AMERICAN RADIUM SOCIETY

95th Annual Meeting
April 27 - May 1, 2013
The Phoenician | Scottsdale, Arizona

Advancing Cancer Care Through Treatment and Biologic Innovation

Final Program

President: Thomas Buchholz, MD – MD Anderson Cancer Center
Program Chair: Theodore DeWeese, MD – The Johns Hopkins University School of Medicine

www.americannradiumsociety.org

ARS 2013 Annual Meeting Mobile Website www.ars2013.org
Advancing Cancer Care Through Treatment and Biologic Innovation

Proceedings of the 95th Annual Meeting of the American Radium Society

APRIL 27–MAY 1, 2013
THE PHOENICIAN
SCOTTSDALE, ARIZONA

PROCEEDINGS
General Information

ACCREDITATION STATEMENT

This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education through the joint sponsorship of the American College of Surgeons and the American Radium Society. The American College of Surgeons is accredited by the ACCME to provide continuing medical education for physicians.

AMA PRA CATEGORY 1 CREDITS™

The American College of Surgeons designates this live activity for a maximum of 25 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

Breakdown of Credit

Saturday = 3.25 credits
Sunday = 5.5 credits
Monday = 6.75 credits
Tuesday = 4.25 credits
Wednesday = 5.25 credits

LEARNING OBJECTIVES

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

1) Understand contemporary molecular imaging and when/how such technologies are best applied to diagnose and follow patients with cancer.
2) Direct care for patients with skin cancer in a multispecialty environment.
3) Direct care for patients with breast cancer and help determine the role of individual therapies for each patient.
4) Have a framework to incorporate proven patient safety protocols and procedures into the clinic to enhance safety and communication of errors from which practitioners can learn.

MEETING GOALS AND EXPECTED OUTCOMES

The goal of this activity is to facilitate a balanced and multidisciplinary discussion of contemporary cancer treatment, using panel discussions and lecture-based didactic sessions, as well as oral and poster discussions of cutting-edge research.

DISCLOSURE INFORMATION

In compliance with ACCME regulations, the American College of Surgeons, as the accredited provider of this activity, must ensure that anyone in a position to control the content of the educational activity has disclosed all relevant financial relationships with any commercial interest. All reported conflicts are managed by a designated official to ensure a bias-free presentation. Please see the insert to this program for the complete disclosure list.
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ROOM ASSIGNMENTS

Exhibit Hall and Poster Session .............................. Camelback Ballroom H, I, J, K
General Sessions .................................................. Camelback Ballroom L, M, N
Hospitality Suite .................................................. Palo Verde
Meet the Professor Luncheons ................................ Pinon
Presidential Categorical Session .............................. Camelback Ballroom L, M, N
Registration ....................................................... Camelback Registration
Speaker Ready Room ............................................ Boojum
Welcome Reception .............................................. Camelback Ballroom H, I, J, K
Social Event ....................................................... Jokake Inn

Registration Hours

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<tr>
<td>Saturday, April 27, 2013</td>
<td>10:00 AM–6:30 PM</td>
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<tr>
<td>Sunday, April 28, 2013</td>
<td>7:00 AM–1:00 PM</td>
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<tr>
<td>Monday, April 29, 2013</td>
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<td>Tuesday, April 30, 2013</td>
<td>7:00 AM–1:00 PM</td>
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<td>Wednesday, May 1, 2013</td>
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Exhibit Hall*/Poster Hours

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<td>Saturday, April 27, 2013</td>
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<tr>
<td>Monday, April 29, 2013</td>
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<td>Tuesday, April 30, 2013</td>
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<td>Wednesday, May 1, 2013</td>
<td>7:00 AM–1:00 PM</td>
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*Exhibits will take place April 27–April 30 only.
The American Radium Society gratefully acknowledges an unrestricted educational grant from Varian Medical Systems in support of the Poster Session.
NEW MEMBERSHIP APPLICATION

AMERICAN RADION SOCIETY
APPLICATION FOR MEMBERSHIP

Instructions to Applicant: Print or type all of the information below. You are required to have three sponsors forward a completed sponsorship form or letter of support directly to ARS. Sponsors must be members of ARS. If you need assistance finding a sponsor, please contact ARS at the email address above. Attach your current CV with bibliography. Return completed application (with dues payment) to ARS. Application and sponsor forms can be downloaded from www.americanradiosociety.org/memberships.

Date:

Type of Membership (please check one):

☐ ACTIVE (Dues are $190.00 for the first year $275 per year thereafter).
☐ RESIDENT MEMBER (No dues are required) – Proof of residency letter required from head of dept. Current year of Residency Anticipated completion date.

Name:

Last

First

Middle or Blvd

Address:

Department

Institution

Street

City/State

Zip Code

Telephone #: __________________ Fax: __________________ E-mail Address: __________________

Alternate Email Address __________________

Place of Birth: __________________ Date (mo/day/year): __________________ Country of Citizenship: __________________

Please list all degrees earned below, including honorary degrees and fellowships:

<table>
<thead>
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<th>Degree</th>
<th>Conferring Institution</th>
<th>Date</th>
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Please list professional training below:

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<th>Type</th>
<th>Place</th>
<th>Date</th>
</tr>
</thead>
</table>

Internship

Residencies

Specialty Training

Fellowship

Other

Specialty of Medical Practice:

<table>
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<tr>
<th>Type</th>
<th>Years in Practice</th>
<th>% of Total Practice in Oncology</th>
</tr>
</thead>
</table>

Hospital (or Professional) affiliations, past and present, with dates:

Current Academic Title (if any): ____________________ Hospital Title: ____________________

Medical and Professional Societies:

Teaching Positions:

State License Number of State License(s): ( )

What part of your activities is devoted to the treatment of patients with cancer, cancer-related research and/or teaching?

Have you attended any meetings of the American Radium Society?

When?

Signature of Applicant:

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Introduction and President’s Welcome

April 27, 2013

Dear Colleagues,

Welcome to the American Radium Society’s 95th Annual Meeting! The theme of this year’s ARS meeting is Advancing Cancer Care Through Treatment and Biologic Innovation, highlighting how the exciting advances in science are advancing the care of patients with cancer. During our meeting, we will hear new, original data that can affect treatment decisions regarding the patients we currently treat, as well as some exciting innovations that will advance the future of our specialties.

The caliber of science received in the abstract submissions this year was outstanding, and we look forward to presenting five Essay Awards and ten Travel Grants to Young Oncologist recipients.

Dr. Theodore DeWeese and the Scientific Program Committee deserve much praise, having recruited an extraordinary group of lecturers and panelists for our four panels that will convene this year. I am honored to extend a special welcome to our distinguished speakers, Dr. Mary Gospodarowicz of Princess Margaret Hospital, who will give the Janeway Lecture, and our Keynote Speakers, Dr. Alfredo Quiñones-Hinojosa of Johns Hopkins and Dr. Amato Giaccia of Stanford University. This year’s debate will pit Dr. Richard Hoppe against Dr. Thomas Miller on the topic: The Role of RT in Lymphoma. We again offer two Self-Assessment Modules for qualification toward the American Board of Radiology’s Maintenance of Certification program, featuring Pancreatic Cancer (Dr. Joseph Herman) and Head and Neck Cancer (Dr. Beth Beadle).

As in past years, we will be preceding the meeting with our annual course, only this year it will be a special Presidential Categorical Session, Difficult Cases in Breast Cancer, and will be included in your registration fee. I will be chairing this session and have invited several fantastic speakers to share their knowledge.

THOMAS BUCHHOLZ, MD
ARS President, 2012–2013
Our deepest gratitude goes to our industry supporters, including Varian Medical Systems, Elekta, Hitachi Ltd, Genomic Health, and Mevion Medical Systems. Finally, all involved with the meeting owe our sincerest gratitude to Jaclyn Weinstein, ARS Executive Director, for her 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. Please take advantage of the beautiful Phoenician Hotel and the surrounding area. We hope you enjoy the academic and social programs, and I welcome any comments for continued improvements to the American Radium Society and its meetings.

Sincerely,

Thomas Buchholz, MD
ARS President, 2012–2013

SAVE THE DATES!
Future Meetings of the American Radium Society

ARS 96th Annual Meeting
April 26–30, 2014
Marriott Frenchman’s Reef
St. Thomas, US Virgin Islands

ARS 97th Annual Meeting
May 2–6, 2015
Grand Hyatt Kauai
Kauai, Hawaii
PAST PRESIDENTS OF THE AMERICAN RADIUM SOCIETY

1916......................... W.H.B. Aikins, MD*
1917......................... W.H.B. Aikins, MD*
1918......................... John M. Lee, MD*
1919......................... J.B. Bissell, MD*
1920................. Henry K. Pancoast, MD*
1921......................... Henry Schmitz, MD*
1922......................... G.E. Pfahler, MD*
1923......................... Robert E. Loucks, MD*
1924......................... James T. Case, MD*
1925......................... William S. Newcomet, MD*
1926......................... Douglas Quick, MD*
1927......................... Albert Soiland, MD*
1928......................... Curtis F. Burnam, MD*
1929......................... Edwin C. Ernset, MD*
1930......................... Harry H. Bowing, MD*
1931......................... Henry J. Ullmann, MD*
1932......................... Sanford Withers, MD*
1933......................... Burton J. Lee, MD*
1934......................... Rollin H. Stevens, MD*
1935......................... William H. Cameron, MD*
1936......................... George W. Grier, MD*
1937......................... Zoe A. Johnston, MD*
1938......................... Edward H. Skinner, MD*
1939......................... William P. Healy, MD*
1940......................... Lawrence A. Pomeroy, MD*
1941......................... Frederick W. O’Brien, MD*
1942......................... Hayes E. Martin, MD*
1946......................... William E. Costolow, MD*
1947......................... Charles L. Martin, MD*
1948......................... A.N. Arneson, MD*
1949......................... Maurice Lenz, MD*
1950......................... William S. Macomb, MD*
1951......................... Leland R. Cowan, MD*
1952......................... Hugh F. Hare, MD*
1953......................... Howard B. Hunt, MD*
1954......................... Edith H. Quimby, ScD*
1955......................... John E. Wirth, MD*
1956......................... Grant Beckstrand, MD*
1957......................... Norman A. McCormick, MD*
1958......................... Douglas J. Roberts, MD*
1959......................... Milford D. Schulz, MD*
1960......................... Theodore R. Miller, MD*
1961......................... Jeshill Love, MD*
1962......................... Robert L. Brown, MD*
1963......................... Gilbert H. Fletcher, MD*
1964......................... Charles G. Stetson, MD*
1965......................... Joseph H. Farrow, MD*
1966......................... Justin J. Stein, MD*
1967......................... Milton Friedman, MD*
1968......................... John L. Pool, MD*
1969......................... Juan A. del Regato, MD*
1970......................... Fernando Bloedorn, MD*
1971......................... James F. Nolan, MD*
1972......................... John V. Blady, MD*
1973......................... Antolin Raventos, MD*
1974......................... Jerome M. Vaeth, MD*
1975......................... Victor A. Marcial, MD*
1976......................... Felix Rutledge, MD*
1977......................... Luther W. Brady, MD*
1978......................... Richard H. Jesse, MD*
1979......................... Frederick W. George III, MD*
1980......................... Alfred S. Ketcham, MD*
1981......................... Simon Kramer, MD*
1982......................... George C. Lewis, Jr, MD*
1983......................... Morton M. Kligerman, MD*
1984......................... Seymour H. Levitt, MD*
1985......................... John R. Durant, MD*
1986......................... Frederick Eilber, MD*
1987......................... Gerald E. Hanks, MD*
1988......................... Morris J. Wizenberg, MD*
1989......................... Carl M. Mansfield, MD*
1990......................... Elliot W. Strong, MD*
1991......................... Robert G. Parker, MD*
1992......................... J. Taylor Wharton, MD*
1993......................... Lawrence W. Davis, MD*
1994......................... Peter H. Wiernik, MD*
1995......................... Marvin Rotman, MD*
1996......................... Robert M. Byers, MD*
1997......................... H. Rodney Withers, MB, BS*
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2003......................... J. Frank Wilson, MD*
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2007......................... Jonathan J. Beitler, MD, MBA*
2008......................... Ritsuko U. Komaki, MD*
2009......................... Bruce G. Haffty, MD*
2010......................... Raymond Sawaya, MD*
2011......................... Peter A.S. Johnstone, MD*
2012......................... Alan Pollack, MD, PhD*

* Deceased
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Steven Frank, MD 2010-2013
Gary Freedman, MD 2010-2013
Mary Katherine Hayes, MD 2010-2013
Mark Henderson, MD 2010-2013
Joseph Herman, MD 2010-2013
Peter Johnstone, MD 2010-2013
Andre Konski, MD 2010-2013
Quynh-Thu Le, MD 2010-2013
Alan Pollack, MD, PhD 2010-2013
Drew Ridge, MD, PhD 2010-2013
Raymond Sawaya, MD 2010-2013
Elin Sigurdson, MD, PhD 2010-2013
Anne Tsao, MD 2010-2013
Sue Yom, MD 2010-2013

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AMERICAN COLLEGE OF RADIOLOGY COUNCILOR
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ON RADIATION PROTECTION & MEASUREMENTS
Ritsuko Komaki, MD 2013-2016

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Bruce Haffty, MD 2009-2013
Lynn Wilson, MD 2011-2015
Kaled Alektiar, MD 2013-2017
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<tr>
<th>Name</th>
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<td>MATTHEW ABRAMOWITZ, MD</td>
<td>University of Miami</td>
<td>Miami, FL</td>
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<tr>
<td>KALED ALEKTIAR, MD</td>
<td>Memorial Sloan-Kettering Cancer Center</td>
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<td>CHISTOPHER BARKER, MD</td>
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<td>BETH BEADLE, MD, PhD</td>
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<td>Houston, TX</td>
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<td>JEFF BRADLEY, MD</td>
<td>Washington University School of Medicine</td>
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<td>University of Michigan</td>
<td>Ann Arbor, MI</td>
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<td>ERIC L. CHANG, MD</td>
<td>USC Keck School of Medicine</td>
<td>Los Angeles, CA</td>
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<td>THEODORE DEWEES, MD</td>
<td>Johns Hopkins University</td>
<td>Baltimore, MD</td>
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<td>SHANNON E. FOGH, MD</td>
<td>University of California, San Francisco</td>
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<td>AMATO GIACCIA, PhD</td>
<td>Stanford University</td>
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<td>MARY GOSPODAROWICZ, MD</td>
<td>Princess Margaret Hospital</td>
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<td>MICHAEL E. KUPFERMAN, MD</td>
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<td>New Haven, CT</td>
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<td>BEN MOVSAS, MD</td>
<td>Henry Ford Hospital Radiology</td>
<td>Detroit, MI</td>
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<td>SASA MUTIC, PhD</td>
<td>Washington University School of Medicine</td>
<td>St. Louis, MO</td>
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<tr>
<td>TODD PAWLICKI, PhD</td>
<td>University of California, San Diego</td>
<td>San Diego, CA</td>
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<td>ALAN POLLACK, MD, PhD</td>
<td>University of Miami</td>
<td>Miami, FL</td>
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<tr>
<td>MARTY POMPER, MD, PhD</td>
<td>Johns Hopkins University</td>
<td>Baltimore, MD</td>
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<tr>
<td>JOHN “DREW” RIDGE, MD, PhD</td>
<td>Fox Chase Cancer Center</td>
<td>Philadelphia, PA</td>
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<td>AYESGUL SAHIN, MD</td>
<td>UT MD Anderson Cancer Center</td>
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<td>STEPHANIE TEREZAKIS, MD</td>
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<td>Baltimore, MD</td>
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<td>DEBU TRIPATHY, MD</td>
<td>USC Keck School of Medicine</td>
<td>Los Angeles, CA</td>
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<td>AKILA N. VISWANATHAN, MD, MPH</td>
<td>Brigham and Women’s Hospital</td>
<td>Boston, MA</td>
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<tr>
<td>CATHERYN YASHAR, MD</td>
<td>UCSD Moores Cancer Center</td>
<td>San Diego, CA</td>
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<td>SUE S. YOM, MD, PhD</td>
<td>University of California, San Francisco</td>
<td>San Francisco, CA</td>
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Mary Gospodarowicz is Professor of Radiation Oncology at the Princess Margaret Cancer Centre and the University of Toronto, the Medical Director of the Princess Margaret Cancer Centre at the University Health Network in Toronto, and the Regional Vice President of Cancer Care Ontario. She has recently completed an 11-year term as the Professor and Chair of the Department of Radiation Oncology at the University of Toronto and Chief of the Radiation Medicine Program at Princess Margaret Hospital. She received her medical degree from the University of Toronto and holds specialty certifications in internal medicine, radiation oncology, and medical oncology. Her clinical practice includes patients with lymphomas and genitourinary cancers. Dr. Gospodarowicz has authored more than 300 peer-reviewed articles and book chapters. Her research interests are in the area of clinical trials evaluating the role of radiation therapy in cancer treatment, image-guided precision radiotherapy, and cancer survivorship, and her work has recently focused on quality of care, partnerships, and international collaboration. She was proud to participate in the work of the Global Task Force on Cancer Care and Control initiated by the Harvard Global Equity Initiative. Her current interests include global cancer control and global access to radiotherapy and quality cancer care.

Dr. Gospodarowicz has held numerous leadership positions, including in the National Cancer Institute of Canada Clinical Trials Group, the Canadian Committee on Cancer Staging, and the Canadian Association of Radiation Oncologists, of which she is a former President. She serves as a member of the Board of Directors of the International Extranodal Lymphoma Site Group. She has been an active member of the American Society for Radiation Oncology (ASTRO) and the European Society for Therapeutic Radiology and Oncology (ESTRO), supporting their education programs, and is an active contributor to the programs of American Society of Clinical Oncology, for which she served on the International Affairs Committee.

Her numerous awards include being named an honorary Fellow of the Royal College of Radiologists in the United Kingdom; receiving honorary membership in ESTRO; being named a Fellow of ASTRO and an honorary Fellow of the Faculty of Radiologists in the Royal College of Surgeons of Ireland; and honors including the Schiffer Exchange Visiting Professorship, Gordon Richards Lecture by the Canadian Association of Radiation Oncologists, and the May Cohen Award for Women Mentors by the Canadian Medical Association.

For the past 20 years, Dr. Gospodarowicz has been actively involved in the work of the Union for International Cancer Control (UICC), an international nongovernmental organization dedicated to the global control of cancer. She has made contributions to the TNM Prognostic Factors Project that she currently co-chairs and served on the UICC’s Executive Committee and subsequently on the Board of Directors. In August 2012, she became President of the UICC.

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 E. Pfeiffer, 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 F. Craver, MD
New York, NY
“Reflections on Malignant Lymphomas”

1957.............................. Simeon T. Cantrill, 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 Radiation 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 Lymphogenous Leukemia”

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

1975.............................. George C. Lewis, Jr., MD
Philadelphia, PA
“Ovarian Cancer: Multifacted 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”
1978 Frank J. Rauscher, Jr., PhD New York, NY
"The National Cancer Program: Progress and Problems"

1979 Oliver H. Beals, MD Rochester, MN
"Treatment of Squamous Cell Epithelioma of the Anus"

1980 Luther W. Brady, MD Philadelphia, PA
"Malignant Tumors of the Eye"

1981 Morton M. Kligerman, MD Philadelphia, PA
"Pions, Protectors: Examples of a Vigorous Decade in Radiotherapy"

1982 Felix N. Rutledge, MD Houston, TX
"Gynecological Oncology – 1982-2002"

1983 Elliot W. Strong, MD New York, NY
"Multidisciplinary Management of Head and Neck Cancer: Update and Prospects"

1984 Willet F. Whitmore, Jr., MD New York, NY
"Surgery and/or Irradiation: Some Areas of Confrontation in Urologic Oncology"

1985 Eleanor Montague, MD Houston, TX
"Radiation Therapy and Breast Cancer – Past, Present, and Future"

1986 John S. Laughlin, PhD New York, NY
"Physical Aspects of Radiation Treatment: Some Developments & Implications for the Future"

1987 Herman D. Suit, MD Boston, MA
"Scope of the Problem of Control of the Primary Tumor"

1988 Alfred S. Ketcham, MD Miami, FL
"The Breast Surgeon's Dilemma"

1989 Seymour H. Levitt, MD Minneapolis, MN
"Role of Radiation Therapy in Hodgkin's Disease: Experience and Controversy"

1990 Alfred G. Knudson, Jr., MD, PhD Philadelphia, PA
"Hereditary Cancer and Tumor Suppressor Genes"

1991 Maurice Tubiana, MD Villejuif, France
"The Treatment of Thyroid Cancer by Ionizing Radiation: A Model for Metabolic Radiotherapy"

1992 Eric J. Hall, ScD New York, NY
"Nine Decades of Radiobiology: Is Radiotherapy the Better for It?"

1993 Theodore L. Phillips, MD San Francisco, CA
"Radiation Effects on Normal Tissue – A Thirty-Year Perspective"

1994 H. Rodney Withers, MB, BS, DSc Los Angeles, CA
"The Biology and Treatment of Subclinical Metastases"

1995 Lester J. Peters, MD East Melbourne, Australia
"Normal Tissue Tolerance Limits: For One or For All?"

1996 Peter H. Wiernik, MD Bronx, NY
"What the Study of Leukemia Has Taught Us About the Common Neoplasms"

1997 Robert G. Parker, MD Los Angeles, CA
"Iatrogenic Carcinogenesis: Clinical Implications"

1998 Harvey E. Averette, MD Miami, FL
"Modern Therapy for Cancer of the Uterine Cervix"

1999 Sarah S. Donaldson, MD Palo Alto, CA
"Hodgkin's Disease – Finding the Balance Between Cure and Late Effects"

2000 James D. Cox, MD, FACR Houston, TX
"Clinical Science and Patient Care: Evidence in Oncology"

2001 Jimmie C. Holland, MD New York, NY
"Improving the Human Side of Cancer Care"

2002 Richard T. Hoppe, MD Stanford, CA
"Hodgkin's Disease, a Model for Interdisciplinary Cancer Management"

2003 Carlos Perez, MD St. Louis, MO
"Breast Conservation Therapy: Past, Present Issues and Future Challenges and Opportunities"

2004 Samuel A. Wells, Jr., MD Durham, NC
"The Multiple Endocrine Neoplasia"

2005 Jean-Claude Horiot, MD, PhD Dijon-Bourgogne, France
"Radiation Oncologists: Endangered Species or Phoenix?"

2006 Andrew C. von Eschenbach, MD Bethesda, MD
"Progress With a Purpose: Eliminating the Suffering and Death Due to Cancer"

2007 Harry Bartelink, MD Amsterdam, the Netherlands
"Moving Towards a New Era in Radiotherapy"

2008 John Mendelsohn, MD Houston, TX
"Targeting EGF Receptors: The Journey Continues"

2009 Larry Kun, MD Memphis, TN
"Radiation Therapy – A Central Role in Pediatric Cancer"

2010 Charles M. Balch, MD Baltimore, MD
"Melanoma as an Example of Evidence-Based Medicine"

2011 Larry Einhorn, MD Indianapolis, IN
"Testicular Cancer: A Model for a Curable Neoplasm"

2012 David Larson, MD San Francisco, CA
"The Fifth 'R' in Radiation Oncology"
KEYNOTE LECTURER BIO

ALFREDO QUIÑONES-HINOJOSA, MD—Dr. Alfredo Quiñones-Hinojosa received a medical degree from Harvard University, where he graduated cum laude. He went on to complete his residency in neurosurgery at the University of California, San Francisco, where he also completed a postdoctoral fellowship in developmental and stem cell biology. At Johns Hopkins University in Baltimore, Maryland, Dr. Quiñones is a Professor of Neurosurgery, Oncology, Neuroscience, and Cellular and Molecular Medicine. In addition to directing the Brain Tumor Surgery Program at Johns Hopkins Bayview Hospital and the Pituitary Surgery Program at Johns Hopkins Hospital, Dr. Quiñones leads the Brain Tumor Stem Cell Laboratory. He focuses on the surgical treatment of primary and metastatic brain tumors, with an emphasis on motor and speech mapping during surgery as well as in the treatment of patients with pituitary and skull base tumors using transsphenoidal, endonasal, and minimally invasive surgical approaches.

“Dr. Q.” is an internationally renowned neurosurgeon and neuroscientist who leads cutting-edge research to cure brain cancer. Named one of the 100 most influential Hispanics in 2008, Dr. Q. was also selected by Popular Science magazine as one of their 6th Annual Brilliant Ten in their search for young geniuses influencing the course of science. He has received an honorary degree from and been appointed to the Board of Trustees at Southern Vermont College. He has published more than 200 peer-reviewed articles and over 40 book chapters, and has edited two books on stem cells. He is the lead editor for the upcoming edition of Schmidek and Sweet’s Operative Neurosurgical Techniques, the world’s preeminent encyclopedia of neurosurgery.

Dr. Q. conducts numerous research efforts to elucidate the role of stem cells in the origin of brain tumors and the potential role stem cells can play in fighting brain cancer and regaining neurological function. He has received R01 funding from the National Institutes of Health for his work with stem cells and cancer, and his awards also include grants from the Physician-Scientist Early Career Award of Howard Hughes Medical Institute, from the Robert Wood Johnson Foundation, and from the Maryland Stem Cell Foundation. Dr. Q. has given more than 200 invited lectures nationally and internationally, including lectures presented during visiting professorships at several universities.

Besides being a constantly in-demand lecturer on an array of subjects, Dr. Q. continues to galvanize public attention. On the award-winning ABC series “Hopkins,” he was featured in the lead episode. Along with appearances on such programs as “NOVA,” CNN features with Sanjay Gupta, CBS News coverage with Katie Couric, and NBC’s “The Today Show,” as well as on National Public Radio, Dr. Q. has been featured in a variety of newspapers and magazines and has a growing online following. Dr. Q is regularly listed as one of the Best Doctors in America and one of America’s Top Surgeons, as well as being included in the Baltimore Top Docs list. He has been the recipient of the Health Care Heroes Award, which recognizes doctors who make a difference in the lives of their patients.

Keynote Lecturer

ALFREDO QUIÑONES-HINOJOSA, MD

Johns Hopkins University, Baltimore
AMATO GIACCIA, PhD—Dr. Giaccia is a Professor of Radiation Oncology, Associate Chair for Research, and Director of the Division of Radiation & Cancer Biology in the Department of Radiation Oncology at Stanford University School of Medicine, in Stanford California. He also heads the Radiation Biology Program at Stanford's Cancer Center, and is Director of the Cancer Biology Interdisciplinary Graduate Program. Professor Giaccia has co-authored more than 200 peer-reviewed articles, as well as the sixth and seventh editions of the textbook, *Radiation Biology for the Radiologist*, with Professor Eric Hall from Columbia (published by Lippincott Williams & Wilkins, in 2006 and 2012, respectively). He is currently the Jack, Lulu and Sam Willson Endowed Professor of Cancer Biology at Stanford University School of Medicine.

Dr. Giaccia’s research interests have focused on understanding the molecular mechanisms underlying the response of tumors and normal tissue to hypoxia. Tumor hypoxia reduces the efficacy of radiotherapy and chemotherapy and increases the invasive and metastatic behavior of tumor cells. Dr. Giaccia and co-investigators have identified several small molecules that selectively kill tumor cells that have elevated levels of the hypoxia-inducible factor (HIF) transcription factor. He and his colleagues are also developing new therapeutics to treat metastatic disease through the targeting of hypoxia-induced genes (such as lysyl oxidase) that are involved in extracellular matrix remodeling.

His group also showed that loss-of-function mutations in the VHL gene or increased HIF activity in osteoblasts results in an increase in hematopoietic stem cells and mature red blood cells. These studies represent a new approach to protecting and/or rescuing the bone marrow after exposure to ionizing radiation.

During the last 5 years, using a synthetic lethal screening approach, Dr. Giaccia and his research team at Stanford have identified several small molecules that kill VHL-deficient renal cancer cells. His laboratory also has identified and characterized several genes that are induced by hypoxia and promote metastases in breast, ovarian, renal, and head and neck cancer, and his team is developing therapeutics against them. His research group is also investigating how hypoxia regulates gene expression epigenetically through regulation of histone demethylases and microRNAs. Dr. Giaccia received a MERIT award from the National Cancer Institute in 2010 for his research project investigating histone demethylases regulated by p53 and HIF. Using mouse tumor models, the studies planned under this MERIT award will determine the importance of histone demethylase targets under hypoxia and after exposure to ionizing radiation in cell culture and in tumors, characterize the importance of p53 in mediating repression under hypoxia, and determine the contribution of the histone demethylases to tumor progression.
2013 Young Oncologist Essay Awards

Andrew McBride
University of Arizona and MD Anderson Cancer Center | Houston | TX
Locoregional Recurrence Risk for Patients With T1,2 Breast Cancer with 1-3 Positive Lymph Nodes Treated With Mastectomy and Systemic Treatment

Adam Ferro, BS
Department of Radiation Oncology, The Cancer Institute of New Jersey UMDNJ/ Robert Wood Johnson Medical School | South River | NJ
Evaluation of Diabetic Patients With Breast Cancer Treated With Metformin During Adjuvant Radiotherapy

Katherine Y. Fan
Johns Hopkins University School of Medicine | Baltimore | MD
Treating Pancreatic Cancer Patients With Erlotinib-Based Adjuvant Therapy Following Pancreatecoduodenectomy or Pancreatectomy

Eugene J. Koay, MD, PhD
MD Anderson Cancer Center, The Methodist Hospital Research Institute, University of New Mexico Cancer Center | Houston | TX
Novel CT-Derived Biophysical Markers Describe Gemcitabine Delivery and Chemoradiation Response in Human Pancreatic Adenocarcinoma

Ravi B. Parikh, BA
Harvard Medical School, Dana-Farber Cancer Institute | Cambridge | MA
Primary Radiotherapy Versus Radical Prostatectomy for High-Risk Prostate Cancer: A Decision Analysis

2013 Young Oncologist Travel Grant Winners

Daniel M. Arsenault, MD
Sylvester Cancer Center, University of Miami | Miami | FL
Are Insurance Companies Influencing the Decision-Making Process for Stage I Non-Small Cell Lung Cancer (NSCLC) Patients?

