherently subject to memory bias. The current Accreditation Council for Graduate Medical Education (ACGME) program requirement for graduate medical education (GME) in radiation oncology has no mention of CAM. Academic programs are engines of innovation in education, with a mandate to produce well-rounded clinicians. Therefore, it is trainees who are in the best position to learn the evidence behind CAM techniques and safely integrate these approaches with current standards of care. The Arizona Center for Integrative Medicine may be an appropriate place to start, as it has developed a variety of targeted modules currently being employed at roughly 45 primary care training programs across the country.

(P143) Advanced Glycation Endproducts: The Sweet Tooth of Radiation Toxicity

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PURPOSE AND OBJECTIVES: The therapeutic index of treating cancer with ionizing radiation (IR) can be increased by minimizing normal tissue toxicity. Unfortunately, the therapies that have been developed to date have had limited efficacy. Therefore, identifying novel targets to protect normal tissue is essential during treatment. Advanced glycation end products (AGEs), such as Nε-(carboxymethyl)-lysine (CML) and pentoside, may be one such class of molecules. AGEs occur when glucose is oxidized and forms irreversible crosslinks with collagen. This allows for sustained/chronic damage. AGEs are thought to be responsible for the end-organ damage noted in diabetics with chronic hyperglycemia, such as nephropathy, cataracts, and retinopathy, when ultraviolet irradiation (UVIR) interacts with the optical structures, inducing collagen crosslinks. Since UVIR induces most of its damage by free radicals, AGEs may be responsible in part for IR treatment–associated normal tissue toxicity. Therefore, we sought to determine if AGEs are induced by IR and if they are sustained over an extended period of time.

MATERIALS AND METHODS: HEP293 cells were exposed to sham irradiation or 6 Gy of ionizing radiation (PanTek X-RAD 320 irradiator) and collected at 0.5, 3, and 24 hours after radiation exposure. Cells were collected, lysed with RIPA buffer (50 mM Tris-Cl, 150 mM NaCl, 1% NP40, 0.25% Na-deoxycholate, 1 × Mini protease inhibitor cocktail and phosphatase inhibitor cocktail), and quantified with BCA protein assay kit (Thermo Scientific, IL). AGE levels were then measured using a CML enzyme-linked immunosorbent assay (ELISA test) in our samples and compared with the four-parameter standard curve for the CML standards (Echelon Bioscience, UT).

RESULTS: Twenty-four hours after irradiation, AGE production was elevated to 101.8 ng/dL vs 74.5 ng/dL in the control arm. The time course revealed that AGEs were induced and maintained at a level above 100 ng/dL at all time points, including 0.5, 3, and 24 hours. At the 0.5- and 24-hour time points, AGE levels were elevated to 103.9 vs 65.6 ng/dL in the control arm 109.4 vs 86.1 ng/dL in the control arm, respectively. This increase was significant at all time points, with a P value < .001.

CONCLUSIONS: AGE formation may be a potential cause of acute and chronic toxicity from radiation. We have demonstrated for the first time that AGEs are induced by IR and may be a potential target to reduce toxicity. AGE inhibitors, such as carnosine, have already been developed and may potentially be used therapeutically to inhibit AGE formation and reduce radiation toxicity.

(P144) Prospective Assessment of Patient-Specific Pulmonary Radiation Pneumonitis

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PURPOSE: Radiation pneumonitis (RP) is a significant toxicity following thoracic radiotherapy, with no method to predict individual risk. Our lab had previously shown that pulmonary metabolic response rate (PMRR) is highly predictive of RP in lung cancer. In this prospective study, we used PMMR as a surrogate marker to predict radiation-induced lung toxicity in lung cancer patients receiving thoracic radiotherapy.