Peyman Kabolizadeh, MD, PhD
Department of Radiation Oncology, University of Pittsburgh Cancer Institute | Pittsburgh | PA
Extent of Perilesional Edema Differentiates Radionecrosis From Tumor Recurrence Following Stereotactic Radiosurgery for Brain Metastasis

Tina Dasgupta, MD, PhD
Department of Radiation Oncology, University of California | San Francisco | CA
Survival Advantage With Everolimus (RAD001) Combined With a Selective BRAFV600E Inhibitor in a Xenograft Model of BRAFV600E-Mutated Pediatric Glioma

Neil C. Estabrook, MD
Department of Radiation Oncology, Indiana University School of Medicine, Indianapolis | IN
Skin Dose of Proton-Scanning Techniques

Benjamin Goodman, DO
Indiana University | Indianapolis | IN
Safety and Efficacy of Stereotactic Body Radiotherapy for Liver Metastasis

Farhaan Hafeez, MS
Department of Therapeutic Radiology, Yale University School of Medicine, Department of Radiation Oncology, UMDNJ-Robert Wood Johnson School of Medicine, Department of Breast Surgery, Shandong University School of Medicine, China | UCSF Medical Center | San Francisco | CA
Prognostic Significance of Ki-67 Expression in Women Treated With Breast Conservation Therapy (BCT)

Minh-Phuong Huynh-Le, SB
Johns Hopkins University School of Medicine | Hanover | MD
Involved Field Radiation Therapy for Pediatric Hodgkin Lymphoma: Treatment Outcomes in a Single-Institution Cohort

Okechukwu Linton, MD
Departments of Radiation Oncology, Otolaryngology/Head & Neck Surgery, and Pathology, Indiana University School of Medicine, Indiana University Health Proton Therapy Center | Bloomington | IN
Initial Clinical Outcomes of Dose-Escalated Proton Therapy for Head and Neck Adenoid Cystic Carcinoma

Geoffrey Martin, BS
University of Texas MD Anderson Cancer Center, University of Cincinnati, Baylor College of Medicine, Rice University | Mason | OH
Utility of Exhaled Nitric Oxide as a Biomarker for Symptomatic Radiation Pneumonitis in Esophageal and Lung Cancer Patients

Roshan Sethi, BS
Massachusetts General Hospital, Harvard Medical School | Boston | MA
Early Clinical Outcomes Using Proton Radiation for Children With Central Nervous System Atypical Teratoid Rhabdoid Tumors
PAST RECIPIENTS OF THE YOUNG ONCOLOGIST ESSAY AWARDS

2012
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

2011
Sanjay Aneja, BS
Matthew R. McCurdy, MD, PhD
Henry S. Park, BS
Hiral Patel Fontanilla, MD

2010
Amol J. Ghia, MD
Matthew Koshy, MD
Baoqing Li, MD, PhD
Jeffrey R. Olsen, MD
Akshar N. Patel, BS
Andris J. Zauls, MD

2009
Leon M. Chen, BS
Camille P. Green, BS
Kilian Salerno May, MD
Thomas J. Pugh, MD
Navesh K. Sharma, DO, PhD
Kevin L. Stephens, MD

2008
Beth M. Beadle, MD, PhD
Mark W. McDonald, MD
Loren K. Mell, MD
James B. Yu, MD

2007
Elizabeth A. Kidd, MD
Daniel J. Indelicato, MD
Erik P. Sulman, MD

2006
Daniel T. Chang, MD
Yee-Lu Tham, MD
Ann H. Klopp, MD, PhD
Anad Parthasarathy, MD

2005
Laura Granville, MD
Andrew Hope, MD
Bridget Koontz, MD
Michael Sinopoli, MD

2004
Ramesh Rengan, MD
Allen Chen, MD
Falguni Amin-Zimmerman, MD

2003
Anesa Ahamad, MD
Anurag Chandra, MD
Robert S. Malyapa, MD
Wendy A. Woodward, MD

2002
Jerry L. Barker, MD
Thomas J. Gergel, MD
Ramesh Gopal, MD

2001
Christopher Chen, MD
Ben Han, MD
Pamela Schlembach, MD

2000
Hany Elsaleh, MBBS
Angela Katz, MD
Jay Locke, MD
Erich M. Sturgis, MD

1999
Kenneth Blank, MD
Heather Curry, MD
Timothy Jameson, MD

1998
Bruce C. Turner, MD
Jennifer B. Sherwood, MD
Oliver Bathe, MD

1997
Eddy C. Hsueh, MD
John P. Geisler, MD

1996
Dong Fu Chen, MD
HuiKuo Shu, MD

1995
Gary M. Proulx, MD

1994
Peter P. Huang, MD
Michael R. MacDonald, MD
Turgut Alagoz, MD
Peter A. S. Johnstone, MD

1993
Edward R. Sauter, MD
Sonia Brisson, MD
Noreen C. Gleeson, MD
Donald J. Martinelli, MD

1992
Edward L. Levine, MD
Seth A. Rosenthal, MD
James R. Wong, MD
Brigette Miller, MD

1991
Thomas Buchholz, MD
Joseph Poen, MD
Paul Monsour, MD
Patrick DePotter, MD

1990
Jerrey Goldstein, MD

1989
Jeffrey Williams, MD

1988
Stephen C. Rush, MD

1987
Richard S. Godfrey, MD

1986
Colleen Lawton, MD
Nabil C. Arlsan, MD

1985
Michelle Burnison, MD
John Zaleberg, MD
David C. Beyer, MD

1984
Michael J. Marchese, MD

1983
Robert A. Rostock, MD

1982
Judith A. Stitt, MD

1980
R. Dirk Noyes, MD

1979
Dennis F. Devereux, MD

1978
Joseph F. Russ, MD
Program at a Glance

SATURDAY, APRIL 27, 2013
10:00 AM–6:00 PM Registration Open
1:00–5:00 PM Presidential Categorical Session: Difficult Cases in Breast Cancer
6:30–7:30 PM ARS Welcome and Exhibit Hall Opening Reception
6:45–7:15 PM Poster Tours

SUNDAY, APRIL 28, 2013
7:00–8:00 AM Continental Breakfast and Exhibit/Poster Session
7:00–8:00 AM Resident Breakfast
8:00–9:15 AM Scientific Session #1: CNS Tumors
9:15–10:15 AM Keynote Lecture: Alfredo Quiñones-Hinojosa, MD, Johns Hopkins Hospital
10:15–10:30 AM Break and Exhibit/Poster Session
10:30–11:30 AM Scientific Session #2: Imaging
11:30 AM–12:30 PM Panel: Image Guidance
12:45–2:15 PM **Meet the Professor Luncheon: CNS Tumors
7:00–10:00 PM ARS Social Event (onsite)

MONDAY, APRIL 29, 2013
7:00–8:00 AM Continental Breakfast and Exhibit/Poster Session
7:00–8:00 AM **Self-Assessment Module (SAM): Pancreatic Cancer
8:00–9:00 AM Scientific Session #3: Head and Neck Cancer
9:00–10:00 AM Janeway Lecture: Mary Gospodarowicz, MD, Princess Margaret Hospital
10:00–10:15 AM Break and Exhibit/Poster Session
10:15–11:10 AM Scientific Session #4: Young Oncologist Essay Awards
11:10–11:45 AM Scientific Session #5: Emerging Biologic and Cell-Based Markers
11:45 AM–12:45 PM Panel: Gynecologic Oncology
12:45–2:15 PM **Meet the Professor Luncheon: Lung Cancer

TUESDAY, April 30, 2013
7:00–8:00 AM Continental Breakfast and Exhibit/Poster Session
7:00–8:00 AM ARS Business Meeting: All ARS Members are welcome to attend. Only Active Members may vote.
8:00–8:45 AM Presidential Address: Thomas Buchholz, MD, UT MD Anderson Cancer Center
8:45–9:30 AM Scientific Session #6: Breast Cancer
9:30–9:45 AM Break and Exhibit/Poster Session
9:45–10:30 AM Debate: The Role of RT in Lymphoma
10:30–11:30 AM Scientific Session #7: Gastrointestinal and Genitourinary Cancer
11:30 AM–12:30 PM Panel: Patient Safety and Quality Assurance

WEDNESDAY, MAY 1, 2013
7:00–8:00 AM Continental Breakfast and Poster Session
7:00–8:00 AM **Self-Assessment Module (SAM): Head and Neck Cancer
8:00–9:15 AM Scientific Session #8: Lung Cancer
9:15–10:15 AM Keynote Lecture: Amato Giaccia, PhD, Stanford University
10:15–10:30 AM Break and Poster Session
10:30–11:30 AM Scientific Session #9: Pediatric Cancers/Sarcoma/Gynecologic Cancers
11:30 AM–12:30 PM Panel: Skin Cancer

** Registration required

ROOM ASSIGNMENTS
Exhibit Hall and Poster Session ............................................................Camelback Ballroom H, I, J, K
General Sessions ......................................................................................Camelback Ballroom L, M, N
Hospitality Suite ......................................................................................Palo Verde
Meet the Professor Luncheons ...............................................................Pinon
Presidential Categorical Session ..........................................................Camelback Ballroom L, M, N
Registration ............................................................................................Camelback Registration
Speaker Ready Room ............................................................................Boojum
Welcome Reception ..............................................................................Camelback Ballroom H, I, J, K
Social Event .............................................................................................Jokake Inn

The American Radium Society gratefully acknowledges Varian Medical Systems in support of the Daily Breakfasts, Breaks, and Poster Session in the Exhibit Hall.
Presidential Categorical Session

CHAIR: THOMAS BUCHHOLZ, MD
SATURDAY, APRIL 27, 2013
1:00–5:00 PM
CAMELBACK BALLROOM

Difficult Cases in Breast Cancer

<table>
<thead>
<tr>
<th>Time</th>
<th>Title</th>
<th>Speaker</th>
<th>Institution</th>
</tr>
</thead>
<tbody>
<tr>
<td>1:00 PM</td>
<td>Welcome and Opening Remarks</td>
<td>Thomas Buchholz, MD</td>
<td>UT MD Anderson Cancer Center</td>
</tr>
<tr>
<td>1:15 PM</td>
<td>Update on Breast Pathology*</td>
<td>Aysegul Sahin, MD</td>
<td>Department of Pathology, UT MD Anderson Cancer Center</td>
</tr>
<tr>
<td>1:45 PM</td>
<td>Timing of SLN and Breast Conservation Therapy With Chemotherapy*</td>
<td>Kelly Hunt, MD</td>
<td>Department of Surgical Oncology, UT MD Anderson Cancer Center</td>
</tr>
<tr>
<td>2:15 PM</td>
<td>Radiation Management of Regional Lymphatics*</td>
<td>Thomas Buchholz, MD</td>
<td>Department of Radiation Oncology, UT MD Anderson Cancer Center</td>
</tr>
<tr>
<td>2:45 PM</td>
<td>Targeted Therapies in Breast Cancer: HER2 and Beyond*</td>
<td>Debu Tripathy, MD</td>
<td>Department of Medical Oncology, USC</td>
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<tr>
<td>3:15 PM</td>
<td>BREAK</td>
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<tr>
<td>3:30 PM</td>
<td>Challenging Case Presentations: Multidisciplinary Panel</td>
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<tr>
<td>4:30 PM</td>
<td>Closing Remarks</td>
<td>Thomas Buchholz, MD</td>
<td>Department of Radiation Oncology, UT MD Anderson Cancer Center</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 appropriate surgical and radiation management of lymph nodes in breast cancer.
Scientific Program

SATURDAY, APRIL 27, 2013

10:00 AM–6:30 PM  REGISTRATION OPEN

1:00–5:00 PM  PRESIDENTIAL CATEGORICAL SESSION: Difficult Cases in Breast Cancer
COURSE CHAIR: Tom Buchholz, MD
MD Anderson Cancer Center
PANELISTS:
Kelly Hunt, MD
MD Anderson Cancer Center
Aysegul Sahin, MD
MD Anderson Cancer Center
Debu Tripathy, MD
University of Southern California

The American Radium Society gratefully acknowledges an unrestricted educational grant from Genomic Health in support of the Presidential Categorical Session: Difficult Cases in Breast Cancer.

6:30–7:30 PM  ARS WELCOME/EXHIBIT HALL OPENING RECEPTION

The American Radium Society gratefully acknowledges Elekta, Inc, Hitachi Ltd, and Varian Medical Systems in support of the Welcome and Exhibit Hall Opening Reception.

6:45–7:15 PM  POSTER WALK
POSTER WALK GUIDES: Andre Konski, MD, and Quynh-Thu Le, MD

SUNDAY, APRIL 28, 2013

7:00–8:00 AM  CONTINENTAL BREAKFAST AND EXHIBIT/POSTER SESSION

7:00–8:00 AM  RESIDENT BREAKFAST

8:00–9:15 AM  SCIENTIFIC SESSION #1: CNS Tumors
MODERATORS: Mark Henderson, MD
Indiana University School of Medicine
Raymond Sawaya, MD
UT MD Anderson Cancer Center

(S001) Survival Advantage With Everolimus (RAD001) Combined With a Selective BRAFV 600E Inhibitor in a Xenograft Model of BRAF V600E–Mutated Pediatric Glioma
TINA DAGGUPATI, MD, PhD – TRAVEL GRANT WINNER

(S002) Patterns of Failure for Glioblastoma Multiforme Following Limited-Margin Radiation and Concurrent Temozolomide
BRIAN J. GEBHARDT, BA

(S003) Temozolomide Use in Adult Patients With Gliosarcoma: An Evolving Clinical Practice
GARY V. WALKER

(S004) Surgical Excision With Adjuvant External Beam Radiation, Temozolomide, and Anti-EGFR Radioimmunotherapy in Treatment of High-Grade Gliomas: A Phase II Study
MICHAEL WONG

(S005) Effect of Treatment Modality on the Hypothalamic-Pituitary Function of Patients Treated With Radiation Therapy for Pituitary Adenomas: Effect of Hypothalamic Dose on Endocrine Outcomes
ANDREW ELSON, MD

(S006) Phase I Preliminary Results of Intraoperative Brachytherapy for Recurrent Glioblastoma Multiforme (GBM) and Atypical Meningioma
A. GABRIELLA WERNICKE, MD, MSC

(S007) Brain Metastases in Patients Diagnosed With a Solid Primary Cancer During Childhood: Experience From a Single Referral Cancer Center
RAYMOND SAWAYA, MD

(S008) A Prospective Study Using Implanted Fiducial Markers to Assess Treatment Accuracy in Spinal Stereotactic Body Radiation Therapy
DAVID C. WEKSBERG, MD, PhD

(S009) Outcomes in Spinal Stereotactic Body Radiotherapy: An Update of the MD Anderson Cancer Center Experience
E.N. CHRISTENSEN, MD, PhD

9:15–10:15 AM  KEYNOTE LECTURE:
Alfredo Quinones-Hinojosa, MD
Johns Hopkins Hospital
“Brain Cancer: Building Bridges as You Walk on Them”

10:15–10:30 AM  BREAK AND EXHIBIT/POSTER SESSION

10:30–11:30 AM  SCIENTIFIC SESSION #2: Imaging
MODERATOR: Alan Pollack, MD, PhD
University of Miami

(S010) Variation in Dose to Organ at Risk, Due to Daily Rectal Filling During Prostate Intensity-Modulated Radiotherapy: A Cone-Beam CT Study
LEONEL A. KAHN, BS

(S011) 18F-FDG PET Definition of Gross Tumor Volume in Pediatric Hodgkin Lymphoma: What Is the Effect of Various SUV Thresholds on Target Volume Delineation?
MINH-PHUONG HUYNH-LE, SB – TRAVEL GRANT WINNER

(S012) PET as a Predictor of Outcomes for Cervical and Vaginal Cancer With HDR Interstitial Brachytherapy Utilizing MRI-Based Planning
J.M. FREILICH, MD

(S013) Noninvasive Real-Time Prostate Tracking Using a Transperineal Ultrasound Approach: Phantom Studies and Initial Clinical Experience
MATTHEW C. ABRAMOWITZ, MD

(S014) Improving Prostate Cancer Risk Stratification Through Multiparametric MRI Prostate Imaging
NICOLO T. KUMMER, MD, PhD

ARS PROCEEDINGS 2013 xix
10:30–11:30 AM  SCIENTIFIC SESSION #2: Imaging (continued)

(S015) Extent of Perilesional Edema Differentiates Radionecrosis From Tumor Recurrence Following Stereotactic Radiosurgery for Brain Metastasis
PEYMAN KABOLIZADEH, MD, PhD  TRAVEL GRANT WINNER

(S016) Optimizing Reconstructive Outcomes in the Radiated Head and Neck Cancer Patient: A Novel Application of Indocyanine Green Angiography
RYAN WINTERS, MD

11:30 AM–12:30 PM  PANEL: Image Guidance
PANEL CHAIR: Thomas Guerrero, MD
MD Anderson Cancer Center
PANELISTS:
Yue Cao, MD; University of Michigan
Steve Jiang, MD; UCSD
Marty Pomper, MD; Johns Hopkins

12:45–2:15 PM  MEET THE PROFESSOR LUNCHEON: CNS Tumors
Come discuss the specialty of CNS tumors with well-known professors. Discuss case studies and get some of your most challenging questions answered.

**Registration is required for this luncheon. Space is limited.

SPEAKERS: Eric Chang, MD; MD Anderson Cancer Center
Ray Sawaya, MD; MD Anderson Cancer Center

7:00–10:00 PM  ARS SOCIAL EVENT (onsite):
COWBOY CORRAL—Enjoy some delicious BBQ and try your hand at one of the various games, such as the Tomahawk Toss or Quick Draw Competition.
ATTIRE: Cowboy 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 in support of the ARS Social Event.

The American Radium Society gratefully acknowledges an unrestricted educational grant from Elekta, Inc, in support of the Scientific Session.

MONDAY, APRIL 29, 2013

7:00–8:00 AM  CONTINENTAL BREAKFAST AND EXHIBIT/POSTER SESSION

7:00–8:00 AM  SELF-ASSESSMENT MODULE (SAM): Pancreatic Cancer
Joseph Herman, MD
Johns Hopkins

8:00–9:00 AM  SCIENTIFIC SESSION #3: Head and Neck Cancer
MODERATORS: Beth Beadle, MD, PhD
UT MD Anderson Cancer Center
Drew Ridge, MD, PhD
Fox Chase Cancer Center

(S017) Initial Clinical Outcomes of Dose-Escalated Proton Therapy for Head and Neck Adenoid Cystic Carcinoma
OKECHUKWU LINTON, MD  TRAVEL GRANT WINNER

(S018) Laryngoesophageal Dysfunction–Free Survival Following Definitive Radiotherapy for Laryngeal and Hypopharyngeal Cancer at UC Davis
CARLIN R. HAUCK

(S019) Dysphagia Following Radiation for Oropharyngeal Squamous Cell Cancer Is Predicted by Dose to the Floor-of-Mouth Muscles
RACHIT KUMAR, MD

(S020) Results of Fractionated Proton Reirradiation for Recurrent Chordoma of the Base of Skull or Spine
OKECHUKWU R. LINTON, MD

(S021) Disease Control and Toxicity Outcomes Using Ruthenium Eye Plaque Brachytherapy in the Treatment of Intraocular Melanoma
VINITA TAKIAR, MD, PhD

(S022) SEER Analysis of Outcomes of Patients With Parotid Cancer Treated With Radiation Therapy
BHUPESH PARASHAR

(S023) Role of TGF-Beta Signaling in PIK3CA-Driven Head and Neck Cancer Invasion and Metastasis
SOPHIA BORNSTEIN, MD, PhD

9:00–10:00 AM  JANeway LECTURE:
Mary Gospodarowicz, MD
Princess Margaret Hospital
“Cancer in the World – The Equity Imperative”

10:00–10:15 AM  BREAK AND EXHIBIT/POSTER SESSION
10:15–11:10 AM  SCIENTIFIC SESSION #4: Young Oncologist Essay Awards
MODERATORS: Thomas Buchholz, MD
UT MD Anderson Cancer Center
Elin Sigurdson, MD, PhD
Fox Chase Cancer Center

(S024) Locoregional Recurrence Risk for Patients With T1,2 Breast Cancer With 1–3 Positive Lymph Nodes Treated With Mastectomy and Systemic Treatment
ANDREW MCBRIDE

(S025) Evaluation of Diabetic Patients With Breast Cancer Treated With Metformin During Adjuvant Radiotherapy
ADAM FERRO, BS

(S026) Treating Pancreatic Cancer Patients With Erlotinib-Based Adjuvant Therapy Following Pancreaticoduodenectomy or Pancreatectomy
KATHERINE Y. FAN

(S027) Novel CT-Derived Biophysical Markers Describe Gemcitabine Delivery and Chemoradiation Response in Human Pancreatic Adenocarcinoma
EUGENE J. KONY, MD, PhD

(S028) Primary Radiotherapy Versus Radical Prostatectomy for High-Risk Prostate Cancer: A Decision Analysis
RAVI B. PARIKH, BA

11:10–11:45 AM  SCIENTIFIC SESSION #5: Emerging Biologic and Cell-Based Markers
MODERATOR: Sue Yom, MD, PhD
University of California, San Francisco

(S029) Expression of Myeloid Differentiation Factor 88 in Neurons Is Not Requisite for the Induction of Anorexia and Lethargy by Interleukin-1 Beta
AARON J. GROSSBERG, PhD

(S030) Developing a Circulating Tumor Cell Assay for Non–Small-Cell Lung Cancer Patients Undergoing Radiation Therapy
LUCAS GILBRIDE

(S031) Epidermal Growth Factor–Mediated Detection of Circulating Tumor Cells in Patients With Head and Neck Cancer: Clinical Results
JONATHAN J. BEITLER, MD, MBA

11:45 AM–12:45 PM  PANEL: Gynecologic Oncology

PANEL CHAIR: Akila Viswanathan, MD
Harvard University

PANELISTS:
Bradley Monk, MD; St Joseph's Hospital
Cate Yashar, MD; UCSD

12:45–2:15 PM  MEET THE PROFESSOR LUNCHEON: Lung Cancer
Come explore various aspects of lung cancer with well-known professors. Discuss case studies and get some of your most challenging questions answered.
**Registration is required for this luncheon. Space is limited.

SPARKERS: Jeffrey Bradley, MD
Washington University in St. Louis
Benjamin Movsas, MD
Henry Ford Hospital

The American Radium Society gratefully acknowledges an unrestricted educational grant from Varian Medical Systems in support of the Meet the Professor Luncheon.

TUESDAY, APRIL 30, 2013

7:00–8:00 AM  CONTINENTAL BREAKFAST AND EXHIBIT/POSTER SESSION

7:00–8:00 AM  ARS BUSINESS MEETING
All ARS Members are welcome to attend. Only Active Members may vote.

8:00–8:45 AM  PRESIDENTIAL ADDRESS:
Thomas Buchholz, MD
MD Anderson Cancer Center
"Breast Cancer: Translating Biology and Clinical Research Into Improved Patient Outcomes"

8:45–9:30 AM  SCIENTIFIC SESSION #6: Breast Cancer
MODERATOR: Meena S. Moran, MD
Yale University School of Medicine

(S032) Prognostic Significance of Ki-67 Expression in Women Treated With Breast Conservation Therapy (BCT)
FARHAAN HAFEZ, MS – TRAVEL GRANT WINNER

(S033) Assessing Breast Cancer–Related Disparities in an Equal-Access-to-Care Health Care System: Data From the VA Central Cancer Registry Database (VACCR)
MEENA S. MORAN, MD

(S034) Post-Mastectomy Radiation Therapy and Tissue Expander–Implant Breast Reconstruction: Effect of Sequencing on Complications and Delays in Therapy
SUSAN A. HIGGINS, MD

(continued)
9:30–9:45 AM  BREAK AND EXHIBIT/POSTER SESSION

9:45–10:30 AM  DEBATE: The Role of RT in Lymphoma
MODERATOR: Theodore DeWeese, MD
Johns Hopkins
DEBATORS:
Richard Hoppe, MD; Stanford University
Thomas Miller, MD; University of Arizona Cancer Center

10:30–11:30 AM  SCIENTIFIC SESSION #7:
Gastrointestinal/Genitourinary Cancer
MODERATORS: Matthew C. Abramowitz, MD
University of Miami
Joseph Herman, MD
Johns Hopkins University

11:30 AM–12:30 PM  PANEL: Patient Safety and Quality Assurance
PANEL CHAIR: Stephanie Terezakis, MD
Johns Hopkins
PANELISTS:
Shannon E. Fogh, MD; University of California, San Francisco
Sasa Mutic, MD; Washington University in St. Louis
Todd Pawlicki, PhD; University of California, San Diego

WEDNESDAY, MAY 1, 2013

7:00–8:00 AM  CONTINENTAL BREAKFAST AND EXHIBIT/POSTER SESSION

8:00–9:15 AM  SCIENTIFIC SESSION #8: Lung Cancer
MODERATORS: Jeffrey Bradley, MD
Washington University School of Medicine
Steven Lin, MD
UT MD Anderson Cancer Center

8:00–9:15 AM  SCIENTIFIC SESSION #7: Gastrointestinal/Genitourinary Cancer
MODERATORS: Matthew C. Abramowitz, MD
University of Miami
Joseph Herman, MD
Johns Hopkins University

The American Radium Society gratefully acknowledges an unrestricted educational grant from Mevion Medical Systems in support of this session.
Utility of Exhaled Nitric Oxide as a Biomarker for Symptomatic Radiation Pneumonitis in Esophageal and Lung Cancer Patients
GEOFFREY MARTIN, BS – TRAVEL GRANT WINNER

Are Insurance Companies Influencing the Decision-Making Process for Stage I Non–Small-Cell Lung Cancer (NSCLC) Patients?
DANIEL M. ARSENAULT, MD – TRAVEL GRANT WINNER

Interfraction Stability of Electromagnetic Navigational Bronchoscopy-Placed Embolization Coil Fiducial Markers for Lung Stereotactic Body Radiation Therapy (SBRT)
NIMA NABAVIZADEH, MD

Predictors of IMRT Utilization for Lung Cancer in the United States: A SEER-Medicare Study
SHERVIN M. SHIRVANI, MD, MPH

The American Radium Society gratefully acknowledges an unrestricted educational grant from Hitachi, Ltd, in support of the Scientific Session.

9:15–10:15 AM
KEYNOTE LECTURE:
Amato Giaccia, PhD
Stanford University
"Is the Tumor Microenvironment an Impediment to Therapy?"

10:15–10:30 AM
BREAK AND EXHIBIT/POSTER SESSION

10:30–11:30 AM
SCIENTIFIC SESSION #9: Pediatric Cancers/Sarcoma/Gynecologic Cancers
MODERATORS: Khaled Alektiar, MD
Memorial Sloan-Kettering Cancer Center
Peter A.S. Johnstone, MD
Indiana University School of Medicine

Early Clinical Outcomes Using Proton Radiation for Children With Central Nervous System Atypical Teratoid Rhabdoid Tumors
ROSHAN SETHI, BS

Local Control Outcomes in Adult and Pediatric Patients With Axial Ewing Sarcoma
LINDSAY L. WARNER

Involved-Field Radiation Therapy for Pediatric Hodgkin Lymphoma: Treatment Outcomes in a Single-Institution Cohort
MINH-PHUONG HUYNH-LE, SB – TRAVEL GRANT WINNER

Using the Toronto Extremity Salvage Score (TESS) to Measure Functional Outcomes After Radiotherapy for Management of Soft Tissue Sarcoma Involving the Distal Extremity
ROBERT A. ZLOTECKI

Skin Dose of Proton Scanning Techniques
NEIL C. ESTABROOK, MD – TRAVEL GRANT WINNER

Improved Node-Positive Cervical Cancer Progression-Free Survival After Triapine Radiochemotherapy
CHARLES A. KUNOS, MD, PhD

Postoperative Radiation Therapy and Concurrent Cisplatin Followed by Carboplatin/Paclitaxel for Stage III Endometrial Cancer
SARAH A. MILGROM, MD

11:30 AM–12:30 PM
PANEL: Skin Cancer
PANEL CHAIR: Sue Yom, MD
University of California, San Francisco

PANELISTS:
Chris Barker, MD
Memorial Sloan-Kettering Cancer Center
Michael Kupferman, MD
MD Anderson Cancer Center
Personalized Radiation Medicine: An Elekta Luncheon Symposium

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

SUNDAY, APRIL 28, 2013

1:00–2:30 PM

**Personalized Radiation Medicine for Prostate Cancer as Practiced at William Beaumont School of Medicine**

Daniel J. Krauss, MD
*Assistant Professor of Radiation Oncology*
*Oakland University William Beaumont School of Medicine*
*Royal Oak, Michigan*

**Personalized Radiation Medicine for Lung Cancer as Practiced at Temple University**

Curtis T. Miyamoto, MD
*Professor and Chairperson*
*Temple University*
*Philadelphia, Pennsylvania*
(S001) Survival Advantage With Everolimus (RAD001) Combined With a Selective BRAFV 600E Inhibitor in a Xenograft Model of BRAF V600E–Mutated Pediatric Glioma

Tina Das Gupta, MD, PhD, Aleksandra Olow, MS, Xiaodong Yang, MS, Theodore Nicolaides, MD, Daphne Haas-Kogan, MD; Department of Radiation Oncology, University of California, San Francisco

PURPOSE: Treatment for pediatric low-grade gliomas (PLGGs) involves maximal safe surgical resection. However, recurrence is common, warranting re-excision, cytotoxic chemotherapy, or adjuvant radiation. Molecular underpinnings of PLGG pathogenesis are rapidly emerging. BRAF is activated through the KIAA1549:BRAF fusion protein in the majority of pilocytic astrocytomas (PAs) and by missense mutation (V600E) in ~25% to 40% of grade 2–4 pediatric gliomas. We have found activation of PI3K/AKT/mTOR in half of PLGGs, providing a preclinical rationale to cooperate with BRAF inhibitors. We aim to test inhibitors of PI3K/AKT/mTOR in PLGGs. In this study, we aimed to determine whether specific inhibitors of mTOR (everolimus [Afinitor]) and of BRAF V600E (PLX4720) cooperate to enhance cytotoxicity against pediatric gliomas. These experiments are conducted in vitro with brain tumor cell lines and in vivo using patient-derived tumor cells from a pediatric pilocytic astrocytoma (PA).

METHODS: In vitro clonogenic assays were performed with varying concentrations of PLX4720 and everolimus using four glioma cell lines with BRAF V600E mutations and four expressing wild-type (WT) BRAF. Expression of mediators of the MAPK and PI3K/mTOR pathways were determined by western blot. Cell cycle effects and markers of apoptosis (annexin V) and of DNA damage (gamma-H2AX) were assayed using flow cytometry. In an in vivo flank model of PLGG, subcutaneous xenografts of BT40 (a BRAF V600E pediatric PA) were treated with vehicle, PLX4720, everolimus, or a combination of PLX4720 + everolimus. The outcome measures were tumor size and animal survival.

RESULTS: Treatment with a combination of PLX4720 + everolimus demonstrated synergistic antiproliferative activity against glioma cell lines expressing BRAF V600E but not those with BRAF WT. In vitro, treatment with PLX4720 decreased pMAPK and p4EBP1 and increased cleaved PARP. These effects were pronounced with the addition of everolimus. Cell cycle analyses demonstrated that PLX4720 caused G1 arrest in BRAF V600E glioma cell lines, an effect that was substantially more pronounced by the addition of everolimus. Both annexin V and gamma-H2AX levels were significantly increased by combination treatment with PLX4720 + everolimus in BRAF V600E–mutated glioma cell lines. In murine xenografts of a PA with mutated BRAF V600E, treatment with PLX4720 + everolimus led to a statistically significant survival advantage, when compared to treatment with vehicle alone (P = .0002), PLX4720 alone (P = .0126), or everolimus alone (P = .0031). Treatment with PLX4720 + everolimus also led to statistically smaller tumors when compared to treatment with vehicle alone (P < .0001), PLX4720 alone (P < .0001), or everolimus alone (P = .0082).

CONCLUSIONS: We report the first in vivo demonstration of combinatorial activity of PLX4720 + everolimus in gliomas—specifically in PLGGs—expressing BRAF V600E. These results implicate increased DNA damage, G1 arrest, and apoptosis as potential mechanisms for this combinatorial activity. Future studies are underway to determine the normal tissue toxicity of this combination. Our data strongly support future, translational, molecularly targeted approaches combining BRAF V600E inhibitors with PI3K/mTOR inhibitors in pediatric patients with BRAF V600E–mutated gliomas.

(S002) Patterns of Failure for Glioblastoma Multiforme Following Limited-Margin Radiation and Concur rent Temozolomide

Brian J. Gebhardt, BA, Michael C. Dobelbower, MD, PhD, Asim K. Bag, MD, James M. Markert, MD, Louis B. Nabors, MD, John B. Fiveash, MD; Medical College of Georgia, University of Alabama at Birmingham

BACKGROUND: To analyze patterns of failure in patients with glioblastoma multiforme treated with limited-margin radiation therapy and concurrent temozolomide (Temodar). We hypothesize that patients treated with margins in accordance with Adult Brain Tumor Consortium guidelines will demonstrate patterns of failure consistent with existing series using 2–3-cm margins.

METHODS: A retrospective review was performed of patients treated at the University of Alabama at Birmingham for glioblastoma multiforme between 2005 and 2011. Seventy-five patients with biopsy-proven disease, documented disease progression after treatment, and adequate radiation dosimetry and imaging records were analyzed. The initial planning target volume included the T1-enhancing tumor and surrounding edema defined by FLAIR imaging plus a 1-cm margin. The boost planning...
target volume included the T1-enhancing tumor plus a 1-cm margin. MRIs documenting failure after therapy were fused to the original treatment plans. Contours of post-treatment tumor volumes were generated from MRIs showing tumor recurrence and were registered to the original planning CTs. Ninety-five percent isodose curves were generated from the completed treatment plans. The tumors were classified as in-field, marginal, or distant if greater than 80%, 20% to 80%, or less than 20% of the recurrent volume fell within the 95% isodose line, respectively. In patients with multiple distinct recurrent lesions, individual sites of recurrence were analyzed independently.

**RESULTS:** The median progression-free survival from the time of diagnosis to documented failure was 11 months (range, 3–49). The median volume of recurrent disease was 19.08 mL (range, 0.11–234.11). Of the 75 documented recurrences, 59 patients (79%) had an in-field component of treatment failure, 4 (6%) had a marginal component, and 23 (31%) had a distant component. Forty-eight patients (64%) demonstrated in-field-only recurrence. Two (3%) failures were marginal only, 14 (19%) were distant only, 2 (3%) were in-field and marginal, and 9 (12%) were in-field and distant. Of the 24 patients with a distant component of failure, 4 (17%) originally had multifocal disease.

**CONCLUSIONS:** The rate of distant failure was higher than rates reported in historical series examining patients treated with radiation only, which suggests that temozolomide acts primarily as a radiosensitizer rather than as an independently cytotoxic agent. The low rate of marginal recurrence suggests that wider margins would have little impact on the pattern of failure, validating the use of limited margins in accordance with Adult Brain Tumor Consortium guidelines.

<table>
<thead>
<tr>
<th>Site of Recurrence</th>
<th>In-field Only</th>
<th>Marginal Only</th>
<th>Distant Only</th>
<th>Central + Marginal</th>
<th>In-field + Distant</th>
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<tr>
<td>Number</td>
<td>48</td>
<td>2</td>
<td>14</td>
<td>2</td>
<td>9</td>
</tr>
<tr>
<td>Percentage</td>
<td>64</td>
<td>3</td>
<td>19</td>
<td>3</td>
<td>12</td>
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</tbody>
</table>

**Table S002**

**Figure:** Kaplan-Meier Overall Survival Curves Comparing Patients Treated for Gliosarcoma Between 2000–2003 versus 2006–2008 (temozolomide era) Identified in the SEER Registry.
AMERICAN RADIUM SOCIETY SCIENTIFIC PAPERS AND POSTERS 2013

(S004) Surgical Excision With Adjuvant External Beam Radiation, Temozolomide, and Anti-EGFR Radioimmunotherapy in Treatment of High-Grade Gliomas: A Phase II Study
Filip T. Troicki, MD, MBA, Larry C. Daugherty, MD, Steven Morales, MD, Ji Kim, MD, Linna Li, MD, Tony S. Quang, MD, Jacqueline Emrich, PhD, Theodore Yaeger, MD, John M. Jenrette, MD, Scott C. Cohen, MD, Lydia T. Komarnicky, MD, Luther W. Brady, MD; Drexel University College of Medicine / Hahnemann University Hospital

PURPOSE/OBJECTIVES: Since 2005, the standard of care for high-grade gliomas has been surgery followed by adjuvant radiotherapy and temozolomide. Despite the survival benefit of adding temozolomide, outcomes for patients with high-grade gliomas remain poor. In our phase II clinical trial, we investigated the efficacy of 125I-labeled anti-epidermal growth factor receptor monoclonal antibody 425 (125I-EGFR MAb 425) in patients with high-grade gliomas. We evaluated the outcomes in terms of survival and disease progression in three treatment groups: surgery+XRT (CTL), 125I-EGFR MAb 425+surgery+XRT (RIT), and TMZ+125I-EGFR MAb 425+surgery+XRT (TMZ+RIT).

MATERIALS AND METHODS: Our single-institution phase II study included 259 patients with newly diagnosed high-grade gliomas, including 207 patients with glioblastoma multiforme (GBM), and 52 patients with astrocytoma with anaplastic foci (AAF). All patients underwent primary debulking surgery followed by postoperative XRT to the tumor bed (median dose of 60 Gy). Fifty microcuries of 125I-EGFR MAb 425 was administered IV once per week for 3 weeks to a total dose of 150 mCi. TMZ was given concomitantly (75 mg/m2/d, 35–42 d) with XRT followed by 6 cycles of adjuvant TMZ (150–200 mg/m2/d × 5 d, q28d). We evaluated the patients in terms of median survival.

RESULTS: Between 1988 and 2007, a total of 259 patients with high-grade gliomas were treated at Hahnemann University Hospital. Of the 207 patients diagnosed with GBM, 39 were in the CTL group, 97 received RIT, and 51 received TMZ+RIT. Median age was 66.0, 52.5, and 53.5 years for each group, respectively. Median survival for all patients was 60.8 months, with median survival for CTL of 18.6 months, RIT of 59.1 months, and TMZ+RIT of 75.2 months.

CONCLUSIONS: The addition of 125I-EGFR MAb 425 radioimmunotherapy to external beam radiation to the tumor bed and temozolomide after surgical excision of high-grade gliomas may have a significant survival benefit. Multi-institutional phase III trials are warranted to confirm our findings.

(S005) Effect of Treatment Modality on the Hypothalamic-Pituitary Function of Patients Treated With Radiation Therapy for Pituitary Adenomas: Effect of Hypothalamic Dose on Endocrine Outcomes
Andrew Elson, MD, Joseph Bovi, MD, Christopher Schultz, MD; Department of Radiation Oncology, Medical College of Wisconsin

OBJECTIVE: To analyze the effect of treatment modality (Linac, TomoTherapy, or Gamma Knife) on hypothalamic dosimetric parameters and correlate them with the onset of new anterior pituitary deficits after radiation for pituitary adenoma.

METHODS: Patients treated postoperatively for pituitary adenomas at the Medical College of Wisconsin using Linac (n = 11), TomoTherapy (n = 10), or Gamma Knife (n = 12) were identified, and hypothalamic contours were added to the plans to allow dose-volume analysis. All patients had undergone prior surgery and had at least one functioning hypothalamic-pituitary axis prior to radiation. The endocrine axes analyzed included growth hormone (GH), thyroid (TSH), adrenal (ACTH), and prolactin (PRL). Dosimetric parameters for the hypothalamus included DMax, DMean, and V12Gy.