MATERIALS AND METHODS: Forty-one patients receiving thoracic radiation for lung cancer were enrolled in a phase II study. Each patient received respiratory surveys before RT initiation and at each weekly follow-up visit. In addition, patients also received restaging positron emission tomography (PET)/CT imaging 30–60 days after completion of RT. The PMRR was determined from the slope of the normalized standardized uptake value (SUV) vs the dose. Deviation of the dose response from a linear model was tested for each case. St. George Respiratory Questionnaire (SGRQ) was used to monitor pneumonitis toxicity. An increase of respiratory efforts in four different activities compared with baseline was considered to be symptomatic. The follow-up endpoint was 1 year after completion of RT, or death. The demographics, dosimetric factors, and PMMRs were evaluated for correlation with RP.

RESULTS: Thirty-eight patients completed the trial. Two patients did not complete the study, and three patients did not qualify due to a restaging PET of more than 3 months. Mean baseline lung function of all patients was 41.46 on the SGRQ. Twenty-two (58%) patients developed RP. Mean ΔSGRQ score for asymptomatic patients was +19.93, and mean ΔSGRQ score for asymptomatic patients was –6.225. No clinical factors (age, tumor size, tumor location, tumor history, or dosimetry parameters) were associated with symptoms. The median PMRR for symptomatic patients was 0.014 (range: 0.002–0.076) and 0.007 for asymptomatic patients (P < .002). Receiver operating characteristics (ROC) analysis yielded an area under the curve (AUC) of 0.79 (95% confidence interval [CI], 0.64–0.94), with a PMMR threshold at 0.0108 providing sen-
sitivity of 64% and specificity of 88%.

**CONCLUSIONS:** The radiation dose response on fluorodeoxyglucose (FDG) PET/CT imaging exhibited a linear relationship on statistical modeling. Patients who developed symptomatic RP had a significantly higher dose-response slope (PMRR) than asymptomatic patients.

(P145) Application of Perfusion SPECT Image-Guided Planning and Clinical Outcomes in Locally Advanced Lung Cancers

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**PURPOSE:** To assess the clinical effect of perfusion single-photon emission computed tomography (SPECT) image-guided planning in patients treated for locally advanced and metastatic lung cancers.

**METHODS:** Seventeen patients with lung cancer who had perfusion imaging obtained in the treatment position fused with treatment planning scans were evaluated to assess the effects of radiation to regions of perfusion, as defined by the pixelated value of the perfusion image (PVPI) method. This method created regions of perfusion, defined as full perfusion (P60–100), moderate perfusion (P40–60), poor perfusion (P20–40), and very poor perfusion (P0–20). All patients were planned prospectively at the time of treatment, with the intent of avoidance of actively perfusing lung while respecting known parameters associated with increased risk of pneumonitis. Volumes of each perfusion region were recorded in all patients, and ratios of planning target volume (PTV) to total lung and active lung were generated. Values for V20, V5, and mean lung dose (MLD) were recorded for whole lung as well as in each perfusion region. Dosimetric variables in each perfusion region were recorded, and patients were retrospectively evaluated for the development of radiation pneumonitis.

**RESULTS:** Five patients required systemic steroids for radiation pneumonitis. There were no significant differences in pretreatment pulmonary function tests (PFTs); dose delivered; PTV volume; or whole-lung V20, V5, or MLD between patients who did and did not require systemic steroids for pneumonitis. There was a trend for less volume of P60–100 in those with pneumonitis (171 cc vs 273 cc; $P = .1$). There were a number of differences noted in P20–40 with regard to trends of increased V20 (28% vs 23%; $P = .1$) and V5 (59% vs 47%; $P = .1$) in patients with pneumonitis. There was also a statistically significant increase in MLD in P20–40 (1.696 cGy vs 1.357 cGy; $P = .04$) as well as V5 in P40–60 (63% vs 40%; $P = .05$). In patients who developed pneumonitis, there was a trend for a decreased ratio of P60–100 to PTV (0.41 vs 1.98; $P = .09$). Of the six patients who were treated using IMRT, there were statistically significant increases in V5 (61% vs 48%; $P = .05$) in the whole lung as well as increases of V20 in P0–20 (23% vs 33%; $P = .02$) and P20–40 (19% vs 27%; $P = .03$).