RESULTS: Eighteen of 33 (54.5%) patients had at least one pre-radiation hormone deficit. Postradiation, 13 of 27 (48%) patients eligible for analysis developed at least one new hormone deficit, of whom 8 of 11 (72%) occurred in the Linac treatment group, 4 of 8 (50%) occurred in the TomoTherapy group, and 1 of 8 (12.5%) occurred in the Gamma Knife group. Kaplan-Meier survival curve analysis showed improved median survival of the intact preradiation HP axis of 48.9 months versus 18.7 months [hazard ratio [HR] = 0.86, NS] in the TomoTherapy versus Linac group, respectively. In comparison with fractionated techniques, Gamma Knife showed significantly improved hypothalamic dosimetric parameters, including DMax.
and V12Gy. For fractionated modalities, TomoTherapy showed improved dosimetric characteristics over Linac-based treatment with hypothalamic DMean (44.8 Gy vs 26.8 Gy, \( P = .02 \)), DMax (49.8 Gy vs 39.1 Gy, \( P = .04 \)), and V12Gy (100% vs 76%, \( P = .004 \)).

CONCLUSION: For patients treated postoperatively for pituitary adenomas, maximal dosimetric conformal avoidance of the hypothalamus was achieved using Gamma Knife–based radiosurgery followed by TomoTherapy-based IMRT, and Linac-based 3D conformal radiation therapy, respectively. Favorable dosimetric characteristics, including reduced dose to the hypothalamus as measured by DMax and V12Gy, were associated with improved endocrine outcomes.

(S006) Phase I Preliminary Results of Intraoperative Brachytherapy for Recurrent Glioblastoma Multiforme and Atypical Meningioma

A. Gabriella Wernicke, MD, MSc, Menachem Yondorf, BA, Bhupesh Parashar, MD, Theodore H. Schwartz, MD, John A. Boockvar, MD, Susan Pannullo, MD, Philip Stieg, MD, PhD, Dattatreyyudu Nori, MD, K.S. Clifford Chao, MD; Weill Cornell Medical College of Cornell University

PURPOSE/OBJECTIVES: Recurrent glioblastoma multiforme (GBM) and recurrent atypical meningioma (AM) have high rates of local recurrence. Treatment at recurrence often consists of additional surgical resections and the use of radiation therapy when possible. Even with these aggressive treatments, these types of tumors are difficult to treat successfully. In this study, we evaluate the safety, feasibility, and efficacy of a novel treatment approach with permanent intraoperative Cs-131 brachytherapy.

MATERIALS AND METHODS: After IRB approval, a total of 17 patients (13 with recurrent GBM and 4 patients with recurrent AM) were accrued on a prospective protocol between 2010 and 2012. Of the GBM patients, there were 4 frontal, 5 parietal, 1 occipital, 3 temporal metastases. For AM patients, there were 1 parafalcine, 2 frontal, and 1 base-of-skull metastases. Based on our physics nomogram and the intracavitary volume of the resected metastasis, Cs-131-stranded seeds were placed as a permanent volume implant. Prescription dose was 80 Gy at 5-mm depth from the resection cavity surface. A postimplant CT scan was performed within 48 hours to determine dose distribution. Follow-up exams included MRI every 2 months. The primary endpoint was resection cavity freedom from progression (FFP). Secondary endpoints included distant metastases FFP, median overall survival (OS), and toxicity.

RESULTS: For the 13 patients with recurrent GBM, median follow-up was 4.4 months (0.4–13.2 months). Median age was 49 years (41–63 years). Median volume of resected tumor was 44.5 cc (16–81 cc). Median number of seeds employed was 42 (44–74), with median activity per seed of 3.8 mCi (range, 2.5–4.3 mCi) and total activity of 171.2 mCi (range, 64.5–280.5 mCi). There were eight cases of local failure, which yielded a median resection cavity FFP of 3.6 months (95% confidence interval [CI] = 2.1–8.6 months), 3-month resection cavity FFP of 66.6% (95% CI = 33.2%–86.1%), and 6-month resection cavity FFP of 33.3% (95% CI = 8.3%–61.5%). There were eight cases of death, which yielded a median OS of 4.9 months (95% CI: 2.8 months, upper limit not estimated), 3-month OS of 81.8% (95% CI = 44.7%–95.1%), and a 6-month OS of 36.4% (95% CI = 11.2%–62.7%). There were seven cases of distant recurrence, which yielded a median distant FFP of 3.7 months (95% CI = 2.1 months, upper limit not estimated), 3-month distant FFP of 76.2% (95% CI = 42.7%–91.7%), and 6-month distant FFP of 39.2% (95% CI = 10.1%–68.1%). Patients tolerated the Cs-131 implant very well, with the following complications: seizure (3), infection (1), and radiation necrosis (0).

For the four patients with recurrent AM, median follow-up was 18.5 months (range, 7.8–22.4 mos), and there have been no cases of local recurrence, distant recurrence, or death. Median age was 65 years (range, 43–66 yrs). Median number of seeds employed was 23 (13–40), with median activity per seed of 2.43 U (2.41–2.45 U). There were two cases of infection and one case of seizure.

CONCLUSIONS: Application of Cs-131 in a resection cavity was safe, well tolerated, and convenient for patients, resulting in a short radiation treatment course and minimal toxicity throughout and following RT. These outcomes for patients with recurrent GBM compare well to the historical data; more results are needed for recurrent AM.

(S007) Brain Metastases in Patients Diagnosed With a Solid Primary Cancer During Childhood: Experience From a Single Referral Cancer Center

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INTRODUCTION: Whereas brain metastases (BM)s occur frequently in adult cancer patients, they are a rare occurrence among children with cancer. More effective treatment to the primary site and prolonged survival may have resulted in an increased frequency of BMs in the pediatric population. We present a large series of BMs in patients diagnosed with a solid primary cancer during childhood and describe tumor type, patterns of occurrence, and prognosis.
RESULTS: Forty-four patients with BMs from a solid primary were identified (43% males; median ages at diagnosis of primary cancer and BMs of 11 and 13 years, respectively). The most frequent primary cancer was sarcoma [24 (54%); osteosarcoma (10); rhabdomyosarcoma (4); Ewing sarcoma (3); unclassified sarcoma (4); clear cell sarcoma of kidney (3)] and melanoma [5 (11%)]. The BMs were symptomatic in 68% of patients; headache, nausea/vomiting, and seizures were the most common symptoms. Thirty-two percent of the BMs were diagnosed at the brain; those receiving treatment survived a median of 0.6 months from diagnosis of metastasis to death. Patients not receiving treatment survived a median Kaplan-Meier estimate of survival from BM diagnosis was 8 months (95% confidence interval [CI]: 5–10 months). The BMs were the first site of metastasis in 12% of patients (19% of sarcoma and 5% of nonsarcoma histologies; \( P \approx 0.34 \)). Sixty-eight percent of patients had a single metastasis and 32% had multiple metastases at the time of diagnosis; 86% had supratentorial lesions. Two had leptomeningeal disease (LMD; retinoblastoma and unclassified sarcoma). Six patients with different primaries subsequently developed LMD. The great majority (91%) received treatment for the BMs; 38% received combination therapy as initial BM treatment; 51% underwent a surgical resection (19% with radiation and/or chemo and 31% without); 14% received radiation alone; and 7% received chemotherapy alone. Twenty-three percent were alive after a median follow-up of 24 months from diagnosis of BMs. The median Kaplan-Meier estimate of survival from BM diagnosis was 8 months (95% confidence interval [CI]: 5–10 months). Patients not receiving treatment survived a median of 0.6 months from diagnosis of metastasis to the brain; those receiving treatment survived a median of 7 months from initiation of therapy, with no difference between different treatment methodologies.

CONCLUSIONS: To our knowledge, this is the largest single-center series of pediatric patients developing BMs in the course of their disease. Almost one-fifth of the patients were diagnosed with BMs at presentation, and half had a sarcoma primary. LMD was a frequent occurrence. Prognosis following BM diagnosis was generally poor, regardless of the treatment method used. A closer look at subsets of patients who may benefit from early screening and treatment will be attempted.

(S008) A Prospective Study Using Implanted Fiducial Markers to Assess Treatment Accuracy in Spinal Stereotactic Body Radiation Therapy

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PURPOSE: Spinal SBRT is a noninvasive treatment for spinal metastases that involves conformal administration of hypofractionated radiation with submillimeter precision. Accuracy in patient positioning is the cornerstone of providing safe and high-quality treatment—our practice utilizes the ExacTrac (Brain Lab) positioning system to simplify this resource-intensive process, bolstered by an independent 3D-3D verification using CT on rails. In our experience, this system accounts well for translational setup error; however, its accuracy with respect to rotational error is not well described.

To this end, we are conducting a prospective study to assess the utility of implanted fiducial markers (NCT-01624220). We aim to characterize the residual translational and rotational error from use of an image fusion approach and further seek to determine whether the use of implanted markers can improve the accuracy of treatment delivery. Here, we report initial results from our ongoing study.

METHODS: Patients undergoing spinal SBRT to T4–L5 are eligible for an IRB-approved protocol with planned accrual of 20. Patients with hardware at the level to be treated (or +/- 1 level) are excluded, as well as patients with comorbidities precluding seed placement. One day prior to simulation, patients undergo placement of 5-mm gold seeds (Best Medical) as an outpatient procedure. Four seeds are placed—two into the pedicles of the vertebral body (VB) above the level to be treated and two into the pedicles of the VB below. At the time of treatment, oblique kV films are obtained using floor-mounted imagers, and ExacTrac software calculates deviation from the treatment isocenter using algorithmic error detection based on image fusion. This calculation is repeated using geometric error detection based on the fiducial position, and independent 3D-3D
RESULTS: To verify the stability of implanted fiducial markers, we obtained three-dimensional position coordinates for each marker from CT data acquired at simulation and treatment. Seed stability is excellent, with measured position change within the margin of detection uncertainty. The average absolute deviation in position (n = 8) between simulation (1 day after implantation) and treatment (average 13.5 days after implantation) was 0.53 mm. No systematic or persistent deviations indicative of seed migration were detected, with an average one-dimensional shift of −0.03 mm. For a patient (n = 4 seeds) receiving three-fraction treatment, the seeds remained stable through the end of treatment (average position change of 0.42 mm after 17 days). Next, we sought to characterize the residual setup error. Our initial experience shows that error detection with bony fusion agrees well with the fiducial-based calculation, with an average residual translation error of −0.12 mm and rotational error of 0.01 degrees (n = 4 treatments).

CONCLUSIONS: We have demonstrated the feasibility of incorporating implanted gold fiducial markers into a spinal SBRT treatment platform built around the ExacTrac patient positioning system. Our results highlight the stability of the implanted seeds, and our initial experience suggests that the algorithmic error detection with ExacTrac correlates well with fiducial-based error detection.

(S009) Outcomes in Spinal Stereotactic Body Radiotherapy: An Update of the MD Anderson Cancer Center Experience

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INTRODUCTION: Stereotactic body radiotherapy is an option for appropriately selected patients with spinal metastases. Here, we update our outcomes data from prospective series of patients treated for spinal metastases with stereotactic body radiotherapy.

METHODS: In all, 218 patients with 242 individual spinal tumors were irradiated with stereotactic radiotherapy between 2002 and 2012 in prospective trials at The University of Texas MD Anderson Cancer Center. Data from stereotactic body radiotherapy delivered as a primary or reirradiation therapy were included. Magnetic resonance imaging of the spine was performed before treatment and at regular follow-up intervals. Stereotactic body radiotherapy was delivered to 16 Gy, 18 Gy, or 24 Gy in one fraction or to 27 Gy in three fractions. Near-simultaneous CT-guided stereotactic intensity-modulated radiotherapy was used for treatment.

RESULTS: The actuarial 1-year, 3-year, and 5-year overall survival rates were 73.3%, 34.8%, and 18.5%, respectively. The median overall survival for all cases was 24.3 months. Actuarial local control at 1, 3, and 5 years was 80.5%, 66.2%, and 56.9%. The median duration of tumor control was 80.6 months. For the 59 tumors that progressed, the median time to tumor progression was 6.6 months (mean, 25.8 months).

CONCLUSIONS: Stereotactic body radiotherapy for spinal metastases provides effective local control. To further optimize local control, further studies are needed to assess targeting, dose, fractionation, and patterns of failure.
**Variation in Dose to Organ at Risk, Due to Daily Rectal Filling During Prostate Intensity-Modulated Radiotherapy: A Cone-Beam CT Study**

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**PURPOSE:** Rectal interfraction motion during prostate radiotherapy has been demonstrated previously, but the dosimetric implications of this phenomenon are not well delineated. The current study aims to: (1) characterize the values of and evaluate daily trends in the rectal volume, rectal anterior-posterior translation, and volume of the rectum receiving 45 Gy, 65 Gy, and 70 Gy (V40/V65/V70) and (2) assess for correlation between the interfraction motion parameters and the dosimetric data.

**MATERIALS AND METHODS:** Sixteen patients undergoing intensity-modulated radiotherapy of the prostate were retrospectively reviewed. Enemas were used prior to simulation. No bowel preparation was performed prior to daily treatment. The outer walls of the rectum were contoured on all on-treatment CBCT series for each patient. Daily rectal volume changes; displacement of the anterior rectal wall at all on-treatment CBCT series for each patient. Daily rectal treatment. The outer walls of the rectum were contoured on each dose level in the absence of any rectal preparation or instructions. No statistically significant correlation between the fraction number and the rectal V40/V65/V70 values, respectively, was noted for any patient (all Pearson coefficients < 0.75). Correlations were found between rectal V40, V65, and V70 and rectal superior/isocenter/inferior translational motion (31.3%/37.5%/0% of cases, respectively), as well as volume change (87.5% of cases).

**RESULTS:** At the superior, isocenter, and inferior rectal level, five, two, and three patients, respectively, had anterior-posterior translations of greater than 0.6 cm. No statistically significant correlation between the translational motion of the rectum and the fraction number was noted for any patient at any rectal level (all Pearson coefficients < 0.75). All but one patient had mean volume changes of greater than 30 cc. No statistically significant correlation between the rectal volume changes and the fraction number and the rectal V40, V65, and V70 and volume of the rectum receiving 45 Gy, 65 Gy, and 70 Gy (V40/V65/V70) and (2) assess for correlation between the interfraction motion parameters and the dosimetric data.

**CONCLUSIONS:** The lack of correlation between the rectal DVH values and the treatment fraction number underscores the random nature of the variation in the rectal DVH. Thus, it is not practical to create a population-based algorithm, applicable to all patients, to ensure reproducible daily rectal DVH parameters. However, rectal DVH values remained under the tolerance limits during the majority of fractions delivered, despite volume and translational changes. Thus, multiadaptive planning to accommodate independent prostate and rectal motion is not needed to improve daily rectal DVH compliance. Only select patients may attain improved rectal DVHs from techniques aimed at maintaining a constant rectal volume. Our results do not obviate the need for daily image-guided RT for prostate motion correction.

**18F-FDG PET Definition of Gross Tumor Volume in Pediatric Hodgkin Lymphoma: What Is the Effect of Various SUV Thresholds on Target Volume Delineation?**

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**PURPOSE/OBJECTIVES:** Accurate target volume delineation in Hodgkin lymphoma (HL) is becoming more important as radiotherapy moves toward more conformal techniques. FDG-PET imaging is used in staging and management of HL and may also be used as a planning tool for radiotherapy. A limitation of FDG-PET in radiation planning for HL is significant variability in interpretation of tumor volume and edge detection, and the best method to incorporate functional PET data into RT planning is still a matter of debate. One approach to reduce variability is to apply automatic or semiautomatic segmentation methods, such as thresholding based on maximum SUV. Accepted SUV max cutoffs range between 15% and 40%. Here, we apply various SUV max thresholds in treatment planning and examine their effects on clinical target volumes in involved-field radiation therapy (IFRT) and involved-node radiation therapy (INRT).
MATERIALS AND METHODS: Twelve pediatric and young adult patients with HL who were treated with IFRT at The Johns Hopkins Hospital from 2006 to 2012 were included in this retrospective analysis. Each patient received a PET-CT prior to chemotherapy that was used for radiation planning purposes. PET-CT datasets were reviewed, and clinical target volumes were generated using the standard qualitative visual method (QVM, so-called CTQVM). The following SUV max thresholds were applied to the prechemotherapy PET: 15%, 20%, 25%, 30%, 35%, and 40%. Clinical target volumes for IFRT and INRT plans (CTVPET) were generated manually based on SUV max threshold volumes for seven patients selected at random. The CTQVM and CTVPET ratios were then compared in order to determine the optimal threshold.

RESULTS: The mean SUV max was 15.0 ± 6.9. On average there was an eightfold increase in PET volume between 40% and 15% max SUV. When applying the seven thresholds in the design of target volumes for IFRT, only 1 out of 12 patients had a change in treatment volume. The mean INRT CTV volume was 1403 (± 945) mL with 15% max SUV, 1,184 (± 840) mL with 25% max SUV, and 701 (± 571) mL with 40% max SUV. The optimal threshold, defined as the CTQVM and CTVPET ratio closest to 1, ranged from 15% to 35% max SUV.

CONCLUSION: In IFRT planning, maximum SUV thresholding had very little effect on final target volumes. In INRT planning, there was a significant amount of variability both within and between patients when max SUV thresholds were used in generating CTVs. Accurate target volume delineation with FDG-PET in HL is challenging and may require more precise and reproducible segmentation methods as we move toward more conformal therapies.

(S012) PET as a Predictor of Outcomes for Cervical and Vaginal Cancer With HDR Interstitial Brachytherapy Utilizing MRI-Based Planning

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PURPOSE: Single-institution data utilizing MRI-based planning for intracavitary brachytherapy for the treatment of cancer of the cervix have demonstrated improved pelvic disease-free survival over historical controls utilizing CT. The purpose of this study is to evaluate our experience with transvaginal and transultrasound-guided interstitial implants of the pelvis with MRI-based planning.

METHODS: A retrospective review was conducted of all vaginal and cervical cancers treated at Moffitt Cancer Center from 2009 to 2011 where 1.5 T, contrast-enhanced, MRI-based high-dose rate (HDR) interstitial brachytherapy was part of the treatment plan. Thirty-five patients were identified, and local recurrence, disease-free survival, metastasis-free survival, and overall survival were analyzed in the whole group and based on prognostic features, PET/CT, and treatment plans.

RESULTS: Mean follow-up was 17 months (range, 2–43). A total of 28 patients had cervical cancer and 7 had vaginal cancer. Four patients had recurrent disease. Total numbers of patients with stage I, II, III, IVA, and IVB were 3, 4, 20, 3, and 1, respectively. A total of 32 patients had squamous cell carcinoma and 3 had adenocarcinoma. Eighty percent received chemotherapy, and 97% received external beam radiation therapy with a median dose (range) of 4,500 cGy (4,320–5,040). Median (range) brachytherapy total dose and dose per fraction were 2,500 cGy (2,000–4,300) and 500 cGy (350–600), respectively. The local recurrence rate was 17%, with a median time to local recurrence of 7 months. In patients with high-risk clinical target volume (HRCTV) D90 greater than 95%, local recurrence was 15% versus 33% if less than or equal to 95%. Disease-free survival was 66%, with a median time-to-event of 11 months. Metastasis-free survival was 85% in patients without metastases on presentation, with a median time to metastasis of 6 months. Overall survival was 71%, with a median time to death of 16 months. Eighty percent of local recurrences and 66% of distant metastases occurred in patients with a primary tumor SUV > 10 on their pretreatment PET scan. Fifty percent of distant metastases occurred in patients with a nodal SUV > 4 on pretreatment PET scan. In patients with posttreatment PET scan (55%, mean time to PET 4.2 months), 40% of patients with an SUV > 4 suffered a local recurrence. Thirty-month estimates for local control, disease-free survival, metastasis-free survival, and overall survival using Kaplan-Meier curves are 80%, 37.5%, 64.7%, and 43%, respectively.

CONCLUSIONS: MRI-based interstitial brachytherapy for locally advanced cancers of the cervix and vagina results in a high rate of local control. Additionally, an HRCTV D90 > 95% correlates well with local control. A pretreatment PET-CT SUV > 10 of the primary appears to correlate well with local recurrence and distant metastases. MRI-based planning appears to provide initial excellent local control and distant metastasis-free survival.
**PURPOSE/OBJECTIVES:** Interfraction image guidance in the management of prostate cancer reduces uncertainty and has become the standard of care. More recently, real-time fiducial/transponder tracking to further reduce uncertainty from intrafraction target motion has become available. Currently available techniques for prostate tracking require the placement of markers. A new transperineal ultrasound (TPUS) system using rigid structure registration (4DTPUS) is a noninvasive technique for accounting for interfraction motions and monitoring intrafraction motion. This technique has potential advantages over historic ultrasound-based interfraction adjustments. It is less affected by user variability, abdominal pressure, approach, anatomy, bowel gas, and bladder filling. As these techniques were transabdominal, they were not amenable to real-time tracking. The transperineal approach significantly reduces these issues. Our objective is to validate the TPUS accuracy of tracking using a motion phantom, visual confirmation of prostate tracking in patients and a direct comparison to prostate motion. TPUS is a noninvasive technique for accounting for interfraction variability, abdominal pressure, approach, anatomy, bowel gas, and bladder filling. As these techniques were transabdominal, they were not amenable to real-time tracking. The transperineal approach significantly reduces these issues. Our objective is to validate the TPUS accuracy of tracking using a motion phantom, visual confirmation of prostate tracking in patients and a direct comparison to prostate motion detected by other approved intrafraction tracking methods.

**MATERIALS AND METHODS:** A programmable 3D motion phantom consisted of a tank filled with a water/Zerdine mixture and motorized control of a target along three translational axes in the liquid. Since the submerged target could only be tracked by the 4DTPUS system, Calypso beacons as well as optical markers were affixed to a rigid surrogate that moved in with the submerged target within approximately 1 mm. Seven motion profiles were programmed and transferred to the phantom. Data were synchronized prior to each fraction. Data from all four sources (Calypso transponders, optical imaging, 4D-US, and the programmed motion) were compared in three directions (antero/posterior, superior/inferior, left/right). In addition, visual tracking of the prostate for four patients was reviewed by three attending physicians as part of an IRB-approved clinical trial. It was rated on a score of 1 to 5 with 1 being the best.

**RESULTS:** Phantom motion, tracked via the optical and the Calypso systems, showed the 95% bound of the maximum distance variation to be less than 0.6 mm. There was no consistent directional error. For the Clarity system, 95% of the maximum distance variation was within 1.3 mm of the Calypso system, the majority being less than 1 mm. No directional preference was identified. The average visual correlation was scored as 1.21. 4DTPUS reviewed for 364 minutes of patient treatment over 62 fractions. Evaluation was somewhat limited in some fractions due to an artifact created by the Calypso magnetic field.

**CONCLUSION:** Phantom and early clinical studies show that a novel 4D transperineal ultrasound system accurately and reproducibly tracked prostate motion. Visual confirmation of prostate tracking was excellent. Transperineal ultrasound tracking of the prostate offers a noninvasive alternative to currently available marker-based systems.

**PURPOSE:** To evaluate how prostate multiparametric (MP-)MRI imaging features might impact National Comprehensive Cancer Network (NCCN) risk stratification relative to standard risk factors by incorporating MRI T stage and attenuation diffusion coefficient (ADC) values of suspect lesions.

**METHODS:** In this IRB-approved retrospective study, prostate cancer patients with MP-MRI imaging performed prior to treatment were reviewed. All MRI studies included T2, diffusion-weighted imaging (DWI), and dynamic contrast-enhanced (DCE) sequences. Patient charts were reviewed for clinical T stage, PSA at diagnosis, biopsy Gleason Score (bGS), and MRI reports that included average ADC values for suspect lesions. MRI T stage was assigned based on the AJCC staging system (7th edition). Differences between the ADC means were analyzed by ANOVA, and correlation was assessed by Hoeffding’s D test.

**RESULTS:** One hundred four patients were included in this study. Prior to MRI staging, patient distribution by NCCN risk groups consisted of 37% low risk, 42% intermediate risk, and 21% high risk. MRI T stage and clinical T stage were discrepant in 51% of cases. A total of 14 of 38 (37%) low-risk and 3 of 44 (7%) intermediate-risk patients would be escalated to the intermediate- and high-risk groups, respectively, based on their MRI T stage. ADC correlated with bGS (D = .0403, P < .001), and the mean ADC±SE for each bGS group was significantly different (3 + 3: 1022 ± 36, 3 + 4: 971 ± 39, 4 + 4: 898 ± 43, P < .001).

**REFERENCES:**

2. (S014) Improving Prostate Cancer Risk Stratification Through Multiparametric MRI Prostate Imaging
4 + 3: 905 ± 66, ≥ 4 + 4: 786.2 ± 47, \( P = .001 \)). Using an ADC cutoff of ≤ 1100, there was a 100% sensitivity and negative predictive value for having bGS ≥ 4 + 4 disease. MRI T stage also correlated better than clinical T stage with bGS (\( D = .018, P < .01 \) vs \( D = –.005, P = .98 \)) and ADC value (\( D = .019, P < .01 \) vs \( D = –.006, P = .99 \)). Additionally, NCCN risk, determined by MRI T stage, correlated better than NCCN risk defined by clinical T stage with ADC values (\( D = .052, P < .0001 \) vs \( D = .035, P = .0008 \)).

**CONCLUSIONS:** MP-MRI provides novel staging information that may improve prostate cancer risk stratification, particularly in clinically defined low-risk patients. Analysis of a larger sample size to determine the degree to which MRI is an independent predictor of overall risk is planned.

**S015) Extent of Perilesional Edema Differentiates Radionecrosis From Tumor Recurrence Following Stereotactic Radiosurgery for Brain Metastasis**

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**INTRODUCTION:** Differentiation of tumor recurrence from radionecrosis is a critical step in the follow-up management of patients treated with stereotactic radiosurgery (SRS) for brain metastases. A method that can reliably differentiate tumor recurrence from radiation necrosis using standard magnetic resonance imaging (MRI) sequences would be of significant value.

**METHODS:** We analyzed the records of 49 patients with 52 brain metastases treated with SRS between May 2005 and August 2011 who subsequently underwent surgical resection of the same lesion. Forty-seven of the lesions had preoperative MRI available for review (90%), including T1 postcontrast, T2, and FLAIR, as well as thin-slice contrast-enhanced spoiled gradient recalled acquisition in steady state (SPGR) sequences. Pre-SRS and preoperative lesion and edema volumes were manually contoured and measured in a blinded fashion using radiation treatment planning software. Samples were then analyzed by a neuropathologist for the presence of tumor and radiation necrosis.

**RESULTS:** A total of 27 of 52 (52%) of the resected lesions had tumor recurrence alone, 14 (27%) were found to contain radionecrosis alone, and 11 (21%) contained both tumor and radionecrosis. Longer time between SRS and resection (\( P < .001 \)) and a larger edema:lesion volume ratio (high T2/T1c, \( P = .002 \)) were found to be predictive of radionecrosis as opposed to tumor recurrence. Using a cutoff value of 10 for the edema:lesion volume ratio, we were able to predict the presence of tumor with a positive predictive value of 92%, which increased to 100% when looking only at patients who underwent resection < 18 months following SRS.

**CONCLUSION:** On follow-up imaging, lesions with a high edema:lesion volume ratio and lesions that progress after a longer period of time after SRS are more likely to contain radionecrosis. These indices may help guide clinical decision-making in the context of evolving lesions after SRS for brain metastases and thereby avoid unnecessary interventions.

**S016) Optimizing Reconstructive Outcomes in the Radiated Head and Neck Cancer Patient: A Novel Optimizing Application of Indocyanine Green Angiography**

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**BACKGROUND:** Radiation therapy is a mainstay of treatment for head and neck squamous cell carcinoma (HNSCC), whether as a solo modality or used in combination with surgery or chemotherapy. The doses necessary for treatment in HNSCC, frequently up to or exceeding 70 Gy, can present significant challenges to patients and surgeons when salvage, postradiation therapy, resection, and subsequent reconstruction are required. Indocyanine green (ICG) is a fluorescent dye with peak absorbance at 800 nm, FDA-approved for cardiac and plastic/reconstructive surgery to evaluate bloodflow. Extrapolating this indication, ICG can be particularly helpful to assess the vascularity in irradiated tissues. The technology allows intraoperative identification of poorly vascularized tissue, which can be immediately debrided or addressed in the reconstruction, thereby avoiding delayed flap or donor site complications stemming from poor perfusion.

**MATERIALS AND METHODS:** We describe our early experience with five patients who had been treated with definitive radiation therapy to 70 Gy for HNSCC, with or without chemotherapy, but subsequently required salvage resection and reconstruction for either recurrent disease or osteoradionecrosis. Intraoperative ICG was employed to ensure the reconstructive flaps were adequately perfused and also that the irradiated recipient tissues had sufficient vascular supply. This technique identified areas of decreased vascular flow in both bone and soft tissue, as well as confirming flow to clinically questionable recipient beds. ICG angiography
was applied to skin flaps surrounding the surgical defect in the operative field, the pharynx, and esophagus after laryngectomy, as well as to tissues immediately adjacent to areas with clinically obvious radionecrosis.

CONCLUSIONS: ICG may be particularly suited to salvage surgery in the radiated patient, since vascularization of native tissues is often in question as a sequel of prior radiation treatment. It can potentially maximize debridement of devitalized tissue and avoid overaggressive resection of vital tissue while maintaining sound oncologic principles, thus potentially optimizing the patient’s chance of efficient healing and successful reconstructive outcomes.

(S017) Initial Clinical Outcomes of Dose-Escalated Proton Therapy for Head and Neck Adenoid Cystic Carcinoma

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PURPOSE: To report outcomes of high-dose proton therapy in head and neck adenoid cystic carcinoma.

METHODS: Retrospective analysis of 27 consecutive patients treated at the Indiana University Health Proton Therapy Center between 2004 and 2012 was performed. A total of 19 (70%) were treated for their initial disease course, and 8 (30%) were treated for recurrent disease, 7 of whom had prior head and neck radiation. A total of 22 patients (82%) were treated after surgery, and 19 had positive margins. The remaining 5 patients (18%) were treated after biopsy alone. The tumor stage was T1 in 2, T3 in 4, and T4 in 21 patients. Base of skull involvement was present in 21 patients (78%). Nodal stage was N0 in 26 patients and N2 in 1 patient. Half of the patients were treated by the senior author. One patient was treated with palliative intent. For the remaining patients, the dose administered was 75.6 Gy (RBE [relative biological effectiveness]) for gross disease and 66–70.2 Gy (RBE) for negative margins. For those with positive margins, the dose was 70.2–72 Gy (RBE), attenuated to 66.6 Gy (RBE) in one patient due to proximity to the optic nerve in a patient with a single sighted eye and to 68.4 Gy (RBE) in one patient due to physician preference. Ipsilateral cervical lymphatics were irradiated in the one node-positive patient, and limited regional nodal irradiation was delivered electively in seven other patients.

RESULTS: Median follow-up on all patients was 22 months (range 6–50 months) — 25 months in patients who are alive. The 2-year Kaplan-Meier estimate of overall survival (OS) was 75%, local control 93%, locoregional control 80%, and development of distant metastasis 14%. On univariate analysis, there was a statistically significant decrease in OS for patients with recurrent disease, with a 2-year OS of 92% in those treated for their initial disease course and 47% for those with recurrent disease (P = .03). Two-year local control for initial treatment was 100% and 88% for recurrent disease (P = .123). Late toxicity of grade 0 or 1 was seen in 19 patients, grade 2 in 4 patients, grade 3 in 3 patients, and grade 4 in 1 patient. The grade 3 toxicities observed were mandibular osteoradionecrosis in one patient, cerebrospinal fluid leak in one patient, and otologic toxicity in one patient requiring tympanic membrane reconstruction. Two of the three patients with grade 3 toxicity had received prior radiation therapy to the same site. The grade 4 toxicity was anticipated unilateral vision loss in a patient irradiated for an orbital tumor involving the optic nerve. Pattern of failure analysis revealed one in-field local recurrence. A second local recurrence occurred out of field in a patient who was irradiated to only a portion of the tumor bed. In three of the five locoregional recurrences, inadequacies in radiation treatment volume likely contributed to regional perineural disease recurrence.

CONCLUSIONS: In this cohort of patients with advanced disease, initial clinical outcomes of dose-escalated proton therapy are encouraging. Careful treatment planning is essential to optimize outcomes.

(S018) Laryngoesophageal Dysfunction–Free Survival Following Definitive Radiotherapy for Laryngeal and Hypopharyngeal Cancer at UC Davis

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BACKGROUND: A 2011 international consensus panel has established laryngoesophageal dysfunction–free survival (LEDFS) as a new endpoint for use in the study of organ-conserving treatment of locally advanced laryngeal and hypopharyngeal cancers. LEDFS assesses an individual’s ability to initiate an effective swallow and survive tracheostomy- and gastric tube–free following treatment. The authors of this report examined factors associated with LEDFS in patients who had received radiation therapy for the treatment of their disease.
METHODS: A retrospective review of 39 patients who have received definitive radiation therapy for the treatment of stage III/IV laryngeal and hypopharyngeal cancer was undertaken. None of the patients had evidence of distant metastasis at diagnosis. A total of 31 patients (80%) were treated by intensity-modulated radiotherapy (IMRT); 7 patients (20%) were treated by 3-D conformal radiotherapy (3D CRT) techniques using initial lateral opposed fields. A total of 29 patients (74%) received concurrent cisplatin-based chemotherapy. The patients’ survival and tracheotomy and gastric tube statuses at 1, 2, and 3 years posttreatment were examined to determine the rate of LEDFS. Clinical and disease-related factors that may have had an influence on patients’ likelihood of achieving LEDFS at 3 years posttreatment were evaluated.

RESULTS: For the entire cohort, the LEDFS rate was 26.7% at 3 years. At 3 years, the LEDFS rate was 29.2% for patients treated with IMRT and 16.7% for patients treated with 3D CRT. LEDFS was 24.1% and 14.3% for patients treated without and with concurrent chemotherapy, respectively ($P < .05$). When stratified by initial Karnofsky Performance Status (KPS), the 3-year rates of LEDFS were 0%, 27%, and 33%, respectively, for patients with scores of 70, 80, and 90 ($P < .05$). Patients who continued to smoke during radiation therapy had inferior LEDFS (22% vs 30%; $P < .05$).

CONCLUSIONS: Efforts to improve LEDFS among patients treated by definitive radiation therapy for locally advanced laryngeal and hypopharyngeal cancer are needed. Treatment with non-IMRT techniques, the use of concurrent chemotherapy, and continued smoking were associated with decreased LEDFS, as was lower KPS at diagnosis.

(S019) Dysphagia Following Radiation for Oropharyngeal Squamous Cell Cancer Is Predicted by Dose to the Floor-of-Mouth Muscles

Rachit Kumar, MD, Sara Madanikia, BS, Heather Starmer, MS, Wuyang Yang, MD, Sara Alcorn, MD, MPH, Emi Murano, MD, PhD, Yi Le, PhD, Harry Quon, MD, MS; The Johns Hopkins University

PURPOSE: Dysphagia is a well-recognized complication following definitive chemoradiation for oropharyngeal squamous cell carcinomas (OPSCCs). While radiation dose to the larynx and pharyngeal constrictors has been the focus of swallowing complications, our previous work has demonstrated the importance of floor-of-mouth (FoM) muscles in predicting dysphasia following definitive chemoradiation. The FoM muscles are critical for hyoid and laryngeal elevation and effective bolus diversion, thus preventing penetration and aspiration (PAS). We hypothesized that radiation dose to the suprahyoid muscles (geniohyoid [GH], genioglossus [GG], hyoglossus [HG], mylohyoid [MH], and anterior digastrics [AD]) are as important as, or more important than, radiation dose to the larynx or constrictor muscles in the development of dysphagia.