**CONCLUSION:** SPECT-based perfusion imaging has utility in terms of functional treatment planning for lung cancer and may assist with avoidance of actively perfusing lung, although the clinical significance of this remains in question due to results suggesting some predictability of pneumonitis associated with higher doses delivered to poorly perfusing regions. Since treatment plans were designed with the intention of minimizing dose to the active regions and thereby pushing this dose to regions of lower perfusion, it can be inferred that the avoidance of highly perfusing regions may make moderately perfusing regions more vulnerable to the effects of radiation pneumonitis, especially in patients with small volumes of active lung. With the advantage of increased conformity, IMRT has utility in avoidance of these concerning regions and is a subject of ongoing research.

(P146) Clinical Outcomes From Frameless Stereotactic Radiosurgery of Arteriovenous Malformations Using High-Resolution 3-Dimensional Rotational Angiography

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**PURPOSE AND OBJECTIVE:** Cerebral arteriovenous malformation (AVM) is defined as a normal collection of vessels with multiple enlarged feeder arteries and dilated venous outflow, associated with risks of blood shunting and hemorrhage. Treatment options include surgery, embolization, or stereotactic radiosurgery (SRS). SRS may be attractive as a safe, noninvasive treatment for small, deep lesions. While techniques and fused imaging modalities for SRS vary across institutions, we have found that 3-dimensional rotational angiography (3DRA) offers superior geometric accuracy. With a lag time of 1–3 years from SRS to complete obliteration, we are able to now report early data for clinical response for AVM lesions treated using 3DRA and image-guided radiosurgery (IGRS) based on our experience.

**MATERIALS AND METHODS:** In 2002, our institution transitioned to the Novalis Extrac IGRS system, with which we have treated over 3,113 lesions. Since 2006, a total of 2,201 of them were treated via frameless IGRS. AVMs were initially excluded due to the need for cerebral angiography for localization, but in 2005, computed tomography angiography (CTA) and magnetic resonance angiography (MRA) were used. In 2009, we transitioned to 3DRA and have treated over 40 AVMs with this technique. Utilizing a phantom model, we have previously shown that 3DCRA offers better geometric accuracy compared with digital angiography orthogonal image pairs (0.27 ± 0.14 mm vs 0.39 ± 0.15 mm, respectively). We reviewed data on response to therapy based on clinical symptoms, events since SRS, and changes on subsequent imaging.

**RESULTS:** Currently, results are available for 12 AVMs (10 patients) that had angiogram repeated 2–3 years following initial SRS date. Initial treatment included embolization for three, craniotomy for hematoma evacuation for two, and ventriculostomy with decompression for one case. SRS pretreatment volume ranged from 0.035 to 27.3 cc, although the majority had volumes ≤ 4 cc. Patients were given single-fraction SRS, with doses ranging from 1,556 to 2,250 cGy prescribed to isocenter using 4–5 arcs. Patients were seen in routine follow-up with serial magnetic resonance imaging (MRI) brain imaging. Angiogram was then repeated (either conventional or 3DRA) after appropriate time elapsed per clinician judgment.
Overall, nine cases had complete resolution of AVM, one had stable-sized lesion, and three had smaller lesions. No patients experienced additional hemorrhage in the interval following SRS. For the four residual lesions, we fused 3DRA data for three using BrainLab. The residual AVM was contoured and compared against pretreatment contoured and treated AVM. We found that the residual size of all three AVMs was drastically decreased, with 85% to 98% resolution in size, including one of a very large lesion (from 27.313 cc to 3.066 cc).

CONCLUSIONS: To date, our results from patients treated with frameless SRS using high-resolution 3DRA and BrainLab treatment planning are encouraging, with the finding of either complete resolution or decrease in size of lesions treated. Furthermore, our results suggest good geometric accuracy using the 3DRA technique, given the small size of most of the lesions treated. Although there is lag time to evaluation to response, we anticipate forthcoming data from evaluation of additional patients treated with this modality to strengthen our current findings.