METHODS: We retrospectively studied 50 patients with OPSCC treated with CRT who prospectively underwent baseline and posttreatment videofluoroscopic swallowing studies (VFSS) from 2007 to 2010. Amongst these patients, those with identified laryngeal penetration or aspiration (PAS) served as the study population, and patients without any identified VFSS complications served as the control cohort. Individual suprahyoid muscles were identified on the planning CT, based on anatomic landmarks provided by an expert otolaryngologist (EM). This process was validated with two independent investigators. The GH, MH, AD, and HG muscle groups were collectively referred to as the FoM muscles. After contouring these structures, the treatment plan for each patient was recalculated to obtain specific doses and dose volumes to these muscle groups. Univariate logistic regression analysis was used to determine parameters of significance between patients with and without PAS. A multivariate regression analysis using factors identified in the univariate analysis was subsequently performed to isolate the most statistically critical structures associated with PAS.

**Table S019: 1** Univariate Analysis

<table>
<thead>
<tr>
<th>Muscle/Group</th>
<th>Parameter</th>
<th>(+) PAS Dose</th>
<th>(-) PAS Dose</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Floor of mouth</td>
<td>Minimum Dose</td>
<td>40.5</td>
<td>34.1</td>
<td>.028</td>
</tr>
<tr>
<td></td>
<td>Mean Dose</td>
<td>61.8</td>
<td>58.8</td>
<td>.080</td>
</tr>
<tr>
<td></td>
<td>V65 Dose</td>
<td>43.1</td>
<td>29.7</td>
<td>.074</td>
</tr>
<tr>
<td>Geniohyoid</td>
<td>Minimum Dose</td>
<td>48.0</td>
<td>40.2</td>
<td>.014</td>
</tr>
<tr>
<td></td>
<td>Mean Dose</td>
<td>61.8</td>
<td>58.1</td>
<td>.072</td>
</tr>
<tr>
<td></td>
<td>V45 &gt; 95% Dose</td>
<td>73.9</td>
<td>44.8</td>
<td>.027</td>
</tr>
<tr>
<td>Genioglossus</td>
<td>Minimum Dose</td>
<td>43.8</td>
<td>35.5</td>
<td>.010</td>
</tr>
<tr>
<td></td>
<td>Mean Dose</td>
<td>63.6</td>
<td>59.4</td>
<td>.044</td>
</tr>
<tr>
<td>Larynx</td>
<td>V60 Dose</td>
<td>36.3</td>
<td>22.7</td>
<td>.065</td>
</tr>
<tr>
<td>MCM</td>
<td>V50 Dose</td>
<td>97.5</td>
<td>89.5</td>
<td>.052</td>
</tr>
<tr>
<td>ICM</td>
<td>V60 Dose</td>
<td>27.4</td>
<td>14.1</td>
<td>.080</td>
</tr>
</tbody>
</table>

RESULTS: Univariate analysis resulted in significance or borderline significance of multiple structures in causing
PAS following radiation therapy (Table 1). However, when a multivariate model was applied, only the mean dose to the FoM and minimum dose to the GH were associated with postradiation PAS (Table 2).

**DISCUSSION:** The data suggest that the dose and volume delivered to the collective FoM muscles may be associated with an increased risk of VFSS-identified laryngeal penetration and aspiration to a greater degree than previously recognized organs at risk, including the larynx and constrictor muscles. MRI-based contouring will help improve the reproducibility of contours. Prospective validation is underway at our institution.

### Table S019: 2 Multivariate Analysis—Statistically Significant Factors

<table>
<thead>
<tr>
<th>Muscle/Group</th>
<th>Parameter</th>
<th>(+) PAS Dose</th>
<th>(–) PAS Dose</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Geniohyoid Minimum</td>
<td>Minimum</td>
<td>48.0</td>
<td>40.2</td>
<td>.008</td>
</tr>
<tr>
<td>Floor of mouth</td>
<td>Mean</td>
<td>61.8</td>
<td>58.8</td>
<td>.011</td>
</tr>
</tbody>
</table>

(S020) Results of Fractionated Proton Reirradiation for Recurrent Chordoma of the Base of Skull or Spine

Okechukwu R. Linton, MD, Mark W. McDonald, MD; Department of Radiation Oncology, Indiana University School of Medicine, Indiana University Health Proton Therapy Center

**PURPOSE:** Patients with recurrent chordoma after prior radiation therapy historically have a poor prognosis. The value of reirradiation is uncertain. We report clinical outcomes for patients who were reirradiated with fractionated proton therapy for skull base or spine chordomas.

**MATERIALS AND METHODS:** We performed a retrospective analysis of 15 consecutive patients (9 male, 6 female) treated at the Indiana University Health Proton Therapy Center between 2005 and 2012. The median age at the time of reirradiation was 59 years (range: 26–78 years). The median time between prior radiation and proton reirradiation was 39 months (range: 12–129 months). Prior therapy consisted of fractionated x-ray therapy in six patients, fractionated proton therapy in five patients, gamma knife radiosurgery in three patients, and stereotactic body radiosurgery in one patient. Ten patients had one prior radiation treatment course, four patients had two prior radiation treatment courses, and one patient had four prior radiation treatment courses. Ten patients underwent surgical debulking prior to proton reirradiation. Fourteen patients (93%) had gross residual disease at the time of proton reirradiation. The site of proton reirradiation was the clivus in seven patients, cervical spine in two patients, thoracic spine in one patient, lumbar spine in two patients, and sacrum in three patients. The median dose of proton reirradiation was 75.6 Gy (RBE [relative biological effectiveness]) with a range of 71.2–79.2 Gy (RBE). Hyperfractionation was used in two patients. Six of 15 patients were treated by the senior author.

**RESULTS:** The median follow-up time after reirradiation was 19 months (range: 6–56 months). The Kaplan-Meier 2-year estimate of overall survival is 87%, local control 93%, and development of distant metastasis 21%. One patient developed an in-field recurrence in a volume that received 71.2 Gy (RBE). One patient developed a recurrence in the surgical tract in the elective treatment volume that received 54 Gy (RBE). Two patients developed distant metastasis in the lung, and one patient developed diffuse leptomeningeal tumor spread. The 2-year estimate of overall survival after proton reirradiation is 100% for women and 78% for men ($P = .06$). Late grade 3 toxicities from proton reirradiation developed in two patients. In one patient, reirradiation may have contributed to vascular stenosis, and the patient developed an out-of-field brainstem stroke, although he made a substantial recovery. In one patient, high cumulative dose to the cervical spinal cord was the likely etiology of spinal cord edema adjacent to the treatment field, which improved with steroids. All five patient deaths that have occurred to date are attributed to disease.

**CONCLUSIONS:** In this population of heavily pretreated patients, salvage reirradiation with proton therapy resulted in good initial local control with tolerable toxicities.

(S021) Disease Control and Toxicity Outcomes Using Ruthenium Eye Plaque Brachytherapy in the Treatment of Intraocular Melanoma

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**PURPOSE:** Ruthenium-106 ($^{106}$Ru) eye plaques have the potential to achieve excellent tumor control with reduced radiation toxicity in lesions < 5 mm in apical dimension. We therefore evaluated our single-institution experience in the management of ocular melanoma treated with $^{106}$Ru plaque brachytherapy.
MATERIALS AND METHODS: The records of 40 patients with uveal melanoma treated with $^{106}$Ru plaque brachytherapy between 2003 and 2007 at UT MD Anderson Cancer Center were retrospectively reviewed. Endpoints assessed included overall survival (OS), tumor control (locoregional control [LRC], progression-free survival [PFS], and enucleation-free survival [EFS]), and toxicity (cataract formation, glaucoma development, visual loss). Patients were subdivided into groups based on preimplant and postimplant visual acuity in the affected eye (20/20 up to 20/40, 20/40 up to 20/200, and worse than 20/200) for detailed analysis, with movement between groups characterized as clinically significant visual loss.

RESULTS: Median age at implant was 59 years. Median follow-up was 67 months (range 6–101 months). Median lesion height and maximum basal diameter were 3.05 mm (range: 1.27–4.94 mm) and 9.6 mm (range: 3.1–13.0 mm), respectively. Median apical dose was 90 Gy. Median dwell time was 89 hours. Actuarial 2-year rates of LRC, PFS, and OS were 97%, 97%, and 97%, respectively. At 5 years, these values were 97%, 94%, and 92%, respectively. There were no enucleations in our cohort, for an EFS of 100%. There were three deaths, two of which were related to melanoma. Fifteen patients (38%) experienced clinically significant visual loss in the treated eye. Two patients (5%) were diagnosed with glaucoma, and 20 patients (50%) developed cataracts. Cataract formation was not associated with apical dose rate or dose at 1-mm depth.

CONCLUSIONS: Our data represent the largest reported US cohort of patients treated with $^{106}$Ru plaque brachytherapy for intraocular melanoma. Our findings suggest that patients with intraocular melanomas < 5 mm in height treated with $^{106}$Ru plaque brachytherapy may achieve excellent rates of tumor control with acceptable toxicity, supporting the reintroduction of this technique in the United States.

(S022) SEER Analysis of Outcomes of Patients With Parotid Cancer Treated With Radiation Therapy

Bhupesh Parashar, Shruthi Arora, Paul Christos, A. Gabriella Wernicke; Weill Cornell Medical Center

PURPOSE: Parotid gland carcinomas are usually treated with surgical resection followed by radiation therapy (RT), if indicated. Indications for RT include high-grade tumors, positive margins, large tumors, and nodal involvement. However, survival outcomes in parotid cancers treated with radiation therapy have not been evaluated in a large population-based sample group. The aim of this study was to evaluate and compare survival outcomes between different parotid cancer histologic types treated with RT using the Surveillance, Epidemiology, and End Results (SEER) database.

MATERIALS AND METHODS: Patients with parotid carcinoma diagnosed from 1973 to 2008 were obtained from the SEER database. All patients received radiation (RT) either as external beam (pre- or postoperative) or implants. Kaplan-Meier survival analysis and log-rank tests were used to examine the (1) effect of histology on overall survival (OS) and cause-specific survival (CSS) and (2) influence of factors, such as treatment, treatment sequence, race, sex, and age, on survival outcomes by stratified histology.

RESULTS: A total of 3,533 patients with parotid cancers were identified. There were 2,076 (58.8%) males and 1,457 (41.2%) females. The most common histologic types were mucoepidermoid (28.3%), adenocarcinomas (30.7%), squamous (24.2%), and acinar (12.7%). Other histologies were mucinous/cystic, acinar, epithelial, and mixed/stromal. Of the known grades, there were 21% grade II tumors, 25.9% grade III tumors, and 11.4% grade IV tumors. Adjuvant RT was given in 95.2% of patients. Whites were 85% of the patient population, followed by blacks (7.1%). Median age was 60 years (range: 6–90 y).

Median CSS was significantly different between histologic types ($P < .001$). Sixteen-year CSS was 79.4% for acinar, 74% for mixed/stromal, 69% for mucoepidermoid, and 50.1% for squamous tumors, and 49.5% for adenocarcinomas. There was no difference in CSS for the kind of RT used ($P = .62$) (external vs implant) or the sequence of RT ($P = .99$) (preop vs adjuvant). Female gender was associated with significantly improved survival—16-year CSS was 69.2% females and 52.4% males ($P < .0001$). Black and nonwhite races were associated with significantly improved CSS—16-year CSS was 71.9% in black patients, 72.8% in nonwhite patients, and 57.3% in white patients ($P < .001$). Hazard ratio (for parotid cancer death) for each 1-year increase in age was 1.03 (95% confidence interval [CI] = 1.03–1.04; $P < .0001$).

CONCLUSION: This is the first large population-based sample study of outcomes in parotid cancer patients treated with radiation therapy. Tumor histology, race, age, and sex were factors affecting cancer-specific survival. This information is useful in clinical decisions regarding the management of this uncommon cancer.
(S023) Role of TGF-Beta Signaling in PIK3CA-Driven Head and Neck Cancer Invasion and Metastasis

Sophia Bornstein, MD, PhD; Jingping Shen, MD, PhD; Frank Hall, BS; Sherif Said, MD, PhD; Xiao-Jing Wang, MD, PhD; Neil Gross, MD; John Song, MD; Natalie Serkova, PhD; Shi-Long Lu, MD, PhD; Department of Otolaryngology, Department of Radiation Medicine, Oregon Health & Science University; Departments of Otolaryngology, Pathology, Anesthesiology, University of Colorado Anschutz Medical Campus, Aurora

BACKGROUND: Head and neck squamous cell carcinoma (HNSCC) patients have a poor prognosis, and mortality is linked to metastatic spread. However, the molecular mechanisms of HNSCC invasion and metastasis are unclear. The phosphatidylinositol 3-kinase (PI3K) pathway regulates a wide range of cellular processes crucial for tumorigenesis. Amplification and mutation of PIK3CA, the gene encoding the catalytic subunit of PI3K, are among the most common genetic alterations in human HNSCC.

METHODS AND RESULTS: To delineate the in vivo roles of PIK3CA during head and neck tumorigenesis, we developed a PIK3CA genetically engineered mouse model (GEMM), in which PIK3CA overexpression is specifically induced in the head and neck epithelia. When we applied 4NQO, a DNA adduct-forming agent widely used as a tobacco surrogate, together with PIK3CA overexpression, the PIK3CA-GEMM developed ~50% poorly differentiated HNSCC compared with ~10% in the control mice. Additionally 40% of 4NQO-treated PIK3CA-GEMM developed metastases compared with 0% in control 4NQO-treated mice. PIK3CA-GEMM tumors showed evidence of epithelial–mesenchymal transition (EMT) with strong vimentin staining and Twist overexpression. Molecular analysis of the PIK3CA tumors suggests that rather than AKT, PDK1 facilitates progression of PI3K-driven HNSCC, potentially through increased TGF-beta signaling. Supporting this hypothesis, PIK3CA tumors expressed increased TGF-beta1 ligand and Smad3, which is associated with TGF-beta-mediated inflammation, angiogenesis, and EMT based on our previous work.

CONCLUSIONS: In summary, our results suggest that the PIK3CA oncoenzyme drives invasion and metastasis of HNSCC through PDK1, possibly through activation of downstream TGF-beta signaling. Combined targeting of these pathways could inhibit cancer progression and metastasis in HNSCC patients with PIK3CA alterations.

(S024) Locoregional Recurrence Risk for Patients With T1,2 Breast Cancer With 1–3 Positive Lymph Nodes Treated With Mastectomy and Systemic Treatment

Andrew McBride, Pamela Allen, PhD; Wendy W. Woodward, MD, PhD; Michelle Kim, MD; Henry Kuerer, MD, PhD; Eva Katherine Drinka, MD; Aysegul Sahin, MD; Eric Strom, MD; Aman Buzdar, MD; Vicente Valero, MD; Gabriel Hortobagyi, MD; Kelly Hunt, MD; Thomas Buchholz, MD; University of Arizona; UT MD Anderson Cancer Center

BACKGROUND/PURPOSE: Randomized trials suggest breast cancer patients with 1–3 positive lymph nodes achieve benefits from postmastectomy radiation (PMRT). However, significant changes in breast cancer management, such as the use of sentinel lymph node surgery and improvements in systemic treatments, have occurred since the conclusion of these trials. We undertook this study to compare the benefits of PMRT in an era prior to and after these changes in breast cancer management.

METHODS: We retrospectively analyzed the locoregional recurrence (LRR) rates of 1,031 patients with a T1,2 breast cancer with 1–3 positive lymph nodes treated with mastectomy and adjuvant chemotherapy with or without PMRT during an early era (1978–1997) and a later era (2000–2007). These eras were selected because they represented periods prior to and after the routine use of sentinel lymph node surgery, taxane chemotherapy, and aromatase inhibitors. To define higher-risk subgroups, we also evaluated the risk factors for LRR for patients who did not receive PMRT.

RESULTS: A total of 506 patients were treated in the early era, 98 (19%) of whom received PMRT, and 522 patients were treated in the later era, 137 (26%) of whom received PMRT. In both cohorts, patients who received PMRT had significantly higher risk disease features. On the basis of our previous studies, we used PMRT more frequently for patients with three positive lymph nodes, T2 tumors, or gross extracapsular extension in the later cohort. PMRT was associated with a lower LRR rate in the early era cohort but not the later era cohort. Specifically, the 5-year LRR rate for patients in the early cohort was 9.5% without PMRT and 3.3% with PMRT (log-rank $P = .028$, 15-year rates 14.5% vs 6.1%, respectively), whereas the 5-year LRR rates of the later cohorts were 2.8% without PMRT and 4.2% with PMRT ($P = .48$). A Cox regression analysis of the early cohort revealed radiation use to be a significant factor predictive of LRR (adjusted hazard ratio [AHR] = 0.37; $P = .035$). In contrast, in the later cohort, radiation was not sig-
significant in a Cox analysis (AHR = 1.41; P = .48). The most significant factor predictive of LRR for the patients who did not receive PMRT was the era in which the patient was treated (AHR = 0.35 for later era; P < .001). In a Cox analysis limited to the data from the new-era no-PMRT cohort, the following factors were independently associated with higher rates of LRR: pathologic tumor size > 3 cm (AHR = 4.56; P = .019) and no sentinel lymph node dissection performed (AHR = 4.74; P = .005). For patients with both of these factors, the 5-year LRR without PMRT (n = 14) was 9.9%.

CONCLUSIONS: The risk of LRR for patients with T1,2 breast cancer with 1–3 positive lymph nodes treated with mastectomy and systemic treatment is highly dependent on the era of treatment. Modern treatment advances and selected use of PMRT for only those with high-risk features have allowed for identification of a cohort at very low risk for LRR without PMRT.

(S025) Evaluation of Diabetic Patients With Breast Cancer Treated With Metformin During Adjuvant Radiotherapy

Adam Ferro, BS, Sharad Goyal, MD, Sinac Kim, PhD, Hao Wu, MD, PhD, Devora Schiff, BS, Aneesh Pirlamarla, Bruce G. Haffty, MD, Department of Radiation Oncology, The Cancer Institute of New Jersey at UMDNJ–Robert Wood Johnson Medical School

PURPOSE: Preclinical studies have shown that metformin, the traditional diabetes mellitus medication and novel anti-cancer agent, combined with radiotherapy (RT) induces a radiosensitizing effect. Published reports regarding the safety of combination therapy involving metformin and RT are lacking. The purpose of this study was to verify metformin’s ability to act as a radiosensitizing agent and to analyze acute locoregional toxicity in patients with breast cancer receiving concurrent metformin plus RT.

MATERIALS AND METHODS: To assess the ability of metformin to cause a radiosensitizing effect when combined with RT, human breast cancer cell lines MDA-MB 468 and MCF-7 and nontumorigenic MCF10A were pretreated with metformin and then treated with ionizing radiation. Cellular survival was compared to cells receiving no treatment, metformin alone, or radiation alone using a trypan blue exclusion assay. For our retrospective analysis, we used the radiation oncology database following approval by the institutional review board to identify patients with breast cancer who were concurrently being treated with metformin for diabetes mellitus (DM) during their radiotherapy.

Patients were matched with nondiabetic patients and diabetic patients using a medication other than metformin. Toxicity was scored by the Common Terminology Criteria for Adverse Events. Primary endpoints in the study included presence of a treatment break and development of desquamation secondary to RT. Statistical analysis was performed to analyze toxicity between groups.

RESULTS: Fifty-one patients were identified to have received metformin plus RT. There was a statistically significant increase in the frequency of treatment breaks for diabetic patients receiving metformin when compared with nondiabetic patients and diabetic patients who received a medication other than metformin. Nine patients (18%) in the metformin group required a treatment break secondary to acute skin toxicity. The diabetic patients not receiving metformin and the nondiabetic patients each had only one treatment break (4% and 2%, respectively). There was also a statistically significant difference in the frequency of development of desquamation when diabetic patients receiving concurrent metformin and RT were compared with diabetic patients receiving a diabetes medication other than metformin and a trend toward significance when compared with nondiabetics. A total of 55% of the patients receiving concurrent metformin and RT developed desquamation, while 32% of diabetic patients being treated with an alternate diabetes medication and 49% of nondiabetic patients developed desquamation.

CONCLUSION: We confirmed the ability of metformin to act as a radiosensitizing agent with in vitro studies and a retrospective analysis. Diabetic patients treated with concurrent metformin and RT developed increased acute locoregional toxicity in comparison with diabetic patients receiving an alternate diabetes medication and with nondiabetic patients. Further clinical investigation should be conducted to determine the potential risks and benefits of metformin in combination with radiation therapy.

(S026) Treating Pancreatic Cancer Patients With Erlotinib-Based Adjuvant Therapy Following Pancreaticoduodenectomy or Pancreatectomy

Katherine Y. Fan, Aaron Wild, Amy Hacker-Prietz, Laura D. Wood, Amanda Blackford, Phuoc Tran, Rachit Kumar, Susannah Ellsworth, Avani Dholakia, Lei Zheng, Dung T. Le, Ana De Jesus-Acosta, Zeshaan Rasheed, Martin Makary, Matthew Weiss, John Cameron, Timothy Pawlik, Daniel Laheru, Ralph Hruban, Elliot Fishman, Christopher Wolfgang, Joseph Herman; Johns Hopkins University School of Medicine
BACKGROUND: Here, we report the first phase II study of erlotinib (Tarceva) in combination with adjuvant chemoradiotherapy (CRT) and chemotherapy for resected pancreatic adenocarcinoma (PDA). Preclinical studies, along with the positive phase III trial of gemcitabine and the EGFR tyrosine kinase inhibitor erlotinib in patients with metastatic PDA, provide a strong rationale to test erlotinib combined with CRT and chemotherapy in the adjuvant setting.

METHODS: A total of 48 patients with resected PDA were treated with adjuvant erlotinib (100 mg daily) and capecitabine (Xeloda) (800 mg/m² twice daily Monday–Friday) concurrently with intensity-modulated radiotherapy (IMRT) (50.4 Gy over 28 fractions) followed by 4 cycles of gemcitabine (1,000 mg/m² on Days 1, 8, and 15 every 28 days) and erlotinib (100 mg daily). Recurrence-free survival (RFS) and overall survival (OS) were calculated from surgery. Toxicity was assessed using the NCI CTCAE, version 4.0.

RESULTS: Median follow-up was 18.2 months (interquartile range [IQR], 13.8–27.1). Eighty-five percent had nodal involvement and 17% had positive resection margins. Median RFS was 15.6 months (95% confidence interval [CI] = 13.4–17.9), and median OS was 24.4 months (95% CI = 18.9–29.7). Multivariate analysis, adjusting for known prognostic factors, showed that tumor diameter > 3 cm was predictive for worse RFS (14.0 vs 17.9 months; hazard ratio [HR] = 4.01; 95% CI = 1.34–12.01; \( P = .01 \)) and OS (18.9 vs 29.7 months; HR = 4.98; 95% CI = 1.58–15.63; \( P = .01 \)), while the presence of dermatitis conferred improved RFS (16.3 vs 9.3 months; HR = 0.27; 95% CI = 0.1–0.72; \( P = .009 \)). During CRT, 31% and 2% experienced grade 3 and 4 toxicity, respectively. During post-CRT chemotherapy, 35% and 0% experienced grade 3 and 4 toxicity, respectively.

CONCLUSIONS: Erlotinib demonstrates acceptable safety in combination with standard adjuvant CRT and chemotherapy. This regimen exhibits promising efficacy that is comparable to or better than existing adjuvant regimens. The current intergroup trial will ultimately determine whether erlotinib confers a survival benefit in the adjuvant setting.

(S027) Novel CT-Derived Biophysical Markers Describe Gemcitabine Delivery and Chemoradiation Response in Human Pancreatic Adenocarcinoma

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PURPOSE: Pancreatic ductal adenocarcinoma (PDAC) lethality is partly ascribed to ineffective chemotherapy delivery to cancer cells, which requires traversal of multiple deranged physical barriers, including abnormal vasculature, characteristically dense stroma, and deregulated intracellular transport proteins. We developed, validated, and applied a method to derive mass transport properties from routine computed tomography (CT) scans to test the hypothesis that transport phenomena would correspond with gemcitabine-based therapy delivery and response.

METHODS: The mathematical model described density changes in pancreatic tissues during contrast-enhanced CT scans, providing mass transport parameters, such as the rate of contrast exchange between microvasculature and tissue (R), maximum enhancement of the tissue (Max Value), and area under the density curve (AUC). The CT analysis was applied to three cohorts: (1) 55 patients with PDAC who served as a learning dataset in model development; (2) 12 patients with PDAC in a prospective “phase 0” clinical trial of intraoperative infusion of gemcitabine, where we sought to prove that gemcitabine incorporated into the DNA of cells in the tumor and determine the factors that influenced the delivery of gemcitabine to the DNA; and (3) 105 patients with PDAC who received preoperative gemcitabine-based chemoradiation and who had evaluable pretherapy CT scans and known pathological response and outcome.

RESULTS: The model was validated by showing a direct correlation between the CT-derived normal pancreas Max Value with the maximum enhancement in the celiac artery (\( P = .0001 \)). There were twofold to 10fold differences in CT-derived parameters between normal pancreas and tumor (\( P < .0001 \)). In the phase 0 trial, there was up to a sixfold difference in tumor gemcitabine incorporation, despite well-controlled infusion conditions and similar intravascular pharmacokinetics. There were significant differences in the tumor gemcitabine incorporation for seven patients with “low” human equilibrative nucleoside transporter (hENT1) and five patients with “high” hENT1 (\( P = .02 \)). Accounting for hENT1 score, surgical pathology-derived fibrosis score had an inverse relationship with tumor gemcitabine incorporation (\( P = .008 \) for “low” and \( P = .004 \) for “high” hENT1). Moreover, the fibrosis score correlated directly with CT-derived Max Value and AUC (\( P = .01 \) and \( P = .007 \), respectively), and these CT-derived parameters also exhibited an inverse correlation with tumor gemcitabine incorporation (\( P = .03 \) for both). In the 105
patients with known pathological response to preoperative gemcitabine-based chemoradiation, lymph node involvement was the only standard clinical variable to correlate with pathological response and disease-specific survival (DSS). Patients with a near-complete pathological response (90% dead cells or greater on surgical pathology after preoperative therapy) had a DSS advantage compared with those who had less than a near-complete response (hazard ratio [HR] = 0.37; 95% confidence interval [CI] = 0.16–0.74; \( P = .004 \)). The CT-derived parameter R had a nearly 1:1 relationship with pathological response (\( P = .0001 \)), and patients with a value \( \geq 0.9 \) had a better prognosis than those with \(< 0.9 \) (DSS: HR = 0.55; 95% CI = 0.33–0.93; \( P = .02 \)). Multivariate analyses confirmed the univariate findings.

**CONCLUSIONS:** CT-derived parameters describe qualities of tumor vasculature and tissue that influence gemcitabine-based therapy delivery, response, and outcome. These quantitative parameters represent biophysical markers of cancer that can be derived prior to therapy, providing clinically relevant information to guide cancer management.

**(S028) Primary Radiotherapy Versus Radical Prostatectomy for High-Risk Prostate Cancer: A Decision Analysis**

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**PURPOSE:** Prostate cancer is diagnosed in over 200,000 men annually in the United States, with up to 25% presenting with high-risk disease. Two evidence-based therapies exist for the treatment of high-risk prostate cancer: external beam radiation therapy with androgen deprivation therapy (RT + H) and radical prostatectomy with adjuvant radiation therapy (S + RT). These strategies have never been compared in a prospective trial. Using decision analysis, we compared the quality-adjusted life expectancy (QALE) among men treated for high-risk prostate cancer with RT + H versus S + RT versus a hypothetical trimodality therapy consisting of S + RT with concurrent androgen blockade (S+ RT + H).

**PATIENTS AND METHODS:** We developed a Markov model to describe lifetime health states after treatment for high-risk prostate cancer. Probabilities and utilities were extrapolated from the literature: local control rates following S + RT were taken from SWOG 8794, and local control rates for RT + H were taken from RTOG 9202. All patients were assumed to have the same rate of distant metastasis (DM) before treatment. The relative efficacy of H in the S + RT + H arm was modeled from RTOG 9202 and 8610. Toxicity rates following RT were based on recent IMRT series, and patients were exposed to risks of diabetes, cardiovascular disease, and osteoporotic fracture for 5 years after completing H. Sensitivity analyses were carried out to model uncertainty in outcome rates, toxicities, and utilities.

**RESULTS:** In the base case, the QALE following treatment with RT + H, S + RT, and S + RT + H was 9.3, 8.0, and 9.5 quality-adjusted life-years (QALYs), respectively. RT + H resulted in an increase of at least 1 QALY compared with S + RT in nearly all one-way sensitivity analyses. The difference between the two treatments was notably less than 1 QALY when assuming a low DM rate. In contrast, S + RT + H was in most cases superior to RT + H but by small margins (\(< 0.5 \) QALY). Differences were highly sensitive to toxicity assumptions, and RT + H was associated with a 0–1 QALY benefit over S + RT + H in five scenarios, including a high risk of bowel toxicity after surgery and low utility of impotence.

**CONCLUSION:** In comparison to prostatectomy and adjuvant RT, radiotherapy with androgen deprivation was the optimal treatment strategy for treatment of high-risk prostate cancer. Furthermore, despite increased morbidity compared to evidence-based strategies, trimodality therapy is associated with local and distant control benefits that may lead to superior outcomes in a meaningful population of men. The sensitivity of this comparison to toxicity assumptions suggests that patient preference of potential outcomes must govern use of trimodality therapy. Such a strategy warrants further study.

**(S029) Expression of Myeloid Differentiation Factor 88 in Neurons Is Not Requisite for the Induction of Anorexia and Lethargy by Interleukin-1 Beta**

Aaron J. Grossberg, PhD, Theodore P. Braun, PhD, Biliana O. Veleva-Rotse, MS, Julia E. Maxson, PhD, Marek Szumowski, BS, Anthony P. Barnes, PhD, Daniel L. Marks, MD, PhD; Oregon Health & Science University

**PURPOSE AND OBJECTIVES:** Cancer and its treatments, including radiation and chemotherapy, induce fatigue and anorexia that significantly impact both quality of life and tolerance to therapy. These symptoms have been linked to an increase in circulating inflammatory cytokines, specifically interleukin-1β (IL-1β). IL-1β inhibits normal feeding and locomotor activity (LMA), via its actions in the brain. Preclinical studies show that these responses to IL-1β are mediated by myeloid differentiation factor 88 (MyD88), although it is unknown in which cells this signal is required.
This study sought to identify the cell type mediating IL-1β–induced fatigue and anorexia, to inform therapeutic approaches to these toxicities of radiotherapy and chemotherapy.

**MATERIALS AND METHODS:** The Nestin-cre mouse was crossed with MyD88loxP mice to delete MyD88 from neurons and glia in the CNS (MyD88CNS). These mice were compared with total body MyD88KO and wild type (WT) mice. Mice had cannulae stereotactically placed in the lateral ventricle and telemetry transponders implanted into the peritoneum. Mice were treated with either intracerebroventricular (ICV) IL-1β (10 ng) or vehicle. Food intake, body weight, and LMA were continuously monitored for 24 h after treatment. ICV TNF (500 ng), a non–MyD88-dependent cytokine, was used as a positive control for normal immune development. Peripheral inflammation was modeled using IP lipopolysaccharide (LPS). Efficacy of recombinase was evaluated using tdTomato reporter mice crossed with the Nestin-cre mouse.

**RESULTS:** ICV IL-1β treatment caused a significant reduction in feeding, body weight, and LMA in WT mice. MyD88KO mice were protected from these effects of ICV IL-1β despite having intact behavioral responses to TNF. Nestin-cre/tdTomato reporter mice exhibited recombination in neurons and astrocytes but not microglia or endothelial cells. In contrast to MyD88KO mice, the behavioral responses of MyD88CNS mice to ICV IL-1β or IP LPS were indistinguishable from those of WT mice.

**CONCLUSIONS:** Our results demonstrate that MyD88 is not required in neurons or astrocytes to induce the behavioral response to ICV IL-1β. This suggests that a non–Nestin-expressing cell population responds to IL-1β in the CNS and transduces the signal to neurons controlling feeding and activity. We posit that cerebrovascular cells are the most likely targets for IL-1β signaling in the brain, implying that systemic therapy addressing anorexia and fatigue need not penetrate the blood-brain barrier.


Lucas Gilbride, Jay F. Dorsey, Sanjay Chandrasekaran, Kelly M. MacArthur, Christina H. Chapman, Joel R. Concepcion, Gary D. Kao, Stephen M. Hahn; Department of Radiation Oncology, University of Pennsylvania

**BACKGROUND:** Non–small-cell lung cancer (NSCLC) is the most common cause of cancer mortality in the United States, with systemic disease and relapse frequent despite definitive therapy. Circulating tumor cell (CTC) assays provide noninvasive and serial interrogations of the status of primary or metastatic NSCLC disease, thus potentially guiding treatment decisions and reflecting prognoses. Substantial technical constraints have impeded efforts with CTC assays based on cell surface markers. We therefore employed a novel approach based on the detection of elevated telomerase activity inherent in tumor cells. This method affords maximal sensitivity, as it is not affected by epithelial-mesenchymal transition (EMT) in cancer cells, and maximal specificity, as among normal cells, only stem cells show activated telomerase. We describe here pilot results with this assay and plans for a more extensive prospective study involving multiple NSCLC patient cohorts.

**PATIENTS AND METHODS:** The feasibility of a telomerase-based method of CTC detection in an NSCLC cancer population was explored in a pilot study of 23 patients enrolled in the tissue collection/registry protocol in the Department of Radiation Oncology. Patients included in the CTC pilot study had biopsy-proven NSCLC and were treated with definitive radiotherapy (RT) as a part of their treatment regimen. CTC analysis was performed on a 10-mL blood sample collected from the patient before, during, and after completion of the RT treatment course. The CTC assay relies on an adenoviral vector expressing the hTERT promoter, which thus drives expression of green fluorescent protein only in the presence of elevated telomerase activity.

**RESULTS:** Of 23 patients with NSCLC, elevated CTC counts were found in all but 1 patient, with the levels of CTCs detected per mL of blood ranging from 0.57 cells to 570.7 cells (mean 62.7, median 9.1, standard error [SE], 28.4). In contrast, the rate of background non-CTC cells detected in four normal healthy controls ranged from 0.1–1.7 (mean 0.76, median 0.72). CTC counts in all but one NSCLC patient decreased as a result of RT, with marked decreases in some. The only patient who did not show a decrease in CTC counts was soon found to have developed new metastases. Representative and notable examples of patient serial CTC counts will be presented.