(P147) Long-Term Outcomes of High-Dose-Rate Interstitial Brachytherapy for Gynecologic Malignancies

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PURPOSE: In this study, we perform a single-institution retrospective analysis of outcomes of patients treated with high-dose-rate interstitial brachytherapy (HDR-ISBT) for gynecologic malignancies. Locoregional control (LRC), disease-free survival (DFS), overall survival (OS), and long-term toxicity were evaluated.

MATERIALS AND METHODS: Patients treated with interstitial brachytherapy for gynecologic malignancies between 1990 and 2013 at the Cancer Therapy and Research Center were identified. Thirteen patients treated from 2008 to 2013 were reviewed for the primary phase of analysis. Site of primary disease was predominantly cervix, with other sites of primary disease to include the vagina and vulva. Patients were treated with a combination of external beam radiation therapy (EBRT) and HDR-ISBT. All patients had locally advanced disease, International Federation of Gynecology and Obstetrics (FIGO) stage IIb–IVA. EBRT dose ranged from 4,500–7,440 cGy to at least the whole pelvis, while HDR-ISBT dose ranged from 1,000–2,900 cGy delivered in 500–700-cGy fractions. HDR-ISBT was delivered via modified Syed applicators on a twice-daily schedule, once per week, with fractions separated by at least 5 hours. Most patients received chemotherapy concurrently with radiation treatments.

RESULTS: Of 12 patients with available follow-up data, 1 patient developed local failure. Three patients developed distant metastatic disease. DFS and OS analyses were deferred for final analysis of all patients to be included in our study. Radiation Therapy Oncology Group (RTOG) grade III late toxicity was seen in two patients in the form of severe urinary incontinence, intractable pelvic pain, vesicovaginal fistula, cystitis, and fibrosis. Two patients experienced RTOG grade IV complications, with development of vesicovaginal fistula requiring surgical repair and skin necrosis requiring surgical debridement (latter complication in patient treated for vulvar cancer). Thus far, no RTOG grade V late complications have been noted.

CONCLUSION: On preliminary analysis, HDR-ISBT appears to be an effective alternative for dose escalation in patients with locally advanced gynecologic malignancies in whom delivery of standard intracavitary BT is not a recommended or feasible option. Acceptability of the toxicity profile from this combined-modality radiotherapy approach requires further evaluation. Expansion of our review to include patients treated prior to 2008, as well as further investigation of the outcomes of those patients initially lost to follow-up, will provide a valuable added perspective to the limited body of existing data evaluating the long-term efficacy and toxicity of this specialized modality of radiotherapy.

(P148) The Use of Updated Dosimetric Guidelines and Independent Dose-Volume Histogram Analysis Improves Treatment Planning for Men Treated With Rapidarc Intensity-Modulated Radiation Therapy for Clinically Localized Prostate Cancer

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PURPOSE: We updated our evidence-based dosimetric guidelines for treatment of men with clinically localized prostate cancer and introduced independent dose-volume histogram (DVH) analysis using MatLab. In doing so, we sought to evaluate whether the interventions above would translate into improvement in dosimetric endpoints for organs at risk (OARs).

METHODS: An internal committee of radiation oncologists, physicists, and dosimetrists reviewed our site’s existing treatment guidelines and updated them based on current Radiation Therapy Oncology Group (RTOG) trials and scientific publications (see Table). In order to efficiently assess which dose constraint objectives passed and which failed, a Matlab program was written to compare an input DVH file from the treatment planning software (Eclipse) with the dose constraint objectives. A report was then generated in Excel through Matlab software, highlighting those objectives that passed (displayed in green) and those that did not (red). Our center began using the updated guidelines and the MatLab program in April 2012. Currently, the independent DVH analysis for each patient is completed prior to plan approval.

All patients were treated with RapidArc intensity-modulated radiation therapy (IMRT), consisting of two full gantry rotations. The clinical target volume (CTV) for intermediate-risk patients was the prostate and seminal vesicles for the initial phase of treatment, fol-
tion described above resulted in treatment plans with less variability.

We retrospectively reviewed treatment plan data for 17 patients treated before and 9 after the interventions above. Groups were defined for analysis as those treated pre- and postintervention. DVH statistics were presented as means and standard deviations (SDs). Independent samples t-tests were used to determine group differences on bladder and rectal doses. The coefficient of variation (SDs) was calculated for the differences between groups (ratio of the sample SD to the sample mean). This coefficient quantifies the extent of the variability in a sample, with higher values representing more variability.

**RESULTS:** Our bladder V75Gy was reduced from 9.5% to 6% (P = .05), and rectum V70Gy and V50Gy were reduced from 12.8% and 29.0% to 9.4% and 22.5%, respectively (P < .05). Moreover, the coefficients of variation for each dosimetric endpoint, except for rectal V75Gy and V70Gy, were higher preintervention compared with patients treated postimplementation of updated guidelines/ MatLab (see Figure).

**CONCLUSION:** Updating our dosimetric guidelines and using independent DVH analysis with MatLab reduced the dose to OARs, as indexed by several key DVH endpoints. In addition, the intervention described above resulted in treatment plans with less variability of dose delivered to OARs.

**P149 Collimator Design and Optimization for an Ir-192 Based Small-Animal Irradiator**

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**BACKGROUND:** Small-animal irradiation is a critical part of translational studies in radiation oncology. The ability to deliver a small, highly focused radiation field allows for evaluation of radiation effects, as well as quantification of acute and late toxicities, in an assortment of tissues. We evaluated a variety of dense metals and alloys to sustain a radiobiologically meaningful dose rate (> 2 Gy/min) using Ir-192 and shield tissue outside of the primary field.

**MATERIALS AND METHODS:** Using a 10-Ci Ir-192 source, we evaluated dose rate and effective shielding of variable-thickness lead and tungsten alloy. With theoretical half-value layers (HVLs) of 5 mm for lead and 3.3 mm for tungsten, we assessed in-field dose rates and doses at specific distances from the block edge using Gafchromic dosimetric film. Collimator dimensions were based on biometric measurements of mature athymic nude mice.

**RESULTS:** Collimator dimensions were based on athymic nude mice hemibrain dimensions and measured 12 mm × 10 mm × 19 mm (length × width × depth) for the lead collimator. Tungsten collimator dimensions were 12 mm × 10 mm × 13.2 mm. Empirically measured density of the lead collimator was 10.92 g/cc and 19.0 g/cc for the tungsten collimator. Depth of the collimator was 4 theoretical HVLs for both lead and tungsten. Dose rates were 0.931 cGy/hr/mCi and 1.56 cGy/hr/mCi for lead and tungsten, respectively. The penumbra and dose profiles for each of the collimators are described, with the dose falling from a maximal dose rate of 260 cGy/min to 26 cGy over a span of 1.2 mm for the tungsten unit and from 155 cGy/min to 15 Gy/min over 1.3 mm for the lead unit.

**CONCLUSIONS:** Using a collimator of high-density tungsten alloy, we were able to deliver radiation at a radiobiologically meaningful dose rate to a small field. The tissue beyond the block edge was well shielded, with < 10% maximal dose received at ~1.5 mm from the collimator’s medial edge, based on Gafchromic dosimetric analysis. Due to the advantage of increased dose rate with the tungsten unit, this collimator design was implemented for a newly developed small-animal irradiator.

**P150 Assessment of Acute and Late Toxicities of Intracranial Stereotactic Radiosurgery in Multiple Sclerosis Patients**

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RESULTS: Eleven patients were identified with proven diagnosis of MS who subsequently underwent SRS for an intracranial lesion. Median age of patients was 58 years. Seventeen distinct targets were treated in among this cohort of patients. The targets of RT included acoustic neuroma, meningioma, and metastatic non–small-cell lung cancer. The target doses varied according to target. Trigeminal nerve doses ranged from 55–90 Gy. Acoustic neuroma dose was 24–25 Gy. One patient with meningioma was treated with 32 Gy to the target. Metastatic disease was treated with 40 Gy. Median follow-up for patients was 301 days. Only one patient experienced an acute toxicity of headache—a grade 1 toxicity. No patients experienced late toxicity.