**CONCLUSIONS:** In a pilot study, we have demonstrated the feasibility to detect CTCs in patients with NSCLC utilizing a novel telomerase-based assay system, with encouraging data showing a reduction in CTC counts in most patients undergoing RT. The assay may thus contribute to: a) predicting response to treatment, b) monitoring response to therapy, and c) early detection of relapse and disease progression. Guided by these promising results, we have initi-
ated a more extensive prospective study involving up to 50 patients with NSCLC in five different cohorts, to validate the potential value of CTC counts in NSCLC patients undergoing various courses of RT. Up to two pretreatment samples will be collected for a baseline reading, followed by one to three on-treatment samples and then 1-, 3-, 6-, 12-, 18-, and 24-month follow-up samples.

**CONCLUSIONS:** Gross disease, group T stage, last disease status, and treatment correlated with CTC measurements. The tumor burden, as measured in our assay of peripheral blood, did not correlate with prognosis. As suggested by Ang et al, EGFR may be a better marker for local rather than distant disease burden. We are expanding our assay to detect other biomarkers in peripheral blood.

**S031** Epidermal Growth Factor–Mediated Detection of Circulating Tumor Cells in Patients With Head and Neck Cancer: Clinical Results

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**PURPOSE:** The epidermal growth factor receptor (EGFR) may be overexpressed in > 90% of malignant cells from patients with squamous cell cancers of the head and neck (SSCHN). Our goal was to count the number of circulating tumor cells (CTCs) by using a tube of peripherally drawn blood and to correlate the quantity of CTCs with the clinical outcome in a population of patients with SSCHN.

**METHODS:** We developed highly sensitive and specific surface-enhanced Raman spectroscopy (SERS) gold nanoparticles for the detection and characterization of CTCs in peripheral blood relying on the presence of EGFR overexpression in CTCs. After QA considerations, samples were available from 90 patients.

**RESULTS:** All patients were analyzed for correlation between CTC/mL and gross disease, T stage (individual T stage and grouped), N stage (individually and grouped), primary site, death related to disease, last disease status, and treatment (N vs Y). Gross disease, grouped T stage (T0–T2 vs T3–4), last disease status, and treatment correlated with CTC measurements. Univariate survival analysis by the Cox model showed statistically significant differences for gross disease. Looking at only nontreated patients with gross disease (n = 43), analysis for an association between CTC/mL and covariates showed no significant associations, and neither univariate analysis nor multivariate analysis showed correlation with survival. Looking at patients without gross disease (n = 40), analysis for an association between CTC/mL and covariates showed a significant association between CTC and grouped T stage. Neither univariate analysis nor multivariate analysis demonstrated CTC correlating with disease-specific survival.

**CONCLUSIONS:**: The human Ki-67 protein is a nuclear protein whose expression is strongly upregulated in proliferating cells. Thus, Ki-67 expression can be used to determine the growth fraction in any clonal population of cells. While the prognostic significance of Ki-67 overexpression in newly diagnosed tumors remains to be elucidated, there are some data to suggest that in breast cancer, Ki-67 overexpression may be prognostic for survival. Whether Ki-67 expression independently predicts for local-regional recurrence after breast conservation therapy (BCT, defined in this setting as breast-conserving surgery and adjuvant radiation therapy) has not been investigated. The purpose of this study was to assess the Ki-67 expression in a cohort of early-stage breast cancer patients with the primary endpoint of assessing its prognostic significance on local-regional relapse, with secondary endpoints of distant metastasis and overall survival, and correlation of Ki-67 to other clinical-pathologic features.

**MATERIALS AND METHODS:** We performed Ki-67 staining on a tissue microarray of 438 patients who were uniformly treated with BCT. Associations of Ki-67 expression and clinical-pathologic features and outcomes were analyzed.

**RESULTS:** We found a significant increase in Ki-67 expression among black patients (blacks: 36.8% vs whites: 16.7%; P < .01), younger patients (age < 50 years: 27.1% vs age > 50 years: 15.4%; P < .01), ER-negative tumors (33.0% ER− vs 16.6% ER+; P = .04), HER2/neu-positive tumors (HER2+ 35.4% vs HER2− 18.4%; P = .01), and larger tumors (T2: 26.5% vs T1: 15.6%; P = .03). On univariate analysis, Ki-67 did not predict for overall survival rate (OS), cause-specific
survival (CSS), ipsilateral breast recurrence survival (IBRS), distant metastasis-free survival (DMS), recurrence-free survival (RFS), or locoregional recurrence-free survival (LRRS) (OS, 74.4% vs 72.6%; CSS, 82.9% vs 82.1%; IBRS, 83.6% vs 88.5%; DMS, 76.1% vs 81.4%; RFS, 65.5% vs 74.6%; LRRS, 81.6% vs 84.7%, respectively; all \( P > .05 \).

**CONCLUSIONS:** To our knowledge, our study is the first to demonstrate the association between Ki-67 and race. Ki-67 appears to be a surrogate marker for aggressive disease and correlates significantly with known prognostic features, such as age, race, and hormone receptor, and HER2 status, but independently does not predict for local-regional outcomes after BCT when taken into consideration these other prognostic clinical-pathologic features.

**RESULTS:** Of the 3,710 patients identified, 2,981 (80%) were white and 729 (20%) were AA. Consistent with other data, AA versus white veterans were of younger age (51 vs 59 years; \( P < .001 \)), had more nodal involvement (29% vs 22%; \( P < .001 \)), hormone receptor negativity (18% vs 13%; \( P = .001 \)), higher grade (grade III: 32% vs 23%; \( P < .001 \)), and higher-stage tumors (stage I: 22% vs 28%; stage II: 30% vs 23%; \( P = .001 \), respectively. On multivariate analysis with adjustment for confounding factors (age, stage, grade, nodal status, treatment), the overall risk of mortality was higher in AA compared to whites (hazard ratio [HR], 1.272; 95% confidence interval [CI]: 1.07–1.5130; \( P = .006 \)). Despite equal access to care for all veterans enrolled in this program, unexpected disparities in treatment delivered were noted, such as a higher percentage of AA patients receiving no treatment after diagnosis (9% vs 6%; \( P = .014 \)), less definitive surgery (16% vs 13%; \( P = .033 \)), less axillary surgery (63% vs 67%; \( P = .044 \)), and less hormone therapy (HR+ subset: 29% vs 44%; \( P < .001 \)).

**CONCLUSIONS:** There are limited data assessing disparities in closed, equal-access-to-care systems. To our knowledge, this is the first study to investigate disparities in female breast cancers from the VACCR. We found similar differences in clinical-pathologic features and outcomes in AA versus white veterans as those reported in the general population. Given the unexpected finding of significant disparities in the delivery of breast cancer treatment for AA versus white veterans in this federally funded organization, which provides comprehensive medical benefits without cost to all enrolled veterans, additional investigations assessing factors influencing treatment decisions, such as physician and patient biases, are needed.

**MATERIALS AND METHODS:** IRB approval was obtained from the VA prior to conducting this study. Breast cancers diagnosed between 1995 and 2009 in the VA health care system were identified through the VA Central Cancer Registry (VACCR) database. Data parameters were analyzed to assess disparities in treatment delivery and differences in clinical-pathologic features and outcomes between the two cohorts.

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sequencing on the time from mastectomy to the initiation of PMRT.

**MATERIALS AND METHODS:** The medical records of all patients undergoing postmastectomy radiation in the setting of tissue expander–implant breast reconstruction at our institution from June 2004 to June 2011 were reviewed retrospectively. Data regarding demographics, oncologic history, radiotherapy, operative details, and clinical outcomes were recorded. All complications requiring additional surgery or hospitalization were recorded. Statistical analysis was performed using multivariate regression, Student’s t-test, and Fischer’s exact test, where appropriate.

**RESULTS:** A total of 55 eligible patients underwent 56 two-stage tissue expander–implant breast reconstructions. A total of 22 patients underwent exchange prior to PMRT (Group 1), and 34 patients underwent exchange following PMRT (Group 2). The mean follow-up time for the two groups was 46 months and 27 months, respectively. The groups were similar with respect to age at mastectomy, BMI, race, comorbidities, oncologic characteristics, and radiation therapy treatment characteristics. There was no significant difference in overall complication rate (54.55% vs 47.06%; P = .785) or reconstruction failure rate (13.64% vs 20.59%; P = .724) between the two cohorts. The most commonly encountered complications were infection, wound dehiscence, and capsular contracture. There was no significant difference in rate of infection (18.18% vs 23.53%; P = .386), wound dehiscence (4.55% vs 14.71%; P = .386). However, there was a statistically significant higher rate of capsular contracture (40.91% vs 11.76%; P = .021) in Group I. To examine the impact of sequencing on delivery of radiation, we excluded all patients who received neoadjuvant chemotherapy. This left 14 patients who underwent exchange prior to PMRT and 17 patients who underwent exchange following PMRT. The group that underwent TEE prior to PMRT experienced a statistically significant increase in the mean number of days from mastectomy-expander placement to initiation of radiation—from 188.0 to 220.4 days (P < .05).

**CONCLUSIONS:** Our findings suggest that the sequencing of TEE in the setting of PMRT had no significant impact on overall complication or reconstruction failure rate. However, there was a higher rate of capsular contracture leading to additional surgical interventions in patients who underwent TEE prior to PMRT. We also noted a relatively high rate of reconstruction failure overall (13% in Group 1 and and 20% in Group 2). In addition, performing TEE prior to PMRT significantly delayed the initiation of PMRT, adding 32 days to the mean time from mastectomy to the start of radiotherapy. The implications of this delay are unknown, but it raises the concern that delays in delivering PMRT secondary to surgery and complications may compromise locoregional control rates.

**RESULTS:** There were a total of 50,815 patients fulfilling the study criteria, between 1992 and 2005. The average number of days in the POI on which patients had imaging, biopsy, and physician encounter claims combined (including their first physician visit date) increased from 3.8 to 5.4 (P < .0001). The average number of dates on which imaging, biopsy, and physician visits were performed during the POI increased from 0.8 to 1.1 (P < .0001), 0.7 to 0.8 (P = .0008), and 2.8 to 4.2 (P < .0001), respectively. The mean number of new patient/consultation encounter dates increased from 1.3 to 1.7 (P < .0001), while established patient visits increased from 1.6 to 2.6 (P < .0001). Excisional biopsy dates dropped from 0.5 to 0.2 (P < .0001), while core needle biopsy dates increased from 0.2 to 0.5 (P = .0004). Over this same period, the mean POI from first physician visit to surgery increased from 33 days in 1992 to 55 days in 2005 (P = .007) (median 21 days, increasing to 30 days; P < .0001). The proportion of patients having consolidation of imaging and biopsy on the same day at least once during the POI increased from 6.9% of patients in 1992 to 23.7% in
Although breast conservation increased from 23.4% of patients to 62.4% during this period (P < .0001), increasing numbers of biopsy dates and imaging dates each independently correlated with mastectomy at first procedure (each P < .001).

**CONCLUSION:** Preoperative evaluation in the Medicare patient has changed, with greater numbers of dates on which imaging, biopsies, and office visits are performed. This may account for the increasing times to surgery. Correlation between outcomes and the increasing time spent in evaluation is needed to determine whether this greater burden for the patient is superfluous or tied directly to improvements in the care of the breast cancer patient.


Steven Register, MD, Cristiane Takita, MD, William Amestoy, Jean Wright, MD; University of Miami/Jackson Memorial Hospital

**PURPOSE:** Optimal sparing of lung and cardiac structures is clinically important for patients receiving adjuvant radiotherapy for breast cancer, given the high probability of long-term survival. We evaluated the influence of treatment planning using deep inspiration breath hold (DIBH) versus free breathing (FB) technique on dosimetric parameters for organs at risk (OAR) and target coverage and evaluated patient/treatment characteristics that may influence OAR sparing.

**METHODS:** We retrospectively reviewed patients with left-sided breast cancer treated with adjuvant radiotherapy to the breast/chest wall +/- regional nodal irradiation (RNI) at our institution from January 2011 to September 2012. All patients had both FB and DIBH image acquisition at CT simulation. The breast/chest wall was contoured per the RTOG atlas, and cardiac structures, including the left anterior descending artery (LAD), were contoured per the validated University of Michigan cardiac atlas. We generated two treatment plans for each patient using the FB and DIBH scans and performed a dosimetric analysis of target coverage and doses to OAR. We analyzed specific patient/treatment characteristics that may influence OAR sparing, including the use of a heart block, maximum heart depth (MHD), heart-chest wall distance (HCWD), lung orthogonal distance (LD), and organ volume. We defined MHD as the maximum distance from the field edge to the heart border. We defined LD as the maximum distance from the field edge to the chest wall at the level of maximum chest separation. Each parameter was compared using a paired two-tailed Student's t-test.

**RESULTS:** We identified 27 patients with both FB and DIBH image sets. The mean patient BMI was 27.3. Seventy-five percent of patients received whole-breast radiation therapy (WBRT), 25% received postmastectomy radiation therapy (PMRT), and 25% received RNI. Both the FB and DIBH plans provided acceptable coverage of breast PTV (planning target volume) V90 of 96.3% and 96.1% (P = .72), respectively. DIBH plans resulted in lower use of a heart block (18 vs 7 patients; P = .0002), smaller heart volume (551.9 vs 524 cc; P = .0007), smaller MHD (1.1 vs 0.26 cm; P ≤ .0001), and larger HCWD (0.41 vs 0.80 cm; P ≤ .001).

DIBH plans showed statistically significant sparing of dosimetric parameters for the heart, as shown in Table 1. DIBH plans also showed statistically significant sparing of the LAD. For the lung, the left lung volume nearly doubled (1036.3 vs 1892.4 cc; P ≤ .0001), and the LD significantly increased from 2.03 to 2.34 cm (P = .0002) in the DIBH plans while showing statistically significant sparing. There were no significant differences in OAR sparing when we compared patients receiving WBRT versus PMRT.

**CONCLUSIONS:** DIBH plans maintained similar PTV coverage while significantly sparing the heart, LAD, and lung at high and low doses for WBRT and PMRT. This pattern of sparing is important, as the relationship between treatment-related cardiac toxicity and dose-volume effects for cardiac structures remains uncertain.

**Table S036**

<table>
<thead>
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<th>Parameter</th>
<th>FB</th>
<th>DIBH</th>
<th>P Value</th>
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<tr>
<td>Heart-mean (cGy)</td>
<td>330.7</td>
<td>190.8</td>
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<tr>
<td>Heart-V5</td>
<td>11.6%</td>
<td>6.1%</td>
<td>&lt; .001</td>
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<td>Heart-V30</td>
<td>1.5%</td>
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<td>Heart-V45</td>
<td>0.8%</td>
<td>0.06%</td>
<td>.006</td>
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<tr>
<td>Lung-mean (cGy)</td>
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<td>.0039</td>
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<td>Lung-V5</td>
<td>40.9%</td>
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<tr>
<td>Lung-V20</td>
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<td>LAD-V40</td>
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(S037) Safety and Efficacy of Stereotactic Body Radiotherapy for Liver Metastasis

Benjamin Goodman, DO, Higinia Cardenes, MD, PhD, Cynthia Calley, MA, Netsanet Gebregziabher, MS, Mary Maluccio, MD, Paul Helft, MD, Elena Chiorean, MD; Indiana University

PURPOSE: Stereotactic body radiation therapy (SBRT) is a noninvasive, effective technique used in the treatment of a limited number of liver metastases from solid tumors. We present our single-institution SBRT experience outcome and toxicity results.

PATIENTS AND METHODS: We treated 64 patients 69 different times, for a total of 78 lesions treated. Inclusion criteria were patients with one to three liver metastases, without evidence of progression outside of the liver and with at least 700 cc of liver (minus the gross tumor volume [GTV]) receiving less than 1,500 cGy. One colorectal patient was treated three times, and four patients were treated twice. Sixty-six percent of the patients had colorectal primary cancers. Noncolorectal gastrointestinal (GI) cancer accounted for 14% of the sites treated, with breast 6%, ovarian 5%, NSCLC 3%, and the other remaining sites 6%. Among the 69 treatments, 85.5% had prior chemotherapy. The mean GTV size was 37.3 cc (range: 3.4–144.8 cc). The mean total dose was 5,254.3 cGy. The median dose was 5,400 cGy (range: 3,000–6,000 cGy). The mean pretreatment CEA level among the 45 colorectal treatments was 65.3 ng/mL (0.7–858 ng/mL).

RESULTS: The median overall survival time was 33.6 months (range: 23.2–38.4 mos). Actuarial survival estimates at 12, 24, 36, and 48 months were 89.1%, 65%, 41.1%, and 17.6%, respectively. The local control rate was 94.2%, with estimates at 12, 24, 36, and 48 months being 96.1%, 87.9%, 87.9%, and 87.9%, respectively. The observed toxicities noted among the 69 treatments included mostly grades 1 and 2 toxicities with only two grade 4 toxicities and one grade 5 toxicity. There was no difference in the toxicity based on the primary site. This included 11 patients with grade 1 and 7 patients with grade 2 nonhepatic GI toxicity. Fifteen patients had grade 1 fatigue and 3 patients had grade 2 fatigue. Grade 1 chest wall pain was seen in three patients, and four patients had grade 2 chest wall pain. There were two patients with grade 1 hepatic toxicity. The most severe toxicity noted was one patient with grade 5 hepatic toxicity and two patients with grade 4 hepatic toxicity. In addition, two patients developed grade 1 pleural effusions thought to be secondary to treatment. Parameters affecting toxicity were evaluated based on grades 4 and 5 hepatic toxicity.

CONCLUSION: Stereotactic body radiation therapy is a safe and effective treatment for patients with one to three liver metastases, with a limited toxicity profile.

(S038) Hemoglobin A1c as a Predictor of Clinical Outcomes in Patients Seen in a Pancreas Multidisciplinary Cancer Clinic

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BACKGROUND: The prevalence of new-onset type 2 diabetes mellitus (DM2) is uniquely high in patients with pancreatic ductal adenocarcinoma (PDAC) compared to other malignancies. Here, we examine poor glycemic control in patients with PDAC compared to benign pancreatic lesions (BPLs) to assess the role of hemoglobin A1c (HbA1c) levels in screening for and management of PDAC.

METHODS: A total of 870 consecutive patients presenting to the Johns Hopkins Pancreas Multidisciplinary Cancer Clinic with suspected pancreatic cancer from 2008 to 2012 were retrospectively reviewed. Patients were diagnosed with BPL or biopsy-confirmed resectable (R), borderline/locally advanced (BRLA), or metastatic (M) PDAC. Patients with prior treatment for PDAC, a history of type 1 diabetes mellitus (DM1), or greater than a 1-year history of DM2 or lacking an HbA1c value (%) at presentation were excluded.

RESULTS: Of 282 patients included in the study, 45 had BPL, 63 had R-PDAC, 112 had BRLA-PDAC, and 62 had...
M-PDAC. Patients with any stage of PDAC had significantly higher HbA1c values than patients with BPL (P < .001, one-way ANOVA). The difference in mean HbA1c values for patients with PDAC compared to those with BPL became more significant as stage increased (R-PDAC: 5.9 vs 5.6, P = .04; BRLA-PDAC: 6.2 vs 5.6, P = .0003; M-PDAC: 6.2 vs 5.6, P < .0001). There was a trend towards higher HbA1c at presentation in patients with advanced PDAC (BRLA and M) compared to patients with R-PDAC (P = .06). Among patients with nonmetastatic disease, univariate analyses showed HbA1c ≥ 6.5, age > 65 years, and BRLA disease to be significantly associated with inferior survival (hazard ratio [HR] = 1.9, 95% confidence interval [CI] = 1.1–3.3, P = .02; HR = 1.7, 95% CI = 1.1–2.5, P = .01; and HR = 1.8, 95% CI = 1.1–2.7, P = .01, respectively), while tumor size and CA19-9 ≥ 90 were not (P > .05). After multivariate analysis, HbA1c (HR, 1.8; 95% CI: 1.1–3.2; P = .03), age (HR, 1.8; 95% CI: 1.2–2.7; P = .006), and resectability (HR, 1.9; 95% CI: 1.2–3.0; P = .009) remained significant independent predictors for poor survival.

CONCLUSIONS: PDAC shows a greater deleterious effect on glycemic control than BPL. Degree of glycemic control appears to correlate with more advanced stage at presentation and, moreover, to independently predict for survival. This study highlights the potential utility of HbA1c as a screening tool and prognostic factor for PDAC.

(S039) Mitomycin in the Context of Dose Intensification Made Possible by Intensity-Modulated Radiation Therapy

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OBJECTIVES: In definitive chemoradiation for squamous cell carcinoma of the anal canal, intensity-modulated radiation therapy (IMRT) allows for dose intensification by decreasing toxicity, reducing frequency of treatment breaks, and thereby increasing average weekly dose (AWD). Mitomycin has long been the preferred chemotherapeutic agent for anal canal carcinoma, but associated dermatologic and hematologic toxicities are significant. We sought to reexamine the necessity of mitomycin in the context of higher average weekly radiation doses made possible by IMRT.

METHODS: We completed an institutional retrospective review of all patients treated with definitive chemoradiation for squamous cell carcinoma of the anal canal between May 2002 and February 2010. After calculating the AWD for each patient, we compared median AWD between groups treated with IMRT and 3-dimensional conformal radiation therapy (3D-CRT) utilizing the Wilcoxon-Mann-Whitney test for significance. Stratifying by AWD greater or less than 875 cGy, we then determined overall survival (OS) and colostomy-free proportion (CFP) estimates for patients treated with or without mitomycin, utilizing the Kaplan-Meier method with the Mantel-Cox test for equality. We also compared Kaplan-Meier survival curves for patients treated with AWD > 875 cGy or mitomycin and those without.

RESULTS: Median follow-up for the cohort was 41.6 months (range: 5.7–111.1 months). A total of 25 (56.8%) patients were treated with IMRT and 19 (43.2%) with 3D-CRT; corresponding median AWD in these groups was 879 and 786 cGy (P = .02), respectively. Eighteen (40.9%) patients attained AWD > 875 cGy, and 23 (52.3%) received mitomycin. In patients not treated with AWD > 875 cGy, mitomycin was associated with an increase in 3-year OS (100% vs 60.8%; P = .005) and a trend toward higher CFP (90.9% vs 80.0%; P = .79). In those treated with AWD > 875 cGy, the difference in 3-year OS between those treated with and without mitomycin was not as large (90.9% vs 83.3%; P = .41). Patients treated with mitomycin or AWD > 875 cGy had more favorable outcomes than those who were not treated with either (3-year OS 92.9% vs 62.8%, P = .002; 3-year CFP 96.4% vs 80.0%, P = .17).

CONCLUSIONS: For squamous cell carcinoma of the anal canal, IMRT allows for dose intensification by reducing frequency of treatment breaks and thereby increasing the AWD. In patients treated with AWD > 875 cGy, incorporation of mitomycin into the chemotherapeutic regimen may not be essential for maintaining excellent disease-related outcomes, though much larger or prospective trials will be required to determine this with significant certainty. For patients treated with AWD < 875 cGy, mitomycin remains integral to ensuring best outcomes and may compensate somewhat for lengthened treatment times and deficits in average weekly dose.

(S040) Combined Transarterial Chemoembolization (TACE) and Stereotactic Body Radiation Therapy (SBRT) for Management of Primary Hepatocellular Carcinoma (HCC)

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PURPOSE: Hepatocellular carcinoma (HCC) is the third leading cause of cancer-related death in the world, with increasing incidence in the United States and central Europe. Surgical resection and orthotopic liver transplant (OLT) have been established as curative options. However, various factors delay surgical therapy, and there is often a long waiting period for donor livers, during which time tumors may increase in size or number. Alternative, as well as temporizing, therapeutic options include transarterial chemoembolization (TACE) and stereotactic body radiation therapy (SBRT). We evaluated the efficacy and safety of combined TACE followed by SBRT for the treatment of primary HCC.

MATERIALS AND METHODS: From August 2011 to October 2012, a total of 25 patients received sequential TACE followed by SBRT for HCC lesions at our institution: 11 Child-Turcotte-Pugh (CTP) Class A and 14 CTP Class B. A total of 24 patients had HCC and 1 patient had mixed histology of HCC with cholangiocarcinoma. A total of 23 patients had a single lesion treated and 2 patients had two lesions treated. A total of 17 patients had hepatitis C and 4 had hepatitis B. The median time from TACE to SBRT was 5 days (range: 2–49). The median dose, dose per fraction, and number of fractions were 4,000 cGy (range: 1,200–4,000 cGy), 800 cGy (range: 600–800 cGy), and 5 (range: 2–5 fractions), respectively. All patients were treated with cone beam CT (CBCT) imaging, with treatment delivered every other day. Abdominal compression was utilized in 21 patients, and an internal target volume (ITV) was generated via 4DCT for 23 patients. The mean gross tumor volume (GTV) and ITV were 32.4 cc (range: 0.5–104.2 cc) and 196.8 cc (range: 2.5–196.8 cc), respectively. Treatment response was scored according to the Modified Response Evaluation Criteria in Solid Tumors (mRECIST). Regional failure was defined as intrahepatic progression of disease outside of the treated lesion. Local control (LC), disease-free survival (DFS), and time to progression (TTP) were calculated according to the method of Kaplan and Meier.

RESULTS: The mean follow-up was 6.9 months (range: 1–12.7 months). Twenty-five (100%) patients experienced local control over this time period. The 8-month DFS was 71%, with four regional and two distant failures occurring in four patients. Median TTP was 7.8 months. Seventeen (68%) patients experienced complete response of tumor to treatment; four (16%) patients had a partial response and one (4%) had stable disease. The mean time to radiographic CR was 4.4 months (range: 1–9 months). Two patients had treatment truncated unrelated to treatment toxicity, and three candidates went on to transplant. Two patients experienced grade 1 nausea 1 month post-treatment, and three experienced abdominal discomfort for which they were prescribed analgesic medicine. Two CTP Class B patients with preexisting ascites experienced an increase in ascites post-treatment.

CONCLUSIONS: Combined TACE followed by SBRT is a feasible therapeutic option that is well tolerated and can provide outstanding local control for primary HCC lesions. Further follow-up is needed to better characterize treatment outcome.

(S041) Improving the Treatment of Primary Prostate Cancers Using a Daily Adaptive Planning Technique, and Its Advantages Over Image-Guided Radiation Therapy

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PURPOSE AND OBJECTIVES: Intensity-modulated radiation therapy (IMRT) coupled with image-guided radiation therapy (IGRT) increases the precision and accuracy of external beam radiation therapy and provides a safer delivery of higher, more curative levels of radiation dose. However, when significant changes to internal anatomy occur, IGRT alone will not be able to compensate for the dose degradation that may occur from using the original IMRT plan created from an earlier static CT scan. A daily adaptive planning technique would better maintain full target coverage and efficient normal tissue sparing, which would therefore more accurately reflect the original documented treatment planning results. Due to these day-to-day anatomic variations and the fact that IGRT only corrects for target location, resulting doses to the surrounding critical structures require examination.

MATERIALS AND METHODS: A total of 100 CT scans were clinically treated with adaptive planning during the course of 10 different primary prostate cancer patients. An in-room diagnostic CT-on-Rails was used for the purposes of performing daily IGRT in conjunction with an adaptive IMRT planning technique. While the daily CT dataset was analyzed for the standard purposes of IGRT, a brand new optimized IMRT plan was also created based on a new set of structures drawn by the on-call physician. This new adapted plan was then compared with the initial IMRT plan, repositioned, and recalculated on the daily IGRT CT.
RESULTS: The adapted plan was consistently equivalent to or better than the initial plan with IGRT in achieving both target coverage and normal tissue dose-sparing. Specifically, target doses were always closely similar, with little to no variation (< 1%) in overall average dose. However, the adaptive planning technique showed a greater reduction in the mean rectal dose of 3% in 32.5% of the cases and 5% to 10% in 8.1% of the cases, and one case showed more than 10% reduction. In addition, these reduced mean dose differences were most significant in the higher V50%, V70%, and V90% ranges.

CONCLUSION: Daily changes of the internal anatomy warrant adaptive planning. In instances of significant dose degradation due to the daily anatomical changes, a new plan can improve normal tissue sparing compared with using IGRT alone. While this process may be more work-intensive than the standard IGRT process, it should not be disregarded as an important tool, since (a) the adapted plan had results that were consistently equivalent to or better than the recalculated IGRT plan and (b) any unforeseen errors incurred during the process can be replaced by utilizing the already approved initial plan with IGRT and therefore prevent any unwanted breaks in the patient’s therapy. Adaptive planning is applicable to other cancer sites as well, and its full potential may be realized once better and faster autosegmentation programs become available.

(S042) Video-Based Educational Tool Improves Patient Comprehension of Common Prostate Health Terminology

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PURPOSE: Health care providers often counsel prostate cancer patients about treatment options using terms that are part of the “core” vocabulary of prostate cancer. However, studies have demonstrated a severe and potentially widespread lack of comprehension of these terms, especially among underserved populations (eg, Kilbridge et al., J Clin Oncol 2009). We hypothesized that a video-based educational tool would significantly improve understanding of these key terms related to prostate health among a predominantly lower-literacy population.

MATERIALS AND METHODS: After obtaining IRB approval, a software application was developed by a team that included a urologist, a radiation oncologist, a psychologist, and human-computer interaction specialists to serve as a video-based educational tool. This tool emphasizes animations to promote understanding. Demographics, education level, and literacy/numeracy (using the standardized REALM, Schwarz-Woloshin, KPTT, and Numeracy tests) were charted for a study population of two low-income safety-net clinics. A previously developed survey (Kilbridge et al., J Clin Oncol 2009) was used on this study population by trained interviewers, to evaluate comprehension of terms related to urinary, bowel, and sexual function both before and after administration of the educational tool. Pre- and postintervention levels of comprehension were assessed in
each case using the paired t-test of percentage of correct responses.

RESULTS: Fifty-six patients completed the study. Their characteristics were as follows: mean age, 54 years; race: African American, 51, white, 3, other, 2; mean education: 12th grade; mean household income: $15,936; mean literacy level: 7th to 8th grade. Patients achieved statistically significant improvement in comprehension (measured by correct survey responses) for 20 of the 32 survey terms after the video intervention. Notable improvements in correct survey responses were exhibited for the terms “rectal urgency” (from 18% to 73%, P < .001), “incontinence” (from 14% to 50%, P < .001), “bowel” (from 14% to 46%, P < .001), and “impotence” (from 58% to 84%, P < .001). Patients also demonstrated significant gains in understanding of the function of the prostate (from 11% to 30%, P < .001) and in ability to locate the prostate on an anatomic drawing (from 50% to 82%, P < .001).

CONCLUSIONS: A video-based educational tool was demonstrated to be an effective method for combatting the severe lack of comprehension of prostate health terminology (along urinary, bowel, and sexual function axes) in an underserved patient population. The improvements in understanding achieved with this intervention have the potential to enhance patient participation in shared and informed decision-making. These results support combined visual and audio multimedia as a promising tool for prostate cancer education and thus as an area for further research and tool development.

(S043) Effect of Hormone Therapy on Quality of Life for Patients Undergoing Brachytherapy With or Without External Beam Radiation for Localized Prostate Cancer

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PURPOSE/OBJECTIVE: Hormone therapy (HT) has been shown to provide benefit in disease control and overall survival when used in combined-modality therapy for prostate cancer. We investigated quality-of-life outcomes of patients with localized prostate cancer treated with or without HT in combination with brachytherapy ± external beam radiation therapy (EBRT).

MATERIALS AND METHODS: At our institution, 2,519 patients with localized prostate cancer underwent brachytherapy ± EBRT with or without HT from 1990 to 2010 (median 6.9 years, range: 1.5–19 years). Of these patients, 44.3% had NCCN low-risk disease, 38.9% had intermediate-risk disease, and 16.8% had high-risk disease. A total of 62.2% of the patients underwent brachytherapy and 37.8% underwent brachytherapy and EBRT; 45.2% underwent HT (median 6 months, range: 1–39) and 54.8% did not. We analyzed mean differences from pretreatment International Prostate Symptom Score (IPSS) and pretreatment Sexual Health Inventory for Men (SHIM) scores at initial 6-month follow-up and subsequent annual follow-up intervals. We also investigated long-term erectile potency preservation per Mount Sinai Erectile Function (MSEF) score ≥ 2 (range: 0–3) as well as rates of potency on final follow-up of patients who had pretreatment potency (n = 1,737). Long-term freedom from RTOG grade ≥ 2 rectal bleeding (FFRB) was also analyzed. T-test, chi-square, and Kaplan-Meier with Mantel-Cox log-rank analyses were utilized.

RESULTS: Up to 4 years after treatment, mean increases from pretreatment IPSS were significantly smaller for patients who underwent HT versus no HT (Figure 1, with 4-year P = .047). Up to 1 year after treatment, mean decreases from pretreatment SHIM were significantly greater for patients who underwent HT versus no HT (Figure 2, with 1-year P < .001). For patients with pretreatment potency who underwent HT versus no HT, actuarial 5- and 10-year erectile potency preservation rates were 51% and 38% versus 67% and 52%, respectively (P < .001). Potency (MSEF ≥ 2) rates on final follow-up for patients who underwent HT versus no HT were 48.4% versus 64.5%, respectively (P < .001). For patients who underwent brachytherapy with HT versus no HT, actuarial 5- and 10-year FFRB was 96.4% and 95.1% versus 92.3% and 90.8%, respectively (P = .005). No significant differences were found in long-term FFRB between patients treated with brachytherapy and EBRT who underwent HT versus no HT.

CONCLUSIONS: For prostate cancer patients treated with brachytherapy ± EBRT, HT is associated with decreased intensity and duration of long-term treatment-related urinary symptoms. Benefit is also seen with decreased long-term risk of rectal bleeding for patients undergoing brachytherapy without EBRT. Negative effects are demonstrated by decreased post-treatment sexual function and long-term erectile potency.

(S044) Thoracic Radiotherapy Within Six Weeks With Concurrent Chemotherapy Improved Outcome of Patients With Limited-Stage Small-Cell Lung Cancer (L-SCLC)

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BACKGROUND: A previous Intergroup study of L-SCLC showed improvement of 5-year survival by twice-daily thoracic radiotherapy (TRT) in 3 weeks with concurrent etoposide and cisplatin (EP) compared with daily TRT in 5 weeks, with significantly more grade 3 acute esophagitis in the 3 weeks regimen. We have compared the duration of TRT ≤ 6 weeks versus > 6 weeks among patients with L-SCLC treated by TRT + concurrent EP at MD Anderson Cancer Center.

MATERIALS AND METHODS: A total of 500 biopsy-proven L-SCLC patients staged by chest/upper abdominal CT and MRI of the brain were treated with TRT/EP between 1985 and 2007. Complete responders received prophylactic cranial irradiation (PCI). The data were analyzed using Kaplan-Meier survival function. The log-rank test was used to assess the quality of survival function using a P value of 0.05. Cox regression analysis was used for univariate and multivariate analysis.