CONCLUSION: In this cohort of patients, only a grade 1 acute toxicity was experienced with RT. The results of our study indicate that SRS is a safe treatment modality for use in patients with MS.

(P151) Poor Long-Term Sexual Recovery With Neoadjuvant Androgen Deprivation Therapy (NADT) Plus Radiotherapy: Results of a Multicenter, Prospective Study

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PURPOSE: Long-term effects of neoadjuvant androgen deprivation therapy (NADT) with radiotherapy (RT) on patient-reported health-related quality of life (HRQOL) have not been characterized in prospective multicenter studies. We evaluated the effects of NADT on HRQOL for 2 years among patients undergoing RT for newly diagnosed prostate cancer.

METHODS: The Prostate Cancer Outcomes and Satisfaction with Treatment Quality Assessment (PROST-QA) Consortium is a prospective, multi-institutional study at nine university-affiliated clinical sites across the US, wherein pretreatment demographic, cancer severity, and treatment details were recorded in a web-based database. HRQOL is measured with the Expanded Prostate Cancer Index Composite (EPIC)-26 questionnaire via a computer-assisted phone interview (CATI) at pretreatment and at 2 months, 6 months, 1 year, and 2 years after the start of NADT. Differences in patient-reported HRQOL were observed between pretreatment and 1 year and 2 years after NADT start (and before definitive RT), with significant differences evaluated by paired t-test.

RESULTS: From among 598 subjects who completed CATI before and 2 years after NADT start, 111 received NADT prior to proceeding with definitive RT. Patients receiving NADT experienced significant impairment in vitality/hormonal (P < .0001), sexual (P < .0001), urinary continence (P = .0005), urinary irritative/obstructive (P = .0001), and bowel (P < .0001) HRQOL after NADT initiation.

CONCLUSIONS: Neoadjuvant ADT with RT has clinically significant long-term effects on sexual, vitality/hormonal, and bowel/rectal HRQOL domains. Most profound are the sexual side effects, which also have the least long-term recovery. The hope of long-term improved sexual QOL should not be an argument when comparing RT with NADT and prostatectomy. The significant impact of this therapy on HRQOL needs to be considered before initiating NADT in men.

(P152) Fiducial-Less SBRT of the Lung: VMAT Versus CK

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PURPOSE AND OBJECTIVE: Advances in radiotherapy technology have led to an increase in stereotactic body radiotherapy (SBRT) treatments. The most recent CyberKnife (CK) tracking algorithm upgrade, Lung-Optimized Treatment (LOT), allows for treatment of lung tumors located anywhere in the lung without the need for fiducial placement by taking orthogonal kV images to locate and track the lesion when it is visible in the camera or taking kV images of the spine if the lesion is not visible. Fiducial-less SBRT can also be delivered using linear accelerator (LINAC)-based systems. Given that the treatment time is substantially greater with the CK-based approach, we performed a dosimetric comparison of these two systems to attempt to quantify any dosimetric advantages that would substantiate the increased treatment time of CK.

MATERIALS AND METHODS: We retrospectively analyzed 10 lung patients who had been treated with LINAC-based SBRT using volumetric arc therapy (VMAT) and generated CK-based treatment plans using the LOT tracking algorithm in 0-View mode. All plans included an internal tumor volume (ITV). All VMAT plans...
were generated using the Eclipse (Varian) treatment planning system (TPS) with the AAA dose calculation algorithm, while the CK plans were generated using the Multiplan (Accuray) TPS with the Monte Carlo dose calculation algorithm. We compared planning target volume (PTV) coverage; conformity index (CI); lung V5, V10, V20, V25, mean lung dose (MLD), 90% IDL/PTV, 80% IDL/PTV, and 70% IDL/PTV; heart V5, V10, and mean heart dose (MHD); and spinal cord maximum and esophagus maximum doses, when applicable. The mean and standard deviations were calculated for all patient parameters, and a paired t-test was used to identify any statistically significant difference in dosimetric parameters between two systems.

RESULTS: Two tumors were located in the left upper lobe, two were located in the right middle lobe, three were located in the left lower lobe one was located in the right upper lobe, and one was located in the right hilum. The mean LINAC lung V5 was 14.43 cc and 23.48 cc in the CK plans (P = .00088). The mean LINAC lung V10 was 8.49 cc and 10.29 cc in the CK plans (P = .04). The mean LINAC MLD was 2.99 Gy and 4.21 Gy in the CK plans (P = .0009). The mean LINAC CI was 1.035 and 1.141 in the CK plans (P = .012). The mean LINAC 90% IDL/PTV was 1.428 and 1.602 in the CK plans (P = .016). There were no other statistically significant differences between dosimetric parameters.

CONCLUSION: When comparing fiducial-less SBRT of the lung using VMAT and CK, we identified statistically significant dosimetric advantages in the LINAC plans as compared with the CK plans. These results may be due to the field size (FS) limitation in the CK, where the largest available FS is 6 cm in diameter and may be suboptimal when treating larger targets. Given the superior dosimetry and decreased treatment time of VMAT plans, fiducial-less SBRT of the lung may be more advantageous and efficient using a LINAC system than CK with LOT in 0-View mode. Future study with an increased number of patients is needed.

(P153) Hypofractionated Radiation for Early Breast Cancer: What Are Reasonable Lung Dose Constraints in the Setting of 3-Dimensional Treatment Planning?

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BACKGROUND: Hypofractionated radiation therapy (HFRT) is being increasingly utilized as a component of breast-conserving therapy for early-stage breast cancer. In the phase III European and Canadian trials investigating the use of HFRT, up to 3 cm of lung measured at the central plane was permitted in the treatment field and resulted in acceptable radiation pneumonitis rates of less than 1%. While these landmark HFRT studies did not report dose-volumes for organs at risk (OARs), an open Radiation Therapy Oncology Group (RTOG) protocol, RTOG 1005, offers ideal and acceptable dose-volume constraints for the ipsilateral lung. These constraints are routinely used at our institution while treatment planning for a hypofractionated course off protocol. Our purpose is to review a series of hypofractionated plans to report our ipsilateral lung dose-volumes and corresponding lung included in the field at the central plane.

METHODS: Ten consecutive radiation plans used in the treatment of early-stage (American Joint Committee on Cancer [AJCC] 7th group stage I, II), right-sided breast cancer were reviewed. All patients included received whole-breast treatment to a total dose of 42.56 Gy in 2.66-Gy fractions with a 10-Gy sequential lumpectomy cavity boost. All patients were planned utilizing forward-planned field-in-field intensity modulation. Patients with left-sided breast cancer and patients treated in the prone position were excluded to most conservatively estimate lung dose-volumes. Percent of the ipsilateral lung receiving 20 Gy or more (V20), V10, and V5 were recorded. Ipsilateral lung included in the field at the central plane was recorded.

RESULTS: All 10 plans that were reviewed met the acceptable target volume coverage recommendations and ipsilateral lung dose constraints as described by RTOG (V20 ≤ 20%, V10 ≤ 40%, and V5 ≤ 55%). Mean ipsilateral lung V20 was 9.7% (median 8.9%; range: 2.4%–19%). Mean ipsilateral lung V10 was 13.8% (median 13.0%; range: 4.7%–22.8%). Mean ipsilateral lung V5 was 23.7% (median 21.7%; range: 10.9%–31.6%). Mean ipsilateral lung included in the field at the central plane was 1.2 cm (median 1.1 cm; range: 0.1–2.7 cm).

CONCLUSIONS: The lung dose constraints as outlined in RTOG 1005 are achievable while still delivering adequate dose to the target volume. Given that all patients in our series had < 3 cm of lung included in the field at the central plane with a mean of just 1.2 cm, it is likely that the patients enrolled in the randomized controlled trials examining HFRT received similar or perhaps higher ipsilateral lung V20, V10, and V5 with acceptable pneumonitis rates. Until the results of RTOG 1005 are available, these data support the use of the RTOG-proposed dose-volumes—lung V20 ≤ 20%, V10 ≤ 40%, and V5 ≤ 55%—as conservative dose restraints during 3-dimensional treatment planning for HFRT.