RESULTS: The median follow-up was 20 months (range: 1–224 months). The median age was 61 years (range: 27–95). Median KPS was 90, weight loss < 5% was 87.8% (439 of 500 patients), 437 patients completed treatment within 6 weeks, and 63 patients took longer than 6 weeks to complete treatment. PCI was given to 270 patients with 2.5 Gy × 10 Fx or 2.0 Gy × 15 Fx (226 patients in the ≤ 6 weeks group compared with 44 patients in the > 6 weeks group). In the comparison between ≤ 6 weeks and > 6 weeks treatment groups in 5 years, the overall survival (OS) rate was 26.4 % versus 13.6% (P = .1131), disease-free survival was 30.4% versus 13.4% (P = .0355), local-regional control was 57.5% versus 34.3% (P = .0241), and distant metastasis-free survival was 38.1% versus 19.4% (P = .0808). Outcomes for all-grade acute dysphagia, pneumonitis, and other toxicities showed no significant difference between the two groups. However, the TRT ≤ 6 weeks group had lower-grade 3+ lung fibrosis (10% vs 22%; P = .01). Multivariate analysis showed that factors influencing overall survival were PCI (P < .001), pleural effusion (P = .02), duration of TRT, LR control (P = .001), and DM failure (P < .001).

CONCLUSIONS: The local-regional control and disease-free survival in 5 years were improved by TRT within ≤ 6 weeks compared to > 6 weeks with concurrent EP. Grade 3+ lung fibrosis was significantly higher in the > 6 weeks TRT group. There was no significant difference regarding acute grade 3+ esophagitis between the two groups. The final recommendation requires the results of a prospective randomized trial.

(S045) Analysis of Local Recurrences After Stereotactic Ablative Radiotherapy (SABR) for Early-Stage Lung Cancer

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INTRODUCTION: For patients with early-stage non–small-cell lung cancer (NSCLC) considered to be at high risk for surgery or patients who refuse an operation, stereotactic ablative radiotherapy (SABR) is a curative alternative treatment option. Long-term local control rates in excess of 90% are being achieved. In this study, we retrospectively analyzed potential causes for local failure.

MATERIALS: In an institutional database containing 729 patients treated with SABR for early-stage NSCLC and with sufficiently long follow-up, all patients with suspicious tumor growth on imaging, even in the absence of histological proof, were coded as local recurrences (n = 32). Kaplan-Meier and Cox regression analyses were used to identify factors prognostic for local failure. We retrospectively reviewed the successive steps from target definition to treatment delivery, to evaluate whether a possible cause for local relapse could be detected. The factors included are the quality of planning 4-dimensional CT (4DCT) scans, the accuracy of target contouring, target mobility, proximity of organs at risk, and target coverage.

RESULTS: Local recurrences were detected in 32 patients after a median interval of 14.9 months. The 3-year actuarial local failure rate was 8.4%. Recurrences were histologically confirmed in 38% of patients, diagnosed by a combination of CT scans and FDG-PET scans in 28%, and by CT scans only in 31% of patients. In a single patient, local recurrence was suspected based on x-ray only. Local recurrences were isolated in 22 patients (69%). In multivariate analysis, TNM stage was a prognostic factor for local failure. The local failure rates at 3 years were 8.2% for T1a, 5.1% for T1b, 10.1% for T2a, and 13.9% for T2b tumors (P = .012). In 18 of the 32 (56%) local recurrences, the tumor was located immediately adjacent to the chest wall. However, in retrospect, target contouring was judged to be too tight in only five of these patients. As only six patients (19%) exhibited tumor motion ≥ 1 cm, geographical misses caused by mobility are unlikely. In a single patient, unnoticed artifacts in the planning 4DCT scan may...
have led to inadequate target definition. In more than half of patients (53%), no apparent explanation could be identified for developing a local recurrence.

CONCLUSIONS: TNM stage is a prognostic factor for local recurrence. A potential explanation for local failure could only be identified in a minority of patients. However, the tumor location immediately adjacent to the chest wall in more than half of patients with local recurrences cautions against undue tight contouring in fear of chest wall toxicity.

(S046) Factors Associated With Grade 3 Acute and Chronic Esophagus Toxicity Following Radiotherapy for Limited-Stage Small-Cell Lung Cancer

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PURPOSE: Concurrent chemoradiotherapy is the standard of care for the treatment of limited-stage small-cell lung cancer (SCLC). Because of the centralized location of most SCLCs, the development of esophagitis is the most significant treatment-limiting toxicity of this therapy. In this study, we investigate the prognostic influence of clinical and dosimetric factors related to the development of both acute and chronic grade 3 esophagitis in a large cohort of SCLC patients.

METHODS: We retrospectively reviewed the medical records and treatment details of 223 patients treated between 1999 and 2009 with limited-stage SCLC who were treated with definitive radiotherapy. The majority of patients was treated with concurrent etoposide and cisplatin to a dose of 45 Gy in 30 fractions administered twice daily. Pertinent clinical, tumor, treatment, and dosimetric covariables were collected for analysis. On review of clinical records, acute and chronic esophageal toxicities were graded according to RTOG criteria. Forward stepwise logistic regression analysis with a multivariable model using all noncollinear variables was performed to identify factors predictive of ≥ grade 3 acute and chronic esophagitis. The median and Fisher’s exact tests were used to find cutpoints significantly associated with outcome.
RESULTS: The rates of grade 3 acute and chronic esophagitis were 22.4% and 6.7%, respectively. Clinical factors associated with a higher rate of grade 3 esophagitis on univariable analysis were performance status ($P = .028$) and tumor stage ($P = .037$). On multivariable analysis for acute toxicity, only the mean esophageal radiation dose (odds ratio [OR] = 1.08; 95% confidence interval [CI] = 1.03–1.12; $P = .001$) was significantly associated with the development of grade 3 acute esophagitis, with a mean dose > 25 Gy serving as a significantly predictive cutoff (Fisher’s exact test, $P = .005$). On multivariable analysis for chronic toxicity, only V45 esophageal dose (OR = 1.04; 95% CI = 1.01–1.07; $P = .017$) was associated with a higher rate of grade 3 chronic esophagitis, with V45 > 35% serving as a significantly predictive cutoff (Fisher’s exact test, $P = .028$).

CONCLUSION: In the treatment of limited-stage SCLC using modern radiotherapy techniques and considering both dosimetric and clinical variables, mean esophageal dose and V45 were the most accurate predictors for grade 3 acute and chronic esophagitis, respectively. There was no difference in the incidence of esophagitis between patients treated with 3DCT and IMRT. Mean esophageal dose of > 25 Gy and V45 > 35% were significantly predictive cutoffs for higher toxicity. Careful attention should be paid to these parameters during the treatment planning process to minimize the risk of grade 3 or higher esophagitis.

(S047) Use of Isodose Levels to Predict Radiation-Induced Fibrosis After Lung Stereotactic Body Radiation Therapy (SBRT): A Quantitative Analysis

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BACKGROUND: After completing stereotactic body radiation therapy (SBRT) for lung cancer, patients are generally followed with computed tomography (CT) to detect treatment response. It is widely known that radiation-induced fibrosis can be detected in the normal lung surrounding the gross tumor volume (GTV). However, the absence of a predictable response can both confound the ability to interpret CT imaging and lead to unnecessary anxiety, follow-up examinations, and biopsies. In this study, we investigated whether treatment isodose levels could be utilized to accurately predict anatomic patterns of radiation-induced fibrosis.

MATERIALS AND METHODS: We selected 12 lesions in 11 patients who were treated with lung SBRT at our institution and who had received two post-treatment CTs at approximately 6 and 12 months. Each patient’s follow-up CT was fused with the patient’s original simulation CT, and the treatment isodose levels were overlaid onto the follow up CT. The pencil beam convolution algorithm was utilized to determine dose distribution in the normal lung. The fibrosis surrounding the GTV was contoured by both a diagnostic radiologist and a radiation oncologist. We calculated the extension of the fibrosis outside a given isodose level, ranging from 5 to 40 Gy, in 5-Gy increments. Specifically, the fibrosis extension index (FEI) was defined as the volume of fibrosis extending outside a given isodose level relative to the total volume of fibrosis seen on follow-up CT and was expressed as a percentage. An FEI of 0% indicated that all of the fibrosis was included within a given isodose curve, while an FEI of 100% indicated that all of the observed fibrosis fell outside a given isodose curve. The FEI was plotted as a function of dose levels of 5, 10, 15, 20, 25, 30, 35, and 40 Gy.

RESULTS: Twelve lesions received definitive doses of SBRT (45–54 Gy). The first follow-up (1st FU) CT was at 5 ± 2 months, and the second follow-up (2nd FU) CT was at 11 ± 3 months. The mean volume of observed total fibrosis at 1st FU was 36.62 cc (range: 0.5–71.2 cc) and 44.08 cc at 2nd FU (range: 3.1–164 cc). As expected, a dose response was observed, and FEI was found to increase with higher dose levels (see Figure). The 20 Gy isodose curve was found to include 90% of the fibrosis at 1st FU and > 90% at 2nd FU. A paired sample t-test determined that the volume of fibrosis did not change significantly between the first and second follow-up ($P > .05$). However, the fibrosis extension index was found to change significantly between the first and second follow-up ($P = .014$).

CONCLUSIONS: In this study, we have shown that the 20 Gy isodose curve correlated well with the pattern of post-SBRT radiation-induced fibrosis. This finding demonstrates predictability in the pattern of treatment response seen on follow-up CT and may be useful in differentiating radiation-induced fibrosis versus recurrence. We advocate communication of treatment isodose information to diagnostic radiologists in order to improve the quality and accuracy of reporting of imaging after SBRT.

(S048) Synchronous Non–Small-Cell Lung Cancer Nodules Treated With Stereotactic Body Radiation Therapy (SBRT)

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3. American Radium Society Scientific Papers and Posters 2013

4. Radiation Therapy (SBRT): A Quantitative Analysis
PURPOSE: Medically inoperable patients diagnosed with presumed synchronous non–small-cell lung cancer (NSCLC) primaries (SPs) present a diagnostic quandary as to whether they have two isolated NSCLCs or early metastatic disease. After appropriate workup and the decision to treat as presumptive early-stage disease, we evaluate our experience with SPs treated with definitive SBRT, as there are limited published outcomes for this presentation.

METHODS: From our IRB-approved prospective registry of 419 patients treated with SBRT for NSCLC between August 2005 and August 2012, a total of 26 (6.2%) patients had SPs identified by biopsy or PET= T and received SBRT using Novalis/Brainlab to both lesions concurrently. The outcomes of SP patients were compared with our institutional single primary stage I experience. SBRT had statistically similar outcomes (local failure, presumed synchronous primary, clinically node-negative disease). After appropriate workup and the decision to treat as presumptive early-stage disease, we evaluate our experience with SPs treated with definitive SBRT, as there are limited published outcomes for this presentation.

RESULTS: There was no significant difference comparing patient characteristics between SP versus non-SP groups (P = NS for all comparisons): median age (years) at treatment of ≤ 75 versus > 75, median KPS of ≤ 80 versus > 80, median Charleston score of 3 versus 2, median smoking pack-years of 40 versus 50, male 42% versus 47.6%, smoking at SBRT 7.7% versus 18%, and median PET SUV of 6.7 (range: 1.0–59) vs 7.3. Eight patients (31%) did not have a diagnostic biopsy, 15 (58%) had biopsy of one nodule, and 3 (11%) had biopsy of both lesions prior to treatment. A total of 5 patients (19.2%) had nodules in the same lobe, 5 (19.2%) had nodules in the same lung, and 16 (61.6%) had nodules bilaterally. All patients were treated with definitive SBRT: 30 Gy/1 fx, 60 Gy/3 fx, 50 Gy/5 fx, or 60 Gy/8 fx. One patient developed grade 3 chest wall pain, and two had grade 2 pneumonitis. There was progression of disease in seven patients (27%). Median follow-up for the SP versus non-SP groups was 12 months (range: 1.5–49.8) versus 15.2 months. Local failure in SP versus non-SP groups was 4% (one patient) versus 7.6% (P = NS), and nodal/distant failure was 23% (six patients) versus 24.6% (P = NS). Median survival for SP versus non-SP groups was 20.7 months versus 28.4 years (P = .3 by log-rank test).

CONCLUSIONS: Patients treated with definitive SBRT for presumed synchronous primary, clinically node-negative NSCLC had statistically similar outcomes (local failure, nodal/distant failure, overall survival) compared with our institutional single primary stage I experience. SBRT offers an effective treatment approach with acceptable toxicity for this population.

(S049) Utility of Exhaled Nitric Oxide as a Biomarker for Symptomatic Radiation Pneumonitis in Esophageal and Lung Cancer Patients

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PURPOSE: Radiation pneumonitis is a common and potentially life-threatening complication of thoracic radiotherapy. Prediction of radiation pneumonitis development has proven to be difficult, however, as the predictive ability of various biomarkers (lung dosimetric parameters, serum markers, radiological imaging, etc) has produced conflicting results. Recent studies on small numbers of patients have suggested that elevated levels of exhaled nitric oxide (eNO) following thoracic radiotherapy may be useful in the prediction of radiation pneumonitis. The purpose of this study was therefore to examine eNO as a predictive biomarker for symptomatic radiation pneumonitis following thoracic radiotherapy in a larger cohort of patients and to investigate whether the source of nitric oxide production (bronchial vs alveolar) is associated with radiation pneumonitis.

METHODS: Patients receiving thoracic radiotherapy for lung or esophageal cancer recorded eNO measurements before and throughout radiotherapy (n = 193). A subset (n = 36) performed multiple eNO flow measurements at each recording, allowing for determination of bronchial (J_{B_{\text{NO}}}) versus alveolar (C_{A_{\text{NO}}}) eNO production using two-compartment modeling techniques. The Common Terminology Criteria for Adverse Events (v 4.0) was used to score pneumonitis toxicity via respiratory questionnaires and chart review. Radiation dose, eNO, J_{B_{\text{NO}}}, and C_{A_{\text{NO}}} were evaluated for predictive potential of symptomatic pneumonitis (grade ≥ 2).

RESULTS: A total of 81 esophageal and 46 lung cancer patients completed the study, with 17 patients performing multiple eNO flow measurements. Symptomatic pneumonitis developed in 10 esophageal (12%) and 30 lung (65%) patients. The mean lung dose and the percentage of the lung volume irradiated to 5, 10, 20, and 30 Gy were not predictive of symptomatic radiation pneumonitis development in either esophageal or lung cancer patients. The median eNO ratio (end radiotherapy/preradiotherapy) was elevated in symptomatic (2.0 ± 1.3) versus asymptomatic (0.7 ± 0.07) esophageal patients (P < .01) but was not associated with symptoms in lung cancer patients. An eNO ratio ≥ 1.5 predicted symptomatic radiation pneumonitis in esophageal cancer patients with a sensitivity of 56%, specificity of 99%, positive predictive value of 83%, and negative predictive value of 94%.
Symptomatic patients with multiple eNO flow measurements had elevated $J_{NO}$ but not $C_{NO}$ at the end of radiotherapy compared with preradiotherapy ($P = .02$).

CONCLUSIONS: Elevation in exhaled nitric oxide was found to be predictive of symptomatic radiation pneumonitis in esophageal cancer patients receiving thoracic radiotherapy, with a high specificity, positive predictive value, and negative predictive value but low sensitivity. An increase in eNO was not predictive of radiation pneumonitis symptoms in lung cancer patients, however. Furthermore, the ability of eNO to predict respiratory symptoms in esophageal cancer patients undergoing radiation therapy may be related to elevations in bronchial airway NO production, as increased bronchial airway NO flux was also associated with symptomatic radiation pneumonitis.

(S050) Are Insurance Companies Influencing the Decision-Making Process for Stage I Non–Small-Cell Lung Cancer (NSCLC) Patients?

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PURPOSE/OBJECTIVES: Recently, there have been advancements in the delivery of radiotherapy that have resulted in two different treatment options with equal efficacy for stage I non–small-cell lung cancer (NSCLC) patients: surgery and stereotactic body radiotherapy (SBRT). Given that lung cancer is the leading cause of cancer death in the United States, an identification of any disparity in access to care may be related to elevations in bronchial airway NO production, as increased bronchial airway NO flux was also associated with symptomatic radiation pneumonitis.

MATERIALS AND METHODS: In this analysis, we used the Florida Cancer Data System (FCDS) to create a cohort of pathologically confirmed stage I NSCLC patients. Patients were included if they had complete information on date of diagnosis, type of insurance (uninsured, insured, Medicare, or Medicaid), and treatment (surgery or SBRT). The chi-square test was used to statistically assess the differences between the groups examined.

RESULTS: A total of 41,470 stage I NSCLC patients were identified between 2005 and 2010. Of this group, 1,379 (3.33%) patients were uninsured, 13,100 (31.6%) were insured, 24,635 (59.4%) had Medicare, and 2,356 (5.7%) had Medicaid. A total of 13,737 patients were treated with surgery, and of this group, 246 (1.8%) patients were uninsured, 4,617 (33.6) patients were insured, 7,975 (58.1%) of patients had Medicare, and 899 (6.5%) patients had Medicaid. A total of 224 patients were treated with SBRT; 2 (0.9%) of these patients were uninsured, 33 (14.7%) patients were insured, 127 (56.7%) patients had Medicare, and 62 (27.7%) patients had Medicaid. There was a statistically significant different usage of treatment modality with respect to insurance status ($P < .0001$).

CONCLUSION: We found a statistically significant difference in treatment modality with respect to insurance status in this cohort of stage I NSCLC patients. Insured patients are more likely to receive surgical treatment, and Medicaid patients are more likely to receive SBRT. Longer follow-up and clinical correlation are needed to determine the clinical significance of this finding, but work is needed to ensure that there is no disparity in access to treatment options. It is imperative that treatment decisions are patient-centered and not influenced by patient insurance.

(S051) Interfraction Stability of Electromagnetic Navigational Bronchoscopy-Placed Embolization Coil Fiducial Markers for Lung Stereotactic Body Radiation Therapy (SBRT)

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INTRODUCTION: SBRT has become a standard of care for patients with early-stage inoperable non–small-cell lung cancers. Commonly, transthoracic-placed gold fiducial markers are utilized as positional surrogates for the lung lesion in pretreatment image guidance. Thus, stable fiducial positioning is essential for effective and safe treatment delivery. However, studies have shown a high dislocation rate of linear gold seeds prior to first radiation treatment, necessitating more reliable markers. Also, pneumothorax rates as high as 23% have been associated with transthoracic procedures. Electromagnetic navigational bronchoscopy (ENB) is a minimally invasive, CT-based localization device that navigates the bronchoscope to peripheral lesions previously inaccessible to traditional bronchoscopy. Our institution has been utilizing fibered platinum embolization coils (VortX-35, Boston Scientific) as fiducial markers, owing to their perceived ability to anchor in small bronchi and soft tissues better. This is the first study to assess the stability of the interfraction position of ENB-placed embolization coil markers throughout courses of SBRT.
**METHODS:** A total of 33 patients with 37 tumors underwent SBRT to 60 Gy in five fractions following ENB placement of three or four embolization coils in the vicinity of the tumor. Patient and tumor positioning was confirmed with cone-beam computed tomography (CBCT) before treatment. Two tumors were excluded from analysis, as infiltrative processes obscured accurate delineation of the tumor. Another tumor was excluded, because the CBCTs did not capture the fiducials. Therefore, simulation CT scans of 34 tumors with 106 embolization coils and the corresponding CBCTs (n = 166, 1 missing CBCT, and 3 CBCTs with poor image quality) were analyzed. The three-dimensional distance between the geometric centers of the coils and the lesion was calculated and compared between daily CBCTs and the respective simulation CT for that patient.

**RESULTS:** Two of 33 patients had pneumothoraces on post-ENB chest x-ray. At simulation, the median distance between the geometric center of the markers and the geometric center of the tumor was 17 mm (range: 3 mm–59 mm). For the two tumors with fiducial placement > 50 mm from the tumor, one incurred a pneumothorax during the procedure, while the other had collapsed airways, resulting in a technically difficult ENB. During SBRT, the median displacement of the geometric center of the markers as compared to the tumor was 1.5 mm (range: 0.01 mm–10 mm). Fiducial displacement was less than 7, 5, and 2 mm in 98%, 96%, and 67% of CBCTs, respectively. For the three tumors with a daily displacement > 7 mm, two had fiducial placements > 50 mm from the tumor while the third exhibited retraction of the tumor to the chest wall.

**CONCLUSIONS:** ENB placement of fibered platinum embolization coils as fiducials for SBRT image guidance of lung tumors was associated with a low rate of iatrogenic pneumothoraces and resulted in reliable placement of the fiducials in close proximity to the lung tumor. Embolization coils retained their relative position to the tumor throughout the course of SBRT and provide an excellent alternative to linear gold seeds. A potential limitation of their use is the relatively low density, limiting their use to kilovoltage imaging for image guidance.

**(S052) Predictors of IMRT Utilization for Lung Cancer in the United States: A SEER-Medicare Study**

Shervin M. Shirvani, MD, MPH; Jing Jiang, MS; Joe Y. Chang, MD, PhD, Benjamin D Smith, MD; UT MD Anderson Cancer Center

**BACKGROUND:** Intensity-modulated radiotherapy (IMRT) for lung cancer has been adopted for use in the clinic without randomized controlled evidence to demonstrate equivalent efficacy or reduced toxicity when compared to 3D conformal radiotherapy. The factors that predict for IMRT use in the absence of such evidence have not been elucidated.

**METHODS:** We used claims data to determine billing for IMRT from Surveillance, Epidemiology, and End Results (SEER)–Medicare records from 2001 to 2007 for 11,484 individuals aged 66 years or older with nonmetastatic lung cancer treated with radiotherapy. The impact of individual covariates (demographic, health services, tumor, and treatment factors) on IMRT utilization was determined using multivariable logistic regression. Performance status and oxygen use covariables were based upon durable medical equipment (DME) claims.

**RESULTS:** The number of patients with IMRT billing claims increased from 0.2% (3 of 1,802) of patients diagnosed in 2001 to 12.4% (168 of 1,355) in 2007. In multivariable analysis, the strongest predictor for receiving IMRT was treatment at a freestanding center (odds ratio [OR] = 2.27; 95% confidence interval [CI] = 1.89–2.78). Other features of the practice environment, including number of radiation oncologists and SEER region, were also significantly associated with IMRT use. Patients who underwent surgery were less likely to receive IMRT (OR = 0.74; 95% CI = 0.57–0.77).

**CONCLUSIONS:** These findings suggest that reimbursement policy and practice environment strongly influence adoption of IMRT for lung cancer.

**(S053) Early Clinical Outcomes Using Proton Radiation for Children With Central Nervous System Atypical Teratoid Rhabdoid Tumors**

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**BACKGROUND/PURPOSE:** Atypical teratoid/rhabdoid tumor (AT/RT) is an uncommon and aggressive tumor that often affects infants. Radiation improves survival but has traditionally been avoided in patients under the age of 3 years. We report the first cohort of AT/RT patients treated with proton therapy. We also perform a dosimetric comparison of 3D conformal proton therapy (3D-CPT), intensity-modulated proton therapy (IMPT), and intensity-modulated radiation therapy (IMRT) plans.
**Materials and Methods:** All patients with AT/RT treated at the Francis H. Burr Proton Facility between July 2004 and November 2011 were included in this study. All patients received chemotherapy. In addition to outcomes, we generated and compared 3D-CPT, IMPT, and IMRT plans for AT/RT cases requiring focal radiation.

**Results:** Ten patients with a median age of 2.3 years and a median follow-up of 27 months were identified. Two patients suffered distant relapse; one patient was successfully treated with involved-field radiation therapy and chemotherapy, while the second patient died of disease. At the last follow-up, nine patients were alive without evidence of disease. Three of seven patients with endocrine follow-up developed growth hormone deficiency, and two of seven patients developed central hypothyroidism. (See the

**Table S053**

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Abbreviations: +, INI-1 was intact; -, INI-1 deficiency; BP, brachial plexus; C, cyclophosphamide; Ca, carboplatin; Cis, cisplatin; COG ACNS 0333, Children’s Oncology Group protocol described in the text; D, doxorubicin; DFCI 02-294, Dana-Farber Cancer Institute protocol described in the text; DOD = died of disease; HSIII, modified Head Start III protocol; I, infratentorial; Mtx = methotrexate; NED = no evidence of disease; NP, test not performed; PBSCR, peripheral blood stem cell rescue; S, supratentorial; Thio, thiotepa; V, vincristine; VP-16 = etoposide.
received chemotherapy; 39% of patients were treated with surgery, 12% received radiation (RT), and 49% were treated with surgery and radiation (S + RT). A greater proportion of patients underwent surgery after 1993, though the difference did not reach statistical significance. Relapses were documented in 32% of patients. Eleven percent of patients received radiation alone, 39% received surgery alone, and 49% received both. The local recurrence rate for radiation was 53%, 88% for surgery, and 96% for radiation and surgery. Univariate analysis of factors potentially associated with local recurrence was performed, including tumor size, treatment era (before or after 1993), age (< 18, 18–25, 26–35, 35+ years), radiation dose, age, sex, osseous versus extraosseous location, chest wall versus spine versus other location, IE (ifosfamide and etoposide)-based chemotherapy, radiation dose, % necrosis at time of surgery, MRI use, and local therapy modality (S vs RT vs S + RT). Era ($P = .03$) and IE-based chemotherapy ($P = .02$) were statistically significant on univariate analysis. Both remained statistically significant on multivariate analysis ($P = .04$).

CONCLUSIONS: Local control in axial ES remains a significant clinical problem. Best outcomes are seen in patients who can have surgery or when surgery and radiotherapy are combined. Treatment in the modern era and use of IE-based chemotherapy were associated with improved local control.

(S054) Local Control Outcomes in Adult and Pediatric Patients With Axial Ewing Sarcoma

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OBJECTIVE: To analyze local control (LC) outcomes in adult and pediatric patients with localized axial Ewing sarcoma (ES).

METHODS: The records of 59 patients with ES seen at Mayo Clinic from 1977 to 2009 were studied retrospectively. Factors relevant to prognosis, survival, and LC were analyzed by Kaplan-Meier methods using JMP statistical software.

RESULTS: The median age at diagnosis was 19 years. Thirty-four percent of patients presented with chest wall tumors, 34% presented with spinal tumors, and 32% presented with other axial tumors (scapula, groin, psoas, brachial plexus, maxilla). Median follow-up for surviving patients was 60 months (range: 5–60). Five-year overall survival and event-free survival rates were 68% (95% confidence interval [CI]: 57%–82%) and 61% (95% CI: 50%–76%), respectively. In total, 100% of patients received chemotherapy; 39% of patients were treated with surgery, 12% received radiation (RT), and 49% were treated with surgery and radiation (S + RT). A greater proportion of patients underwent surgery after 1993, though the difference did not reach statistical significance. Relapses were documented in 32% of patients. Eleven percent of patients received radiation alone, 39% received surgery alone, and 49% received both. The local recurrence rate for radiation was 53%, 88% for surgery, and 96% for radiation and surgery. Univariate analysis of factors potentially associated with local recurrence was performed, including tumor size, treatment era (before or after 1993), age (< 18, 18–25, 26–35, 35+ years), radiation dose, age, sex, osseous versus extraosseous location, chest wall versus spine versus other location, IE (ifosfamide and etoposide)-based chemotherapy, radiation dose, % necrosis at time of surgery, MRI use, and local therapy modality (S vs RT vs S + RT). Era ($P = .03$) and IE-based chemotherapy ($P = .02$) were statistically significant on univariate analysis. Both remained statistically significant on multivariate analysis ($P = .04$).

CONCLUSIONS: Local control in axial ES remains a significant clinical problem. Best outcomes are seen in patients who can have surgery or when surgery and radiotherapy are combined. Treatment in the modern era and use of IE-based chemotherapy were associated with improved local control.

(S055) Involved-Field Radiation Therapy for Pediatric Hodgkin Lymphoma: Treatment Outcomes in a Single-Institution Cohort

Minh-Phuong Huynh-Le, SB, Amanda J. Walker, MD, Moody
Wharam, MD, Ido Paz Priel, MD, Stephanie A. Terezakis, MD; Johns Hopkins University School of Medicine

OBJECTIVES: Hodgkin lymphoma (HL) constitutes 6% of pediatric malignancies. Radiation therapy (RT) remains an integral component of curative therapy, although it is primarily used in intermediate-risk and high-risk patients. Here, we present clinical outcomes, including patterns of failure, in a cohort of pediatric and young adult HL patients with long-term follow-up treated with RT at The Johns Hopkins Hospital (JHH).

METHODS: Pediatric and adolescent/young adult patients 40 years of age or younger with intermediate-risk and high-risk HL who received involved-field radiation therapy (IFRT) at JHH from 1985 to 2012 were included in this retrospective analysis. Patients were evaluated for overall survival (OS), progression-free survival (PFS), and patterns of recurrence. Kaplan-Meier curves and descriptive statistics were used for analysis.

RESULTS: A total of 76 patients with intermediate-risk or high-risk HL (stages II–IV) were retrospectively reviewed with a median follow-up of 4.4 years (range: 0.5–18.3 years). The mean age at diagnosis was 21.5 years (range: 4.1–39.9), and 45 were male (59%). Forty-seven patients had stage II disease (62%), 12 had stage III disease (16%), and 17 had stage IV disease (22%). The majority of patients had nodular sclerosing subtype (82%, n = 62). Patients were treated with chemotherapy, followed by consolidative radiation to a median dose of 2550 cGy (range: 750–3960 cGy). The majority of patients received ABVD (n = 28, 37%) or ABVE-PC (n = 25, 33%) chemotherapy. Nearly all patients received conventional radiation (n = 69, 91%), one received 3D-CRT (1%), one received IMRT (1%), and five were unspecified (7%). Overall survival and progression-free survival rates of the entire cohort at 6 years were 96% and 81.6%, respectively. A total of 40 patients received < 30 Gy of IFRT (53%), and 36 patients received ≥ 30 Gy (47%). The 6-year survival rate of the cohort receiving ≥ 30 Gy was 92%, compared with 96% 6-year survival among those who received < 30 Gy of radiation (P = .63). The cohort receiving ≥ 30 Gy had a 17% overall recurrence rate, while the cohort receiving < 30 Gy had a 23% recurrence rate. Of the patients who recurred, 33% had in-field recurrences (n = 5), 33% had out-of-field recurrences (n = 5), and 33% had local and distant recurrences (n = 5). The majority of patients with an in-field recurrence alone (80%) received < 30 Gy of IFRT. Among the 15 patients with ≥ 1 recurrence of HL, the 6-year survival rate was 76%, compared with 100% in the 61 patients without recurrence (P = .0003). At last follow-up, no second malignancies were reported in any patient. All deaths (n = 6) in the cohort were related to recurrent disease.

CONCLUSIONS: The current paradigm for treatment of pediatric HL utilizes RT primarily in slow, early-responding, intermediate-risk and high-risk patients—both groups with overall lower event-free survival rates in large studies. Patients in this cohort who recurred had a significantly lower 6-year survival rate, and HL was the primary cause of all deaths. This study demonstrates that RT is an important component of therapy for these patients, with higher radiation doses resulting in better local control. Therapeutic optimization of combination chemotherapy and RT is essential for further improvement of clinical outcomes.

(S056) Using the Toronto Extremity Salvage Score (TESS) to Measure Functional Outcomes After Radiotherapy for Management of Soft Tissue Sarcoma Involving the Distal Extremity

Richard J. Cassidy, Christopher G. Morris, C. Parker Gibbs, Mark T. Scarborough, Daniel J. Indelicato, Robert A. Zlotecki; University of Florida

OBJECTIVE: The management of soft tissue sarcoma (STS) of the distal extremity is challenging in terms of achieving local control, avoiding treatment-related complications, and thus conserving functional limb capacity. This report evaluates the functional outcomes of limb-conserving oncologic management by using the validated Toronto Extremity Salvage Score (TESS) questionnaire and quantifies potential treatment-related toxicities utilizing the Common Terminology Criteria for Adverse Events (CTCAE), v4.0 guidelines.

METHODS: Thirty-three patients with STS involving the hand-wrist or foot-ankle complex received adjuvant radiotherapy with limb-conservative resections and were evaluated to determine if local control, survival, and objective functional ability were achieved. The median patient age was 49 years, and the median time of follow-up was 11.5 years. Eighteen patients had sarcomas of the hand-wrist complex, and 15 patients had sarcomas of the foot-ankle complex. Eight patients were treated with preoperative radiotherapy (median dose, 50.4 Gy), and 25 were treated with postoperative radiotherapy (median dose, 51.8 Gy). Functional outcomes were measured using TESS; patients with amputations were excluded. Potential adverse-event toxicities related to gait, limb edema, skin infection, wound complication, and wound dehiscence were assessed using the CTCAE guidelines.
RESULTS: The 5- and 10-year rates of local control were both 90%. The 10-year rates of cause-specific survival and absolute survival were 97% and 87%, respectively. The 10-year rate of distant metastasis–free survival was 84%. Four patients required an amputation for reasons other than a local recurrence or treatment complications. Eleven patients were able to complete the TESS questionnaire; scores ranged from 88 to 100 (mean, 98.2). One patient had a grade 3 skin infection. Another patient had a grade 2 wound complication and grade 2 wound dehiscence.

CONCLUSIONS: The combination of adjuvant radiotherapy and limb-conserving surgery achieves excellent local control and overall survival rates, with few toxicities. Additionally, through the TESS questionnaire, we found that this treatment modality provides robust functional preservation.

(S057) Skin Dose of Proton Scanning Techniques
Neil C. Estabrook, MD, Vadim P. Moskvin, PhD, Chee-Wai Cheng, PhD, Indra J. Das, PhD, Peter A. Johnstone, MD; Department of Radiation Oncology, Indiana University School of Medicine

OBJECTIVES: Most proton therapy (PT) currently uses passive scattering (PS) techniques, although active direction of the beam is possible using uniform scanning (US), also called “wobbling,” and spot scanning (SS) techniques are available at some centers. Scanning techniques are widely being touted as superior to PS, since scanning beams provide a reduction in neutron dose. However, today’s SS beam is too broad (1.2-cm diameter) for precise intensity modulation, and the clinical advantage of SS is not essential when treating a uniform dose across a large target, as in the cranial irradiation portion of craniospinal irradiation (CSI). It has been previously demonstrated that for narrow proton beams (< 10 mm in diameter), a higher relative dose is being deposited at the surface; thus, skin dose could be a limiting factor for clinical care. Our objective was to ascertain the relative superficial depth dose of scanning techniques using Monte Carlo simulation.

METHODS: A proton beam of 206.8 MeV (range of 27 cm) was modeled using FLUKA Monte Carlo simulation for a 250-cm source-to-axis distance with 32-cm distance from the nozzle exit. Dose distributions with spot sizes in air and water were calculated for a field width of 7 cm, typical for spinal irradiation. US and SS techniques were simulated for the same irradiation geometry.

RESULTS: Scatter within nozzle components is a major contributor to beam spread, and beam spread is responsible for a higher skin dose. The dose at 1-mm depth for a 7-cm field was 21% to 26% Bragg peak dose (Bpd) for US compared with 23% to 28% for SS (see Figure).

CONCLUSIONS: Though target coverage between US and SS is nearly the same, the skin dose for SS is relatively higher and increases with width of the spread-out Bragg peak. Future developments in reducing the spot beam size will create even higher doses at shallow depths.

(S058) Improved Node-Positive Cervical Cancer Progression-Free Survival After Triapine Radiochemotherapy
Charles A. Kunos, MD, PhD; Case Western Reserve University and Summa Health Systems

PURPOSE: Triapine potently inhibits cervical cancer ribonucleotide reductase, an overexpressed enzyme that generates deoxynucleotides used to repair radiochemotherapy-induced DNA damage. The goal here was to study prognosis after triapine radiochemotherapy in women with node-positive cervical cancer detected by computed tomography (CT) and positron emission tomography (PET) with [18F]-fluoro-2-deoxy-D-glucose (FDG).

MATERIALS AND METHODS: A total of 35 women with cervical cancer underwent CT lymph node staging and whole-body FDG-PET. Women were treated with intravenous triapine three times weekly (25 or 50 mg/m²), once-weekly cisplatin (40 mg/m²), and daily pelvic radiation (45
Gy) followed by brachytherapy (30–40 Gy). They were observed afterward for a median 24 months (range: 2–78 months). Progression-free survival was evaluated by the Kaplan-Meier method.

RESULTS: Pretherapy FDG-PET/CT detected abnormal FDG uptake in pelvic lymph nodes in 21 (60%) and in para-aortic lymph nodes in 10 (29%) of the 35 women. The 2-year progression-free survival rate for women with FDG-PET/CT node-positive pelvic lymph node status was 68% (95% confidence interval [CI] = 55%–81%), which compares favorably to a 49% historical control. The 2-year progression-free survival rate, based solely on node-positive para-aortic lymph node status, was 52% (95% CI = 29%–75%), which weighs against an 18% historical control.

CONCLUSIONS: Findings indicate that triapine radiochemotherapy provides improved progression-free survival in women with FDG-PET node-positive cervical cancer. A prospective NCI-sponsored randomized phase II trial of triapine radiochemotherapy versus radiochemotherapy is planned utilizing 3-month post-therapy FDG-PET/CT as a response indicator.

(S059) Postoperative Radiation Therapy and Concurrent Cisplatin Followed by Carboplatin/Paclitaxel for Stage III Endometrial Cancer

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PURPOSE: The optimal sequencing of adjuvant chemotherapy for advanced endometrial cancer is controversial. One approach is concurrent pelvic irradiation (RT) and cisplatin, followed by 4 cycles of carboplatin/paclitaxel, as in RTOG 9708. Opponents of this approach cite the small number of stage III patients enrolled (n = 27). The aim of this study is to report an institutional experience using this regimen for FIGO 2009 stage III endometrial cancer.

METHODS: From January 2004 to December 2009, 40 stage III endometrial cancer patients were treated at a single institution with definitive hysterectomy/bilateral salpingo-oophorectomy, RT with concurrent cisplatin, and carboplatin/paclitaxel. Seven patients were stage IIIA and 33 were stage IIIC. Histology was endometrioid in 31 patients (77.5%; 15 grade 1, 11 grade 2, 5 grade 3), papillary serous in 6 patients (15%), clear cell in 2 patients (5%), and mucinous in 1 patient (2.5%). Nineteen patients (47.5%) were ≥ 60 years of age, 23 (57.5%) had ≥ 50% myometrial invasion, 30 (75%) had lymphovascular invasion, and 11 (27.5%) had cervical stromal invasion. A total of 39 patients (97.5%) underwent pelvic lymphadenectomy (median 16 lymph nodes [LNs], range: 2–45), and 28 (70%) underwent para-aortic lymphadenectomy (median 8 LNs, range 2–32). Peritoneal washings were performed in all cases and positive in five (12.5%). No patient had residual disease postoperatively. RT was given to a median dose of 50.4 Gy. Patients received concurrent cisplatin, followed by carboplatin and paclitaxel.

RESULTS: At a median of 49 months (range: 11–101), there were eight recurrences and six deaths, all from endometrial cancer. The 5-year freedom from progression rate was 79% (95% confidence interval [CI] = 67%–91%), and the overall survival rate was 85% (95% CI = 73%–97%). At 5 years, the rate of vaginal recurrence was 3% (95% CI = 0%–9%), 3% for nonvaginal pelvic recurrence (95% CI = 0%–8%), 11% for para-aortic recurrence (95% CI = 0%–22%), 5% for peritoneal recurrence (95% CI = 0%–12%), and 11% for other distant recurrences (95% CI = 0%–22%). Thirty-three patients (82.5%) were able to complete the planned regimen of cisplatin-RT and 4 cycles of carboplatin/paclitaxel. Acute toxicities included 11 cases of neutropenia (27.5%; 3 grade 1, 4 grade 2, 4 grade 3, no febrile neutropenia), 31 cases of anemia (77.5%; 16 grade 1, 13 grade 2, 2 grade 3), and 19 cases of thrombocytopenia (47.5%; 18 grade 1, 1 grade 2). Acute nonhematologic toxicity included 19 cases of nausea/vomiting (47.5%; 15 grade 1, 3 grade 2, 1 grade 3), 18 cases of proctitis (45%; 17 grade 1, 1 grade 2), 34 cases of diarrhea (85%; 18 grade 1, 14 grade 2, 2 grade 3), and 11 cases of cystitis/frequency (30%; 11 grade 1, 1 grade 2). Late toxicities included 2 cases of proctitis (5%; 2 grade 1), 5 cases of diarrhea (12.5%; 5 grade 1), 2 bowel obstructions (5%; 2 grade 2), 12 cases of cystitis/frequency (30%; 11 grade 1, 1 grade 2), 2 cases of vaginal dryness (5%; 2 grade 1), 2 vaginal stenoses (5%; 2 grade 1), 10 cases of lower extremity edema (25%; 9 grade 1, 1 grade 2), and 5 cases of peripheral neuropathy (12.5%; 5 grade 1).

CONCLUSIONS: These excellent outcomes for stage III endometrial cancer patients confirm the results of RTOG 9708. Whether this regimen is superior to chemotherapy or RT alone must await the results of the GOG and PORTEC trials, respectively.
(P001) Features of Radiation Reactions in Cancer Patients Previously Subjected to Chronic Accidental Exposure

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OBJECTIVE: The purpose of this study was to determine the characteristics of radiation reactions in cancer patients with chronic radiation exposure history, identifying the factors influencing the response of normal tissues, the dynamics of the tumor, and changes in hematological parameters in cancer patients previously exposed to chronic accidental exposure associated with activity of the Mayak nuclear facility.

MATERIALS AND METHODS: We have carried out a retrospective analysis of medical data of patients treated with external beam radiotherapy for solid tumors of various localizations. The study group comprised 89 patients who had an indication of chronic radiation exposure history. A total of 182 patients in the control group had not been exposed to radiation. Patients in the study and control groups were matched for age, sex, diagnosis, and treatment.

RESULTS: The frequency of radiation reactions did not differ significantly \((P = .957)\): 59.6% in the study group (53 patients) and 60.3% in the control group (108 patients). The distribution of reaction severity did not differ significantly between groups \((P = .176)\). However, the main group was dominated by second-degree reactions, the frequency of which was 64.15%, while first- and second-degree reactions in the control group were distributed almost equally (51.4% and 48.6%, respectively). In some cases, symptoms of the reactions caused the need to interrupt treatment. The number of breaks was significantly higher in the study group than in controls \((10 [11.2\%] \text{ versus } 7 \text{ patients } [3.8\%]; P = .018)\). The presence and frequency of breaks in the course of radiotherapy can be considered one of the objective indicators of tolerance to radiation therapy. There was a statistically significant difference in the dynamics of the process \((P = .048)\), indicating a lower frequency of the positive effect of radiotherapy in previously irradiated patients. The erythrocyte, hemoglobin, and white blood cell content did not undergo significant changes during radiotherapy. The lymphocyte content in the peripheral blood of patients from the study group decreased during radiation therapy by 40%. In the control group, the reduction of lymphocytes was 16%. These differences in the dynamics of lymphocytes were statistically significant \((P < .001)\). Reactions were more severe in the main group of patients with head and neck tumors \((P = .004)\). Among patients with tumors of the lung, such an effect was not observed. There was no statistically significant effect of absorbed doses by red bone marrow \((P = .534)\) or soft tissue \((P = .359)\) on the frequency of radiation reactions (CMC).

CONCLUSIONS: These data suggest that the main factors affecting the frequency of radiation reactions in cancer patients with chronic radiation exposure history are similar to those in patients without prior exposure to radiation. However, we can make a conclusion about some changes in radiosensitivity in patients previously exposed to chronic irradiation. Implementation of these data into the clinic will help to optimize treatment plans and reduce the incidence and severity of reactions, thereby improving the quality of life in cancer patients.

(P002) Clinical Outcomes of Patients Treated for Bilateral Breast Carcinomas With Accelerated Partial Breast Irradiation (APBI) Using a Multilumen Catheter

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BACKGROUND: Reports on accelerated partial breast irradiation (APBI) for synchronous bilateral breast cancers are lacking. In this study, we review and report the outcomes of patients with bilateral breast carcinomas treated with APBI using a multilumen catheter.

MATERIALS AND METHODS: Between August 2008 and September 2012, a total of 90 patients were treated with breast-conserving therapy and adjuvant APBI. Five patients with bilateral ductal carcinoma in situ (DCIS) were treated with bilateral APBI at the same time. All of them received 3,400 cGy in 10 fractions delivered twice daily using high-dose-rate radiation with iridium-192. The dose was prescribed to 1 cm from the applicator surface. We report on the tumor characteristics and dosimetric data, and evaluate patients’ clinical outcomes and toxicities according to RTOG 9517 and RTOG 9804.

RESULTS: The median age was 61 years (range: 61–75). All patients had bilateral biopsy-proven DCIS. Contralateral DCIS was detected with preoperative MRI performed before lumpectomy. Median tumor size was 4.8 mm on the right and 10 mm on the left. Three patients had positive ER.
and PR receptor status in both breasts, and two had positive receptors on one side and was negative on the other. Margins were negative in the 10 pathology specimens. Seven specimens had a high nuclear grade, and three had a low to intermediate grade by SBR criteria. Two patients received hormone therapy. All five patients were treated with the Contura Multi-Lumen balloon. Median follow-up was 35 months (range: 8–37 months). The average tumor bed–to-skin distance was 7.5 mm (range: 3.6–10) on the right side and 13.1 mm on the left (range: 6.7–25). The average PTV (planning target volume) and PTV-eval were 92% and 73% on the right and 91% and 79% on the left, respectively. The median maximal skin dose was 115% on the right (range: 100%–128%) and 106% (range: 49%–128%) on the left. The median maximal rib dose was 87% (range: 63%–133%) on the right and 105% (range: 70%–120%) on the left side. The median V90, V95, and V100 were 99%, 97%, and 93% on the right side and 99%, 98%, and 95% on the left, respectively. The average V150 and V200 were 31 cc and 8.5 cc on the right and 32 cc and 9.6 cc on the left, respectively. At a median of 3 weeks after treatment, all of the patients had good to excellent cosmetic outcomes: two patients had grade 1 skin toxicity, one patient had grade 2 skin toxicity, and two did not have any skin reaction. At the last follow-up, grade 1 skin toxicity was reported in two patients, and the remaining patients did not have any residual late skin reaction. Cosmesis was excellent in all of the patients. There was no locoregional recurrence.

**CONCLUSION:** To our knowledge, this is the largest series including patients treated for bilateral breast cancer with APBI using a multilumen catheter. APBI is safe and effective and was associated with excellent cosmetic outcomes in this small population of patients with bilateral DCIS and MRI-detected contralateral DCIS. Long-term results in a larger population are needed.

**(P003) Once-Daily Radiation Therapy for Inflammatory Breast Cancer: The Northwestern Experience**

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**PURPOSE:** To report contemporary outcomes for inflammatory breast cancer (IBC) patients treated with once-daily radiation therapy at Northwestern University.

**MATERIALS AND METHODS:** We retrospectively reviewed the charts of 41 IBC patients treated with curative intent between July 1995 and April 2012. Seven patients presented with distant metastatic (DM) disease, six patients did not undergo surgery as part of a multimodality approach, and five patients received a second course of local radiation therapy (RT). A single patient received twice-daily radiation therapy. Kaplan-Meier estimation was used to assess locoregional control (LRC), disease-free survival (DFS), and overall survival (OS).

**RESULTS:** The median follow-up time was 29 months; 17 (41%) patients were ER/PR-negative, and 15 (37%) patients were HER2/neu-amplified. Of the 35 (85%) patients who underwent surgery, 32 (91%) received postoperative RT and completed all of the intended therapy. As part of their chemotherapy regimen, 33 (80%) patients received a taxane, and 8 of 15 (53%) HER2/neu-amplified patients received trastuzumab (Herceptin). With RT, 14 (34%) patients received concurrent hyperthermia, and 12 (29%) patients received concurrent chemotherapy, most frequently capecitabine (Xeloda). Of the total of 13 patients who initially presented with metastatic disease, did not undergo surgery as a component of multimodality treatment, and/or received a second course of RT, 8 patients (61%) experienced a local recurrence (chest wall = 6, axilla = 1, SCV fossa = 1, and concurrent DM = 6). In comparison, in the entire cohort 15 patients (37%) experienced a local recurrence (chest wall = 13, axilla = 1, SCV fossa = 1, and concurrent DM = 8). For the entire cohort, the 5-year rates of OS, LRC, and DFS were 43%, 33%, and 32%, respectively. The ER/PR-negative patients had a 5-year OS of 46% versus 41% for ER/PR-positive patients (P = .99). Those patients who received ≥ 60.4 Gy to the chest wall had 5-year OS and LRC rates of 45% and 43%, respectively, versus 43% and 24%, respectively, for patients who received < 60.4 Gy to the chest wall (P = .77 and .40, respectively).

**CONCLUSIONS:** Outcomes for IBC patients remain modest and may vary between institutions. A higher dose to the chest wall may possibly improve local regional control but does not appear to significantly affect overall survival. Further analysis is needed to report the benefit of patients who underwent a single course of RT as part of a trimodality approach, as well as the potential benefit of concurrent hyperthermia or chemotherapy.

**(P004) Quantitative Assessment of Thyroid Gland Dosimetry in Breast Cancer Patients Receiving Supraclavicular Radiation**

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INTRODUCTION: In patients with breast cancer, incidental inclusion of a portion of the thyroid lobe may occur when treatment fields are designed to target the supraclavicular nodes. The aim of this study is to evaluate the dose distribution to the thyroid gland in patients with breast cancer who require supraclavicular radiation (SCV RT).

MATERIALS AND METHODS: The treatment plans of 50 consecutive patients with breast cancer treated with standard tangential fields to the intact breast (n = 14) or chest wall (n = 36) were reviewed. All included patients received SCV RT using a standard anterior field arrangement with a 10-degree (n = 35) or 15-degree (n = 15) gantry offset from midline, typically with a 6-MV beam. The prescription dose to the SCV field was 50 Gy at 2 Gy/fraction, with the maximum dose (Dmax) limited to less than 110% of the prescribed dose. The calculation point depth was selected to allow the 45 Gy isodose line (IDL) to encompass the SCV nodes. SCV nodal volume contours specifically excluded overlap with the thyroid gland, as endorsed by the Radiation Therapy Oncology Group (RTOG) consensus breast contouring atlas. The thyroid gland (including the left lobe, isthmus, and right lobe) of each patient was delineated on the CT radiation planning scan using a predefined, optimized auto-window level. A dose-volume histogram (DVH) was generated using Eclipse treatment planning software. Dosimetric analysis of the thyroid organ at risk (T-OAR) was performed with quantification of Dmax and mean dose (Dmean). Values for the % of T-OAR volumes receiving 45 Gy, 25 Gy, 5 Gy, 2 Gy, and 1 Gy (V45, V25, V5, V2, and V1) were collected from the DVH.

RESULTS: Median patient age was 52 years (range: 28–80 years). Six patients required use of a mixed 6-MV/18-MV beam for the SCV field, while all other patients were treated with only a 6-MV beam. The median depth of the SCV calculation point was 3 cm (range: 2–5). In all patients, a minimum of 90% of the SCV nodal volume received at least 45 Gy. The median Dmax and Dmean to the thyroid gland were 54 Gy (range: 47–56) and 14 Gy (range: 3–28) respectively. The median V45, V25, V5, V2, and V1 of the T-OAR were 14% (range: 0%–38%), 26% (range: 2%–55%), 40% (range: 8%–61%), 54% (range: 18%–84%), and 85% (range: 43%–100%), respectively.

CONCLUSIONS: The addition of an SCV field for regional nodal RT exposed small volumes of the thyroid gland to substantially high doses of radiation. Over one-fourth of the total gland volume was routinely receiving 50% of the prescription dose. The possibility of increasing the risk of thyroid disorders must be considered in the context of clinical decision-making, and patients should be appropriately counseled about potential side effects to the thyroid gland when receiving SCV RT for breast cancer.

(P005) Quantifying the Benefit of Pathologic Complete Response After Neoadjuvant Chemoradiotherapy in the Treatment of Rectal Cancer

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PURPOSE: Patients achieving a pathologic complete response (pCR) to neoadjuvant therapy for esophageal cancer have better outcomes than patients with residual disease at time of resection. There are fewer data available in rectal cancer (RCa) regarding the prognostic utility of pCR status at time of resection. We completed a comprehensive literature review to quantify the benefit of pCR versus the presence of residual disease after neoadjuvant chemoradiation for RCa.

MATERIALS AND METHODS: A comprehensive search of publication databases was performed using the keywords “rectal,” “rectum,” “carcinoma,” “cancer,” and “complete response,” with review of the referenced articles. Forty-six articles were initially selected as appropriate, of which 15 provided survival data for patients obtaining a pCR versus those with residual disease. Eight studies were excluded, resulting in a final analysis of seven studies (n = 1,279). All included papers stratified patients obtaining a pCR at surgery and those who did not. Data were analyzed by publication and in pooled fashion where the data allowed.

RESULTS: In six of the seven studies, patients received 5-FU–based chemotherapy with neoadjuvant radiotherapy of 45 to 50.4 Gy. Total mesorectal excision (TME) as the type of surgery was specifically mentioned for 626 patients (49%). The frequency of a pCR ranged from 9% to 26% (mean 15.3%). Three of the seven studies documented a significant difference in overall survival (OS) between patients with a pCR and those without; four studies documented a significant difference in disease-free survival (DFS). Only three of the five studies noted a significant difference in local control (LC).

CONCLUSION: In esophageal cancer, patients achieving a pCR to neoadjuvant chemoradiation uniformly experience a survival benefit; this is not clearly the case with RCa.
**Borderline Resectable Pancreatic Adenocarcinoma Following Neoadjuvant Radiation Therapy for**

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**BACKGROUND:** Margin-negative (R0) surgical resection is the only potentially curative therapy for pancreatic cancer. For patients deemed borderline resectable (BL), neoadjuvant chemoradiotherapy (NCRT) increases the likelihood of subsequent R0 resection and improves overall survival. Prognostic factors for achieving resection following NCRT have yet to be clearly identified.

**METHODS:** A total of 50 consecutive patients diagnosed with BL pancreatic cancer by a multidisciplinary tumor board from 2008 to 2012 were retrospectively identified. Pre- and post-NCRT CT scans and surgical specimens were centrally reviewed by a blinded radiologist and pathologist, respectively.

**RESULTS:** A total of 29 patients underwent resection following NCRT, while 21 remained unresectable. Between the two groups, age, gender, mean RT dose, and proportion of pancreatic head tumors were not significantly different. Lack of the following factors was favorably associated with resection: SMV/PV encasement ($P = .01$), SMA involvement ($P = .02$), ascites ($P = .01$), and questionable/overt metastases ($P = .01$). Notably, celiac artery involvement/encasement, common hepatic artery encasement, and percentage change in tumor volume were not significant predictors of resectability (all $P > .05$). Additionally, tumor volume and degree of individual vessel involvement did not significantly change from scans before and after NCRT (all $P > .05$). Median OS rate was 22.9 versus 13.0 months in resected and unresected patients, respectively ($P < .001$). Of resected patients, 93% had negative margins, 28% had positive nodes, 27% demonstrated < 10% viable tumor, and 12% had a pathologic complete response at surgery.

**CONCLUSION:** Certain radiographic features appear to be more strongly associated with resectability after NCRT than others. Despite the fact that tumor-vessel interactions do not change significantly due to NCRT, subsequent R0 resection rates are high, nodal involvement is low, nearly one-third of patients have minimal residual tumor, and outcomes are improved. Further studies are needed to elucidate novel biomarkers or functional imaging predictors for successful resection following neoadjuvant therapy.

**A Novel Method of Dose Calculation Utilizing PET-CT in Patients Treated With Radioembolization**

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**BACKGROUND:** Radioembolization is an emerging therapeutic option for the treatment of metastatic and primary tumors of the liver. Two devices, TheraSphere and SIR-Spheres, are available to treat patients. Simple formulas are currently utilized in order to prescribe the appropriate activity to treat a liver volume, ranging from a segment to the whole liver. While the activity infused to each patient is known, limited data are available concerning the dose delivered to tumor volumes from this activity. This makes correlation of the response to dose impossible and also makes integration of traditional external beam radiotherapy challenging. The aim of this study is to establish a method for calculation of the dose delivered to intrahepatic targets.

**MATERIALS AND METHODS:** Six patients were enrolled in this study as part of one approved clinical trial and one approved humanitarian device exemption. All patients underwent radioembolization for primary or metastatic liver tumor(s). Each patient underwent a posttreatment PET-CT for the quantification of activity of yttrium-90–labeled microspheres using the small probability of pair production from yttrium-90 beta decay. The last four patients also underwent a pretreatment PET-CT in order to quantify the background noise activity so that it could be subtracted from the posttreatment PET activity. The dose kernel was calculated using the Fluka Monte Carlo code, which was subsequently convolved with the PET-measured activity. Dose-volume histograms were created for up to three target tumors, liver, and right kidney. Descriptive statistics were calculated.

**RESULTS:** Four patients underwent treatment with SIR-Spheres for liver metastases from colorectal cancer, and two patients were treated with Therасhphere for hepatocellular cancer. A total of 11 target tumors were contoured on posttreatment PET-CT scans for dosimetric evaluation. Mean prescription activity was 1.51 GBq (range: 0.58–3.29 GBq). The resulting mean maximum measured dose to targets was 167 Gy (range: 71–311 Gy). Mean minimum dose to 70% of
target (D70) was 54 Gy (range: 29–83 Gy). Mean minimum dose to 90% of target (D90) was 36 Gy (range: 13–58 Gy). The mean volume of liver receiving at least 30 Gy (V30) was 856 cc (range: 257–1,199 cc). The mean maximum dose to 1 cc of the right kidney was 42 Gy (range: 28–60 Gy). The mean maximum dose for Therasphere and SIR-Spheres was 266 Gy versus 111 Gy, respectively. The mean D70 for Therasphere and SIR-Spheres was 79 Gy vs 40 Gy, respectively. The mean D90 for Therasphere vs SIR-Spheres was 48 Gy and 28 Gy, respectively.

CONCLUSIONS: This pilot project demonstrates that dose can be calculated in patients after radioembolization, utilizing PET-CT–measured activity. Although this represents preliminary work with a small number of patients, the doses to patients treated with Therasphere may be larger. This process could lay the foundation for more sophisticated dose prescription methods in the future.

(P008) Cost-Effectiveness Analysis of Stereotactic Body Radiotherapy and Percutaneous Radiofrequency Ablation for Medically Inoperable Isolated Liver Metastases From Colorectal Cancer

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INTRODUCTION: Regional treatment of isolated hepatic metastases from colorectal cancer delays the need for systemic chemotherapy and may prolong overall survival. The standard treatment is surgical resection. For patients who are not surgical candidates, local control can be achieved via radiofrequency ablation (RFA) or stereotactic body radiation therapy (SBRT). These two minimally invasive approaches have never been directly compared to each other, and no expert consensus exists as to the standard of care. The cost-effectiveness of these techniques has not been compared in this setting.

MATERIALS AND METHODS: A retrospective cohort of rectal carcinoma patients treated with radiation therapy at Montefiore Medical Center from 1999 to 2011 was considered for this study.

RESULTS: The incremental cost-effectiveness ratio (ICER) for SBRT over RFA was estimated to be $33,602/quality-adjusted life-year (QALY). Sensitivity analysis shows that the following factors had the greatest impact on ICER: cost of RFA, likelihood of re-treatment, RFA complication rate, and liver-only recurrence rate after RFA.

CONCLUSION: Compared with RFA, SBRT has an estimated ICER of $33,602/QALY. This ICER value falls well within the range of what is considered reasonable and acceptable in the literature for the cost per QALY from the societal perspective. Cost-effectiveness models such as this one can inform clinical decision-making and help guide prospective clinical trials that incorporate economic evaluation and measure patient utility preference for various health states.

(P009) Neoadjuvant Versus Adjuvant Radiation Therapy for the Treatment of Rectal Cancer

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PURPOSE/OBJECTIVE: Recent randomized trials suggest that neoadjuvant radiotherapy in the treatment of rectal cancer may result in better outcomes than adjuvant radiation treatment. These benefits include decreased tumor recurrence, reduced preoperative tumor stage, and increased rates of sphincter-sparing surgery. However, not all institutions are convinced, and many still prefer the upfront surgical approach. Here, we review the Montefiore Medical Center experience of rectal cancer patients treated with either neoadjuvant or adjuvant radiation therapy to evaluate the benefit of the neoadjuvant approach.

MATERIALS AND METHODS: A retrospective cohort of rectal carcinoma patients treated with radiation therapy at Montefiore Medical Center from 1999 to 2011 was considered for this study.

RESULTS: Of the 109 evaluable patients included in the study, 69 (63.3%) were treated with neoadjuvant radiotherapy +/- chemotherapy followed by surgery, and 40 (36.7%) were treated with surgery upfront followed by adjuvant radiotherapy +/- chemotherapy. Tumor recurrence was observed in 14.5% and 20.0% (P = .69) among the neoadjuvant and adjuvant treatment groups, respectively. In the neoadjuvant group, 20.3% of patients demonstrated a complete response, 11.6% had an excellent response, and 18.8%
had a moderate response to neoadjuvant therapy, with the levels of response corresponding to a graded reduction of T-stage preoperatively versus postoperatively. Furthermore, 26.8% of patients originally only eligible for an abdomino-perineal resection were converted to a sphincter-sparing, low anterior resection after neoadjuvant treatment.

CONCLUSION: Neoadjuvant radiotherapy conferred a trend toward lower local recurrence rates compared with adjuvant radiotherapy for the treatment of rectal cancer. There was also a dramatic tumor response to neoadjuvant therapy in half of all patients, allowing some cases to convert to a sphincter-sparing operation.

(P010) Image-Guided Radiation Treatment Planning for Rectal Cancer Using MRI and PET-CT
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PURPOSE/OBJECTIVE: To precisely visualize the rectal tumor mass for image-guided radiation therapy planning for preoperative treatment in rectal cancer patients.

MATERIALS AND METHODS: High-resolution MRI scans were performed in 26 patients with biopsy-proven, endoscopic, ultrasound-staged rectal cancer. All MRI scans were obtained on a 3T (Siemens TRIO TIM) scanner using a six-element body RF matrix coil. The contrast-enhanced 3D T1-weighted images were acquired using a volumetric interpolated breath-hold exam (VIBE) sequence with TR/TE: 3.87/1.44 ms, 4 NEX at 1.2 × 0.9 × 3.0 mm spatial resolution in parallel imaging mode (acceleration factor of 2), yielding 60 slices in 2:54 min. T2-weighted images were obtained using a turbo spin-echo sequence with TR/TE: 6,440/130 ms, 3 NEX at 1.2 × 0.9 × 3.0 mm resolution with an acceleration factor of 2, yielding 56 slices in 2:48 min. All patients underwent PET-CT simulation, and MR/PET-CT registration was performed to delineate the gross tumor volume (GTV).

RESULTS: Tumor extent was clearly outlined in all 26 patients with the help of MRI images, and MR/PET-CT fusion scans helped to localize the tumor mass and its extensions more clearly than CT alone. GTV was therefore more accurate with the use of MR/PET-CT fusion. This resulted in appropriate coverage of the tumor and allowed for highly conformal treatment fields.

CONCLUSIONS: Accurate delineation of rectal tumor mass is necessary in our transition from three-field radiation treatment fields to highly conformal image-guided intensity-modulated radiation therapy techniques. The use of high-resolution MRI and functional imaging with PET-CT for preoperative radiation treatment planning allows precision in conformal targeted therapy for rectal cancer.

(P011) Chemoradiation Therapy Versus Chemotherapy Alone for Gastric Cancer After R0 Surgical Resection: A Meta-Analysis of Randomized Trials
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BACKGROUND AND OBJECTIVES: The standard of care for locally advanced gastric cancers (T2–4 or node-positive) is surgical resection with either chemoradiation therapy or chemotherapy alone. Current national guidelines include category 1 recommendations for either perioperative chemotherapy or adjuvant chemoradiation, at the discretion of the treating physician. Gastric cancer trials have suggested a local control and disease-free survival advantage for chemoradiation when compared to chemotherapy alone. However, no large, randomized trials demonstrating a statistically significant benefit of adjuvant chemoradiation compared to chemotherapy alone have been reported. It remains unclear whether one strategy is better than the other.

METHODS: Electronic searches were conducted on PubMed and EMBASE for randomized, controlled clinical trials with results reported before November 2012. Only randomized, controlled clinical trials involving patients with histologically confirmed gastric cancer status postcurative resection with negative surgical margins were included. The interventions being compared were adjuvant chemoradiation therapy versus chemotherapy alone with any chemotherapy regimen. The primary outcome of interest was disease-free survival. Two authors assessed trial eligibility and extracted data. The primary outcome of the study was disease-free survival. The secondary outcome was overall survival. Events were defined as disease-free and overall survival failures, respectively. The Mantel-Haenszel fixed effects odds ratio method was used to calculate effect sizes.

RESULTS: Five randomized, controlled clinical trials satisfied the inclusion criteria and were included in the current meta-analysis. A total of 820 patients were evaluated in these studies, with 413 patients randomized to chemoradiation therapy and 407 patients randomized to chemotherapy alone. Adjuvant therapy with chemoradiation was associated with a significant increase in disease-free survival.
when compared with chemotherapy alone, with 138 events in the chemoradiation group and 169 events in the chemoradiation group (odds ratio [OR] = 1.45; 95% confidence interval [CI] = 1.08–1.94; \( P = .01 \)). Three of the five trials reported on overall survival, and we were unable to detect a significant difference in overall survival between the two groups.

**CONCLUSIONS:** In patients with gastric cancer postsurgical resection, adjuvant chemoradiation therapy was associated with higher disease-free survival when compared with chemotherapy alone. Future gastric cancer trials should directly examine subsets of patients who benefit most from chemoradiation.

**(P012) Feasibility of Stereotactic Body Radiotherapy (SBRT) Dose Escalation Using Simultaneous Integrated Boost (SIB) in Patients With Locally Advanced Pancreatic Cancer (LAPC)**

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**BACKGROUND:** Forty percent of locally advanced pancreatic cancer (LAPC) patients have unresectable disease. Local control rates with concurrent chemoradiation have been inadequate, and down-staging rates have been poor. Recent studies suggest that stereotactic body radiotherapy (SBRT) may be a promising treatment strategy for LAPC. SBRT with simultaneous integrated boost (SIB) may allow dose escalation to the superior mesenteric artery (SMA) and/or celiac axis. Boost to areas that limit resectability may increase downstaging, enhance resectability of borderline resectable tumors, and increase the margin-negative resection rate, while potentially improving local control. Here, we evaluate dose escalation possibilities using SIB-based SBRT for LAPC patients.

**METHODS:** Ten consecutive patients previously treated with conventional SBRT (5 Gy \( \times \) 5) were selected. Planning target volumes (PTVs) ranged from 29 to 132 cc. Volumes within the PTV involving the SMA and/or celiac axis were contoured as boost target volumes (BTVs) (range: 2–14 cc). Volumetric modulated arc optimization (2–3 arcs) was performed with BTV dose 60 Gy and PTV prescription 25 Gy. Our standard clinical normal tissue dose goals were used: spinal cord V8Gy = 0.3 cc, total kidneys D75% = 12 Gy, liver D50% = 12 Gy, stomach/duodenum/bowel V15Gy = 9 cc, V20Gy = 3 cc, V33Gy = 0.3 cc, and D50% = 12 Gy. Boost efficiency (ratio of BTV mean dose to 95% PTV dose) was calculated.

**RESULTS:** No patient experienced CTCAE v.4 grade 3 toxicity after conventional SBRT (5 Gy \( \times \) 5, median follow-up 3 months), confirming adequacy of the normal tissue limits used. SIB-escalated plans for 9 of 10 patients achieved the same PTV coverage obtained in the respective non-SIB plans while still meeting all normal tissue dose limits. Those nine patients had an average boost efficiency of 2.0 (range: 1.9–2.1), average BTV mean dose of 52 Gy (range: 49–59 Gy), and average BTV minimum dose of 47 Gy (range: 34–57 Gy). The average GTV mean dose was 38 Gy (range: 31–51 Gy), 39% higher than that for non-SIB plans.

**CONCLUSIONS:** Dose-escalated SIB SBRT for LAPC is dosimetrically achievable without exceeding normal tissue limits. The achievable BTV dose is anatomy-dependent; we suggest a BTV dose prescription of 34 to 57 Gy for a prospective study to assess clinical outcomes in LAPC patients using SIB-based dose escalation.

**(P013) Improved Biochemical Outcomes in Patients With Prostate Cancers With Dose-Escalated Radiation and Hormones: A Single-Institution Experience**

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**BACKGROUND:** Short-term androgen deprivation therapy (ADT) combined with radiation therapy (RT) reduces biochemical failures and improves disease-free and overall survival in patients with early-stage and intermediate- and high-risk prostate cancer. This improvement was seen in RT doses of 66.6 Gy and lower; yet, dose escalation trials have shown a clear benefit in disease control when treating the prostate beyond 70 Gy. Our single-institution retrospective study was done to determine whether the use of ADT is still beneficial in patients who received escalated RT doses.

**METHODS:** We performed a retrospective review of all early-stage and intermediate-risk (26) and high-risk (3) patients who received RT to their prostate above 66.6 Gy (median dose 75.6 Gy, range: 68 Gy–79.8 Gy) at Hahnemann University Hospital in Philadelphia, Pennsylvania between October 1999 and March 2011. We analyzed a total of 29 patients who received external beam radiation (23 treated with IMRT, 6 with 3D CRT), 15 of whom received short-term hormones and 14 who did not. Median pretreatment PSA for both groups was 11.0 ng/mL (range: 4.1–38), with a median PSA for the no-hormone group of 5.4 (range: 6.0–19.0) and 14.0 (range: 5–38) for the group that received ADT. One patient had a Gleason score of 5, three patients had a Gleason score of 6, and 22 patients had a Gleason...
respectively. There was no significant difference in median dose received by the bladder or rectum between IMRT and VMAT, but there was an increase in median dose received by the femoral heads in VMAT plans. The mean NTCPs for grade ≥ 4 bladder and rectal toxicities for IMRT and VMAT were 0.0, 0.0 and 3.3, 3.2, respectively. There was no statistically significant difference between the two. The total MUs and treatment delivery time were reduced by 17.3% and 17.3%, respectively.