(P154) Variation in Severity of Acute Skin Toxicity by Race and Ethnicity in a Prospective Cohort of Patients Receiving Postmastectomy Radiation

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PURPOSE AND OBJECTIVES: Risk factors for radiation-induced skin toxicity (ST) are poorly understood, and there are limited data examining the relationship between race/ethnicity and the development of ST. We evaluated risk factors for radiation-induced ST in a racially and ethnically diverse cohort of patients receiving postmastectomy radiation therapy (PMRT) for breast cancer.

MATERIALS AND METHODS: We evaluated the first 108 patients in an ongoing prospective study assessing radiation-induced ST in patients receiving PMRT. We assessed ST using a variation of the National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events version 3.0 (CTCAE v3.0), which divides skin reaction into six categories in order to capture the presence of dry and moist desquamation as follows: 1- faint or dull erythema and/or follicular reaction and/or itching (CTCAE grade 1); 2- bright erythema and/or tender to touch (CTCAE grade 2); 3- dry desquamation with or without erythema (CTCAE grade 2); 4- small or
moderate amount of wet desquamation (CTCAE grade 2); 5- confluent moist desquamation and/or edema (CTCAE grade 3); and 6- ulceration, hemorrhage, and/or necrosis (CTCAE grade 4). ST was evaluated at Week 3 of RT and RT completion. We recorded patient demographics, smoking history, body mass index (BMI), and disease and treatment characteristics. We used Pearson's chi-square test or Fisher's exact test for differences in the distributions of patient and disease characteristics and ST grade.

RESULTS: Overall, 5.6% self-identified as non-Hispanic white, 68.2% Hispanic white, 24.2% black, and 2% other. Further, 20.8% was premenopausal; 28% had BMI < 25, 37.4% 25–29.9, and 34.6% ≥ 30. In addition, 65.4% of patients were never-smokers, and 34.6% of subjects were current/former smokers. Disease stage was 4.7% stage I, 26.1% stage II, 66.3% stage III, and 1.9% stage IV. Also, 67.3% had estrogen receptor (ER)+ tumors, 25% were human epidermal growth factor receptor 2 (HER2)+, and 20.8% had triple-negative disease. All had mastectomy +/- reconstruction and axillary dissection or sentinel node biopsy. Further, 91.5% received systemic chemotherapy, and 67.3% received endocrine therapy. Median chest wall dose was 50 Gy vs 60 Gy for mastectomy scar, using photon tangents alone or matched to a medial electron field.

Of all patients, 93.9% were treated with bolus throughout treatment, most commonly 0.5 cm daily. Dosimetric analysis showed that the mean chest wall volume receiving > 105% of prescription dose was 29.1%, and 2.5% received > 110%. Overall at RT completion, 15.9% developed grade 1 ST, 9.3% grade 2, 20.6% grade 3, 47.7% grade 4, and 6.5% grade 5. There were no significant differences in patient, disease, or treatment characteristics by race or ethnicity, including BMI. Grade 4–5 ST (moist desquamation) was more common in black patients than nonblack patients (73.1% vs 48.1%; P = .026) and in those with PR-positive tumors (64.2% vs 43.1%; P = .031). Those with BMI ≥ 25 exhibited a trend toward grade 4–5 ST (59.7 vs 40%; P = .066). No other factors significantly associated with ST.

CONCLUSION: In a racially and ethnically diverse prospectively studied cohort of breast cancer patients receiving PMRT, black race was a significant predictor of moist desquamation. CTCAE grading alone would not capture this difference; improved scales with sensitive criteria for grading radiation-induced ST in breast cancer are needed. Our ongoing study with a targeted sample size of 240 may shed light on the mechanisms of racial/ethnic disparities in radiation-induced ST.
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