**CONCLUSIONS:** VMAT and IMRT plans for stereotactic postprostatectomy radiation therapy yield similar risks for late stage 4 rectal and bladder toxicity. VMAT is associated with fewer monitor units and a faster time of delivery.

(P016) The Impact of the Intensified Bimodality Approach on Low-Risk Prostate Cancer Outcomes
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**PURPOSE:** The discrepancy between biopsy-based Gleason score (GS) and postprostatectomy findings suggests that low-risk disease may harbor more aggressive pathology. The purpose of the current study is to investigate the impact of bimodality-intensified treatment (I-125 brachytherapy [BT] boost and external beam radiotherapy [EBRT]) on outcomes.

**MATERIALS AND METHODS:** This is a single-institution retrospective study that was fully approved by our IRB. From January 2000 to December 2010, a total of 60 patients with low-risk prostate adenocarcinoma were identified. All patients underwent initial I-125 BT (108 Gy) followed by EBRT (50.4 Gy at 1.8 Gy/fraction) to the prostate only. RT was delivered via either 3-D RT (10%) or intensity-modulated radiation therapy (IMRT) (90%) after 3 weeks from the BT. The rationale of that sequence was to use the I-125 physical decay as a simultaneous integrated BT boost (SIBB) during EBRT. Eligible criteria were PSA ≤ 10, ≤ T2a, and GS ≤ 6. RT-induced toxicity was scored using the RTOG genitourinary (GU) and gastrointestinal (GI) toxicity scores. Biochemical failure (BF) was defined as nadir + 2. Chi-square and Cox proportional hazards multivariable analyses were performed for all factors predicting for biochemical failure (BF), biochemical progression-free survival (BPFS), clinical progression-free survival (CPFS), metastasis-free survival (MFS), and cause-specific survival (CCS). BF was defined as nadir + 2.

**RESULTS:** The median age of the whole cohort at BT was 60 years (range: 44–77); 45% were Caucasian, 31% were
African American, 20% were Hispanic, and 4% were Asian. After a median follow-up of 4 years (range: 2–12) for the whole cohort, late RT-related grade ≤ 2 GU and GI toxicity rates were 14% and 11%, respectively, with no grades ≥ 3 reported. There were 2 BF’s, with no local or distant failures. The median time to BF was 14.2 months (range: 8–24). The 4-year BPFS, CPFS, MFS, and CCS rates were 96.7%, 100%, 100%, and 100%, respectively. Chi-square test and logistic regression analysis did not show a significant relationship between clinical outcomes and any factor (eg, prostate size, pretreatment PSA, age, Gleason score, and duration between BT and EBRT).

CONCLUSIONS: Intensified bimodality treatment of low-risk prostate cancer via simultaneous I-125 integrated brachytherapy boost to EBRT yielded excellent results with very tolerable late toxicity compared with historical data. Further studies are warranted to identify patients at higher risk of BF despite delivery of intensified RT.

(P016) Biochemical Outcomes in Patients With Adenocarcinoma of the Prostate With a Very High Presenting PSA of Greater Than 50 ng/mL

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PURPOSE: The optimal treatment of patients with prostate cancer with a high presenting PSA (> 50 ng/mL) is debated within and between specialties, as reflected in variable PSA outcomes for data reported. We present our clinical outcomes in irradiated patients for this population.

MATERIALS AND METHODS: With approval of our institutional protocol and ethics panel, prospectively collected patient, disease, treatment, and biochemical data were analyzed in patients with a presenting PSA > 50 ng/mL treated by a single physician (DS) at Beth Israel Medical Center from 1997 to 2012. External beam radiation therapy (EBRT) was delivered using 15 to 18 MV photons to an initial portal, including prostate, seminal vesicles, and draining pelvic lymph nodes, to 45 Gy, followed by a conformal cone down to 50.4 Gy, then a boost with either brachytherapy or 30.6 Gy conformal EBRT. PSA was routinely checked every 6 months in the follow-up after treatment was completed. Biochemical failure (BF) was defined as posttreatment PSA nadir + 2 ng/mL.

RESULTS: A total of 36 patients with a presenting PSA > 50 ng/mL underwent curative intent irradiation; 44% of patients were African American, 22% were Hispanic, 22% were Caucasian, and 6% were Asian. The median patient age, Gleason score (GS), PSA, and T stage were 67 years (range: 48–83), 7 (range: 6–9), 80 ng/mL (range: 51–280), and stage 2 (17% TX, 28% T1, 19% T2, 19% T3a/b, 14% T3c, 3% T4), respectively. Combined EBRT and permanent radioactive seed implant (CMT) was used in 64% (n = 23); EBRT alone was used in 36% (n = 13). Hormone therapy (HT) was administered to 89% (n = 32) of patients and was used for a median duration of 29 months. Of the patients receiving brachytherapy as part of their treatment, 83% (n = 19) received an I-125 permanent seed implant, and 17% (n = 4) received a Pd-103 implant. With a minimum follow-up of 2 years and a median follow-up of 5.0 years (range: 2.0–12.2), overall biochemical failure was 22.2% (n = 8), and median time to failure was 4.9 years (range: 2.5–9.3 years). Of those who failed, median age was 63 years (range: 55–83 years), and 50% were African American; median pretreatment PSA was 79 ng/mL (range: 53–238 ng/mL), and median AJCC stage was 3. BF occurred in 5 of 23 (21.7%) CMT patients (3 of 5 with I-125 and 2 of 5 with Pd-103) and 3 of 13 (23.0%) EBRT patients. All patients who failed received HT.

CONCLUSIONS: Our data demonstrate excellent overall biochemical outcomes in patients with a high presenting PSA level, with only approximately 22.2% of patients experiencing BF at a median follow-up of 5.0 years. Of all treatments analyzed, combined EBRT and permanent seed implant yielded the highest rate of biochemical control. Further prospective analyses comparing EBRT +/− brachytherapy in this population are warranted.

(P017) Current Outcome and Morbidity for Non-metastatic High-Grade Prostate Cancer Treated by Definitive Radiation Therapy

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INTRODUCTION: Patients with nonmetastatic prostate cancer and a high Gleason score of 8, 9, or 10 are often treated by radiation therapy. As this is considered aggressive disease, intense treatment regimens of high-dose radiation in combination with androgen deprivation may be employed. However, treatment success and morbidity for this subset of prostate cancer patients are not as well defined as might be expected. We report on a large cohort of these individuals treated with current techniques.

MATERIALS AND METHODS: An IRB-approved chart review of the 21st Century Oncology database returned 316...
patients (mean age 73.6 years) with histologically confirmed Gleason 8 (n = 200), 9 (n = 109), and 10 (n = 7) prostate cancer. All patients were without evidence of metastatic disease on pelvic/abdominal CT and bone scan and therefore were treated with curative intent. Pretreatment PSA was a mean of 15.3 ng/mL (range: 0.7–211). Photon radiation was delivered by intensity-modulated radiation therapy (IMRT) in almost all cases, with 58% also undergoing image guidance. Definitive external beam radiation therapy (XRT) alone was undertaken in 78%, achieving doses up to 84.6 Gy (median 75.8 Gy), while a total of 69 patients underwent the combination of external beam (median dose 45 Gy) followed by high-dose-rate brachytherapy boost. Pre-XRT hormonal blockade was delivered to 91.5%, and 35% had hormonal blockade during XRT.

**RESULTS**: All patients have been followed for a mean of 35.6 months. Treatment was generally well tolerated, with a reported 15% acute genitourinary (GU) morbidity of grade 3 and 4% with grade 4. Acute gastrointestinal (GI) morbidity was 4% grade 3, and one patient had grade 4 morbidity. Chronic GU morbidity of grade 3 was 7%, and of grade 4 was 2%. Chronic GI morbidity was grade 3 in one patient, and none had grade 4. A statistically increased rate of acute and late GU toxicity was found in patients undergoing brachytherapy (P = .03 and P < .0001, respectively). On analysis of outcome, age, Karnofsky performance status, T-stage, dose, Gleason score, hormones, treatment technique, and baseline PSA did not predict outcome. At last follow-up, 73% of patients are alive (n = 230), and 70% are disease-free (n = 220).

**CONCLUSION**: High-grade, nonmetastatic prostate cancer at diagnosis can be successfully treated by the combination of radiation therapy with androgen deprivation. The use of brachytherapy increases morbidity without additional disease control. Relatively high survival and disease control can be achieved with this strategy in the majority of patients. Further, elderly patients and those with high PSA at workup can have long-term disease-free survival with definitive XRT and hormonal blockade.

(P018) Do Testosterone Kinetics After Radiation Therapy (RT) Predict Sexual Function for Low- and Intermediate-Risk Prostate Cancer (CaP)? The Fox Chase Cancer Center Experience

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**PURPOSE/OBJECTIVES**: A modest decrease in testosterone has been reported after conventional-dose 3D-conformal RT with no change in testosterone reported after low-dose-rate brachytherapy (LDR) or proton therapy. We investigated whether dose-escalated intensity-modulated radiation therapy (IMRT) and LDR are associated with a change in testosterone and if any association exists between testosterone after RT and sexual function.

**MATERIALS AND METHODS**: We queried our prospective database for patients with low- and intermediate-risk prostate cancer (CaP), treated with IMRT or LDR between 2002 and 2008, who had post-RT testosterone levels ≥ 3. Patients were excluded if they received androgen deprivation therapy or had their first testosterone measured > 12 months after RT. Testosterone results were normalized for comparison. Wilcoxon rank-sum test was used to assess changes in normalized testosterone at 3, 9, 15, and 21 months post-RT. Information on patients’ self-reported sexual activity (SA) and erectile function (EF) was queried from the database. SA was reported as active or not active. EF was reported as full, none, partial, or intact (unknown if full or partial). Fisher’s exact test was used to assess for a difference in SA or EF.

**RESULTS**: A total of 544 patients with a median follow-up of 49 months (range: 4–105) were analyzed. Of the 259 patients with a pre-RT testosterone level, a decrease in median testosterone from baseline was observed after both IMRT (n = 174) and LDR (n = 85), which was independent of age and initial testosterone level. In this subset of patients, the median change in testosterone at 3, 9, 15, and 21 months post-RT was −45, −42, −33, and −54 ng/dL for IMRT patients (P < .05 for all) and −24, −24, −24, and −63 ng/dL for LDR patients (P = .084, .048, .055, and .005, respectively). From this set, 71 patients had both pre- and post-RT data for either SA or EF. SA data were available for 54 patients, and EF data were available for 46 patients. Patients were stratified by testosterone increase (n = 28) or decrease (n = 43) after RT. SA results for patients with a testosterone drop were as follows: 88% stayed the same, 3% decreased, and 9% increased; in patients with a rise in testosterone, 91% stayed the same, 9% dropped, and 0% increased. EF results for patients with a testosterone drop, revealed that 72% stayed the same, 17% decreased, and 10% increased, whereas for patients with a rise in testosterone, 70% stayed the same, 18% decreased, and 12% increased. There was no statistically significant difference in either SA or EF, independent of the change in testosterone.

**CONCLUSION**: IMRT and LDR were both associated with a post-RT decrease in testosterone. An initial decrease in tes-
tosterone after RT was not associated with decreased sexual activity or erectile function. This information may be helpful in counseling patients about testosterone levels and the impact on sexual function after RT.

(P019) Office-Based Assessment of Quality of Life After Robot-Assisted Radical Prostatectomy

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INTRODUCTION: We report our experience with quality-of-life assessments of robot-assisted radical prostatectomy patients in the setting of routine care in the office using comprehensive, validated survey instruments. Currently, there is an unmet need for such a feasibility and outcomes study from experienced surgeons in a routine clinical care setting—ie, outside of a funded study using mailed surveys or telephone interviews.

METHODS: From May 2006 to August 16, 2012, two surgeons from a single, academic institution completed 1,224 robot-assisted radical prostatectomy (RARP) procedures. The surgeons had previously completed over 150 cases each of laparoscopic and/or RARP. The patients were inclusive of all primary RARP treatments with or without neoadjuvant systemic therapy. Patients completed surveys within 30 days of surgery and at routine postoperative intervals, including 6 weeks, 6 months, 1 year, and 2 years. The instruments included the Expanded Prostate Cancer Index (EPIC), which was utilized in the pivotal study by Sanda et al. (NEJM, 2008). The survey includes functional, bother, and summary scores for sexual, urinary, bowel, and hormonal domains and is scored from 0 to 100, with 100 always being the optimal result, and was not feasible for real-time feedback or use with the patient. In total, 3,872 surveys were entered for an estimated 645 work-hours. Review of the hormonal and bowel summary and subscales showed baseline scores > 90 and no treatment-related effect. Urinary summary and bother returned to baseline by 6 months, while urinary irritative/obstructive domains improved slightly at 6 months and beyond. Urinary incontinence was 72, 40, 42, 51, and 56, respectively.

RESULTS: EPIC surveys take patients approximately 20 minutes to complete with high (unmeasured) compliance in the course of an office visit. Translating the scores into scales takes a skilled data-entry assistant 10 minutes each and was not feasible for real-time feedback or use with the patient. In total, 3,872 surveys were entered for an estimated 645 work-hours. Review of the hormonal and bowel summary and subscales showed baseline scores > 90 and no treatment-related effect. Urinary summary and bother returned to baseline by 6 months, while urinary irritative/obstructive domains improved slightly at 6 months and beyond. Urinary incontinence was 92 at baseline, 49 at 6 weeks, 74 at 6 months, and 82 at 1 and 2 years. Sexual function at the same intervals was 57, 24, 30, 37, and 39, while bother was 72, 40, 42, 51, and 56, respectively.

CONCLUSIONS: EPIC surveys provide quality of life data that are comprehensive, informative, and comparable across studies and modalities. Patients appear willing to complete them routinely during an office setting, but the scoring is likely too burdensome for routine clinical care. Our results suggest an opportunity to delete the bowel and hormonal scales in the surgical setting and to place greater emphasis on a subset analysis of urinary and sexual domains. The urinary summary and bother scales suggest excellent post-operative recovery, despite a decline in the urinary incontinence domain that is minimally significant.

(P020) Short-Term and Long-Term Changes in Urinary Function in Prostate Cancer Patients Treated With IMRT: Effect of Real-Time Tumor Tracking

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PURPOSE: To compare urinary function in two groups of patients treated for prostate cancer: patients treated with intensity-modulated radiation therapy (IMRT) in conjunction with the Calypso real-time tumor tracking system and patients treated with IMRT utilizing implantable fiducial gold markers (gold seeds) with cone beam CT (CBCT) for image guidance.

METHODS: With IRB approval, we reviewed 261 patients consecutively treated with IMRT for prostate cancer between July 2007, when the Calypso system was introduced in our department, and April 2011. A total of 87 patients were treated with gold seed implants to track target position, and 174 were treated with the Calypso real-time tumor tracking system. Since both standard IMRT (sIMRT, 78 Gy over 39 fractions) and hypofractionated IMRT (hIMRT, 70 Gy over 28 fractions) regimens have been used in our department, we compared outcomes in Gold and Calypso patients within each regimen. To evaluate urinary function, we used the AUA BPH Symptom Score Index, measured at baseline (before the treatment) and at follow-up visits every 6 months. We also recorded nocturia and use of a-blockers. Subjects were followed for up to 24 months, with a median follow-up of 18 months. Linear mixed models were fit, taking into consideration the following covariates: tumor tracking modality, age, BMI, and baseline prostate volume. Changes in the outcomes over time and relative to baseline were compared among the cohorts.

RESULTS: Overall, AUA BPH scores were not significantly different between the Gold and Calypso cohorts. However, the change over time was significantly different (P = .006)
between Gold and Calypso patients treated with sIMRT. Relative to the baseline and compared with the Gold patients, mean AUA BPH score in Calypso patients was 1.54 points lower at 6 months, 2.94 points lower at 12 months, 2.42 points higher at 18 months, and 0.30 points higher at 24 months. Similar but statistically nonsignificant changes in the mean AUA BPH score were observed in hIMRT patients. Both Gold and Calypso cohorts experienced a substantial increase in nocturia at the end of treatment. Calypso patients had a 0.3-point greater increase in mean nocturia score at the end of treatment compared with Gold patients; however, this difference was not statistically significant. No significant difference in mean nocturia scores across time was found between the Gold and Calypso cohorts. The prevalence of α-blocker use at the end of treatment was estimated to be 18 pp greater (95% confidence interval [CI] = 2–34 pp greater) in Gold patients compared to Calypso patients when treated with sIMRT, with no significant difference at baseline and other time points.

**CONCLUSIONS**: The trends of change in AUA BPH scores over time, relative to baseline, and the difference in prevalence of α-blocker use suggest lower short-term and higher long-term urinary toxicity of real-time tumor tracking with the Calypso system compared to the use of gold fiducials. However, the magnitude of this difference is clinically small.

**(P021) High-Dose-Rate Brachytherapy With or Without Intensity-Modulated Radiation Therapy for a Local Recurrence of Prostate Cancer**

**Tobin Strom, MD, Richard B. Wilder, MD, Daniel Fernandez, MD, PhD, Matthew C. Biagioli, MD; H. Lee Moffitt Cancer Center**

**INTRODUCTION**: Few articles have been published on brachytherapy as salvage therapy for recurrent prostate cancer after prostatectomy. We hypothesized that high-dose-rate (HDR) brachytherapy ± intensity-modulated radiation therapy (IMRT) could effectively treat patients with a local recurrence of prostate cancer.

**METHODS**: From October 2009 to July 2012, we treated three patients with a local recurrence after radical prostatectomy with HDR brachytherapy ± IMRT. Recurrent prostate cancer was defined based on the NCCN definitions of detectable postprostatectomy prostate-specific antigen (PSA) or postprostatectomy PSA ≥ 0.1 ng/mL that increases on two subsequent measurements. All three patients initially underwent prostatectomy with negative margins. No patients had extraprostatic extension, one patient had seminal vesicle invasion, and two patients had a PSA that was initially detectable after prostatectomy. The median pre-HDR PSA value was 0.6 ng/mL (range: 0.3–2.3 ng/mL). The median time from prostatectomy to salvage HDR treatment was 116 months (range: 25–194 months). A pelvic MRI, CT, or PET scan demonstrated an identifiable mass in the prostate bed with no regional (nodal) or distant metastases. Two patients had recurrences > 2 cm in the prostate bed and were treated with two 950-cGy fractions of HDR brachytherapy and 4,500 to 5,040 cGy in 25 to 28 fractions of IMRT to the prostate bed, one of whom also received androgen deprivation therapy (ADT). The third patient had a palpable 5-cm recurrence in the left seminal vesicle and underwent HDR brachytherapy consisting of four 950-cGy fractions and ADT but no IMRT. Rectal toxicities were graded according to the Common Terminology Criteria for Adverse Events, version 4.

**RESULTS**: At a median follow-up of 22 months, all three patients have undetectable PSA levels. The two patients who were initially on ADT have been able to stop the therapy. No patients report late grade 1 or higher rectal toxicities.

**CONCLUSIONS**: HDR brachytherapy ± IMRT is an option for salvage therapy after prostatectomy for patients with a local recurrence and no regional or distant metastases, and it deserves further study.

**(P022) Dosimetric and Body Mass Index Analysis of Polyethylene Glycol Gel in Prostate Cancer Patients Undergoing Radiotherapy**

**Tobin Strom, MD, Matthew C. Biagioli, MD, Daniel Fernandez, MD, PhD, Richard B. Wilder, MD; H. Lee Moffitt Cancer Center**

**INTRODUCTION**: Use of a gel to increase the distance between the rectum and prostate decreases the radiation dose delivered to the rectum in prostate cancer patients undergoing high-dose-rate (HDR) brachytherapy ± intensity-modulated radiation therapy (IMRT). One group reported that men with a lower body mass index (BMI) have less fatty tissue between the rectum and prostate and consequently receive a higher rectal wall dose from brachytherapy. Based on this report, we hypothesized that BMI would correlate with rectal-prostate distance, rectal V75, and rectal D2cc.

**METHODS**: Between May 2010 and October 2012, we treated 125 clinically localized prostate cancer patients with HDR brachytherapy ± IMRT ± polyethylene glycol gel. Low-risk and favorable intermediate-risk patients under-
went HDR brachytherapy monotherapy to 2,700–2,800 cGy in two 1,350–1,400-cGy fractions separated by 2 to 3 weeks. Higher-risk patients received two 1,050–1,150-cGy fractions of HDR brachytherapy and IMRT to 4,500–5,040 cGy in 25–28 fractions. Beginning in September 2011, we also treated 59 patients with a transrectal ultrasound–guided transperineal injection of 5–10 mL polyethylene glycol gel (DuraSeal; Covidien, Mansfield, MA) mixed with 1 mL iohexol (Omnipaque 300; GE Healthcare; Waukesha, WI) nonionic contrast. This mixture was injected into anterior perirectal fat immediately prior to the first ± second HDR brachytherapy fraction. Patients who were treated beginning in September 2011 did not receive gel if magnetic resonance imaging showed posterior extraprostatic extension of their cancer or if their serum creatinine was > 1.5 mg/dL. Gel volumes were contoured on treatment planning computed tomography (CT) scans using Oncentra v4.1 (Nucletron, Netherlands). The Mann-Whitney U test and Spearman’s rank order correlation were used.

**RESULTS:** BMI was 29.3 ± 5.2 kg/m² (mean ± standard deviation). Mean rectal-prostate distance in the group with gel was significantly greater than in the group without gel (14 mm vs 4 mm, respectively; \( P < .001 \)). Rectal-prostate separation correlated negatively with rectal V75 (\( r = –0.36; \ P < .001 \)) and rectal D2cc (\( r = –0.75; \ P < .001 \)). In the group without gel, BMI did not correlate with rectal-prostate distance (\( r = 0.14; \ P = .28 \)), rectal V75 (\( r = 0.16; \ P = .20 \)), or rectal D2cc (\( r = –0.03; \ P = .82 \)).

**CONCLUSIONS:** Use of a bioabsorbable polyethylene glycol gel as a temporary tissue spacer decreases the radiation dose delivered to the rectum, as measured by rectal V75 and rectal D2cc. However, BMI does not correlate with rectal-prostate distance, rectal V75, or rectal D2cc.

**P023** Prospective Evaluation of Patient-Reported Outcomes After IG-IMRT for Prostate Cancer

**James B. Yu, MD, Jenerius A. Aminawung, MD, MPH, Jessica B. Long, MPH, Cary P. Gross, MD; Yale School of Medicine**

**INTRODUCTION:** Image-guided intensity-modulated radiation therapy (IG-IMRT) as primary or salvage treatment for prostate cancer is reported to have low side effects and toxicity. In addition to physician-reported toxicity, patient-reported outcomes (PROs) and quality of life are important measures of how patients are actually feeling and functioning. The Expanded Prostate Index Composite (EPIC) survey is a commonly used and validated survey instrument that measures prostate cancer-related PROs in four domains: urinary, bowel, sexual, and hormonal. EPIC scores range from 0 to 100, with 100 indicating perfect function.

**METHODS:** Patients undergoing IG-IMRT prostate radiotherapy from 2009 to 2012 for prostate and prostate bed radiotherapy at Yale-New Haven Hospital and affiliated centers were enrolled on a prospective patient-reported quality of life study. Patients included a mix of patients undergoing radiotherapy with or without pelvic radiotherapy, also with or without androgen deprivation. The EPIC survey was given to patients at baseline and 1, 6, 12, 18, and 24 months after completion of radiotherapy. Patients who completed 24 months of follow-up are reported. Using paired samples T-tests, we compared EPIC scores at 6, 12, and 24 months to baseline scores.

**RESULTS:** Eighteen patients have completed 24 months of follow-up. Two patients received prostate bed radiation, and 16 had primary prostate radiotherapy. Median age of the 18 patients was 69.5 years. Mean EPIC urinary scores at baseline and 6, 12, and 24 months after treatment were 83.6, 83.9, 87.1, and 86.1, respectively. Mean EPIC bowel scores at these times were 94.5, 85.2, 91.6, and 93.0, respectively. Mean EPIC sexual scores were 38.4, 28.8, 32.1, and 36.7, respectively. Mean EPIC hormonal scores were 92.6, 84.1, 90.1, and 90.4, respectively. Mean EPIC scores are shown below (see Figure). Though EPIC scores appeared to drop at 6 months, the mean EPIC scores were similar to baseline values at all three follow-up periods.

**CONCLUSIONS:** Patient-reported quality of life recovered 24 months after treatment. Mean urinary and bowel scores remained relatively stable through 24 months of follow-up. Mean sexual and hormonal scores declined early and were followed by an eventual return to baseline. This likely represents patients who underwent short-term androgen deprivation therapy as a part
of their treatment who subsequently recovered after return of testosterone.

(P024) Prostate Volume as a Predictor of Toxicity in Men Treated With Conventional Versus Hypofractionated Intensity-Modulated Radiation Therapy for Localized Prostate Cancer

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PURPOSE: To determine predictors of toxicity related to hypofractionated versus conventionally fractionated external beam radiation for localized prostate cancer.

MATERIALS AND METHODS: We performed an analysis of a prospective randomized trial conducted at a single tertiary cancer center that compared conventional fractionation IMRT (75.6 Gy at 1.8 Gy per fraction, CIMRT) to hypofractionated IMRT (72 Gy at 2.4 Gy per fraction, HIMRT). Radiation Therapy Oncology Group genitourinary (GU) and gastrointestinal (GI) toxicity was prospectively recorded for all patients. Univariate and multivariate analyses were performed to identify associations between recorded variables and toxicity. Log-rank tests were used to compare any toxicity and grade ≥ 2 GU and GI toxicity between CIMRT and HIMRT.

RESULTS: Two hundred four men were randomized and treated from March 2001 to May 2010. Median follow-up was 71 months. Baseline characteristics and median follow-up were no different between the two groups. Any-grade GU, grade ≥ 2 GU, and grade ≥ 2 GI were equivalent between the two arms (P > .05). Any-grade GI was increased in the HIMRT arm (P < .05). There were four grade 3 events (CIMRT n = 2, HIMRT n = 2). There were no grade 4 events. On univariate analysis, age, race, clinical T-stage, Gleason score, pretreatment PSA, use of androgen deprivation therapy, protocol arm, and baseline AUA symptom score were not significantly associated with increased GU or GI toxicity. Larger prostate volume was associated with an increased risk of any GU toxicity, grade ≥ 2 GU toxicity, and grade ≥ 2 GI toxicity in men treated with HIMRT (P < .05).

CONCLUSION: Severe GU or GI toxicity is uncommon with CIMRT or HIMRT. Contoured prostate volume predicts for any grade GU toxicity and grade ≥ 2 GU and GI toxicity. Men with larger prostate volumes were at greater risk of toxicity when treated with HIMRT. Other identified variables, including baseline AUA symptom score, were not predictive of increased toxicity. Prostate volume should be a consideration when delivering dose-escalated HIMRT for localized prostate cancer.

(P025) Extended-Field Intensity-Modulated Radiation Therapy (EF-IMRT) With Simultaneous Integrated Boost (SIB) for Locally Advanced Gynecological Malignancies With Radiographic Lymph Node Involvement: Efficacy and Toxicity

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OBJECTIVE: To assess the efficacy and toxicity of extended-field intensity-modulated radiation therapy (EF-IMRT) with simultaneous integrated boost (SIB) in the treatment of women with advanced cervical and endometrial malignancies with radiographic pelvic and paraaortic lymph node involvement.

METHODS: Between July 2010 and June 2012, 16 consecutive patients with advanced cervical (n = 12; stage IIIB–IVB) and endometrial (n = 4, stage III–IVB) malignancies with pelvic and paraaortic lymph node involvement were identified. Lymph node involvement was determined by positron emission tomography–computed tomography (PET-CT). All patients received EF-IMRT of 45–50.4 Gy to a large-field planning target volume (PTV) in addition to a SIB of 50–59.36 Gy to PET-positive lymph nodes. Cervical cancer patients received concomitant chemotherapy during IMRT. All patients received high-dose-rate (HDR) brachytherapy (12–30 Gy in 2–5 applications). Acute and late toxicities were assessed using the Common Toxicity Criteria for Adverse Events (CTCAE, version 3.0) and the RTOG-EORTC late radiation morbidity scoring scheme.

RESULTS: Fifteen patients completed their planned treatment. Median follow-up was 10 months (range: 3–26 months); no patient experienced acute grade 3 or higher gastrointestinal (GI), genitourinary (GU), or skin toxicity. Among the patients receiving concomitant chemoradiotherapy, two patients (17%) experienced grade 3 hematological toxicity. Likewise, late toxicity was limited, with two patients (12%) developing grade 3 GI toxicity and one patient (6%) developing grade 3 GU toxicity. The estimated 1-year locoregional control rate was 87%. Two patients (12%) had in-field failures, diagnosed 3 and 12 months after completion of treatment. Five patients (31%) had distant metastases at diagnosis, and 3 patients (19%) developed distant metastases at 3, 7, and 9 months after completion.
CONCLUSION: Treatment of women with advanced cervical and endometrial cancers with EF-IMRT with SIB demonstrates good locoregional control with few grade 3 or higher GU, GI, or skin toxicities. Further prospective evaluation of this technique is warranted.

(P026) How the Type of Pelvic Radiation Therapy Influences Urinary Tract Infection Rates During Treatment

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PURPOSE: The purpose of this study was to compare the rates of urinary tract infection (UTI) among patients with endometrial cancer receiving vaginal brachytherapy alone and brachytherapy plus three-dimensional conformal radiation therapy (3D-CRT) or intensity-modulated radiation therapy (IMRT).

MATERIALS AND METHODS: We retrospectively evaluated the rates of UTI among 585 patients diagnosed with endometrial cancer, treated between 2004 and 2012—37% (216/585) received brachytherapy alone, 28% (164/585) received brachytherapy plus 3D-CRT, and 35% (205/585) received brachytherapy plus IMRT. UTI during the treatment was defined as evidence of pyuria detected by either urine dipstick or urinalysis. All specimens were collected as a clean-catch, midstream void to avoid contamination and resultant false positives. Chi-square and logistic regression analyses were subsequently employed for statistical analyses.

RESULTS: UTI was diagnosed in 14.5% (85/585) of all patients. Only 2.7% (6/216) of patients receiving brachytherapy were diagnosed with a UTI during treatment, whereas UTI was diagnosed in 36.6% (60/164) of patients receiving brachytherapy plus 3D-CRT, and 35% (20/585) received brachytherapy plus IMRT. UTI during the treatment was defined as evidence of pyuria detected by either urine dipstick or urinalysis. All specimens were collected as a clean-catch, midstream void to avoid contamination and resultant false positives. Chi-square and logistic regression analyses were subsequently employed for statistical analyses.

LOGISTIC REGRESSION ANALYSIS FOUNDED A DECREASED ASSOCIATION BETWEEN UTI AND STAGE 3 ENDOMETRIAL CANCER (ODDS RATIO [OR] = 0.46; 95% CONFIDENCE INTERVAL [CI] = 0.24–0.87; P = .017). WHEN COMPARED WITH BRACHYTHERAPY, BOTH TYPES OF EBRT WERE ASSOCIATED WITH AN INCREASED RISK OF UTI, THOUGH ADJUVANT 3D-CRT (OR = 28.256; 95% CI = 11.112–71.853; P ≤ .001) HAD A MORE DRAMATIC RISK INCREASE THAN IMRT (OR = 4.154; 95% CI: 2.269–4.154; P = .003).

CONCLUSION: When compared with IMRT, 3D-CRT is associated with a significantly increased risk of UTI, supporting the use of IMRT as the preferred EBRT for endometrial cancer.

(P027) Radiosurgery for Endometrial Recurrences

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INTRODUCTION: Radiation therapy has been shown to be effective in decreasing the risk of local recurrences in endometrial cancer. However, in patients who present with local endometrial cancer recurrences, further radiation has often had a limited role in patients who have received prior radiotherapy, due to critical structure constraints. The use of radiosurgery may be an effective means of delivering reirradiation to previously treated tissue safely while addressing the area of recurrence. This study is a retrospective chart review of the Winthrop University Hospital experience using radiosurgery for isolated local endometrial recurrences.

METHODS: A retrospective chart review of 19 patients with endometrial primaries treated with whole pelvic radiotherapy plus or minus vaginal brachytherapy. Patients presented with radiographically confirmed areas of local recurrence and metastatic disease. The patients were subsequently treated with stereotactic radiosurgery from August 2006 to February 2012.

RESULTS: Of the 19 endometrial patients, 8 patients recurred in the vaginal cuff or pelvic and paraaortic lymph nodes. One patient presented with a recurrence to the sacrum. Four patients presented with pulmonary metastasis. The rest of the six patients presented with distant metastasis to the liver, brain, or colon. The median dose of pelvic radiotherapy given prior to the recurrences was 4,980 cGy. Doses of radiosurgery to the pelvis ranged from 1,800–2,500 cGy, with a median dose of 1,800 cGy. The BED of 1,800 cGy/5 fractions was 415 cGy per fraction and a total of 2,075 cGy. Of the eight patients with local recurrences, four had no evidence of disease following radiosurgery with a median follow-up interval of 17.2 months, two had stable disease at 0.5 months, and two had disease progression with a median follow-up of 12 months. The two patients with disease progression developed distant metastases after completion of their radiosurgery. Three of eight patients developed grade 1 gastrointestinal (GI) toxicity and zero of eight patients developed genitourinary (GU) toxicity based on CTCAE v4.0 criteria.

CONCLUSIONS: The use of reirradiation for local recurrences of endometrial cancer has been limited historically
due to dose constraints posed by critical structures in the pelvis. Our retrospective review demonstrates that radiosurgery can potentially offer a safe and effective means to provide additional local control. The majority of patients with pelvic recurrences had stable disease following radiosurgery. The procedure was well tolerated, with only 40% of patients developing grade 1 GI toxicity. The results of this chart review warrant further investigation of radiosurgery for locally recurrent endometrial cancer.

(P028) Radiation Therapy in the Treatment of Vulvar and Vaginal Melanoma

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OBJECTIVE: Melanoma of the female genital tract is a rare tumor type with a poor prognosis. We sought to evaluate the role of radiation therapy (RT) in the management of vulvar and vaginal melanoma by reviewing the experience from a single referral center.

METHODS: We identified all patients presenting to our institution for management of vulvar or vaginal melanoma from 2000 to 2012. Demographics, clinicopathologic data, and treatment information were abstracted from the medical record.

RESULTS: Sixty-one patients were identified, of whom 22 (36%) received radiation therapy and constituted the study group. There were 16 (73%) vaginal primaries and 6 (27%) vulvar primaries. The median age was 68.5 years (range: 53–87). The most common presenting symptoms were vaginal bleeding (12, 54.5%), incidental lesion (5, 22.7%), palpable mass (2, 9.1%), and pruritis (2, 9.1%). Radiation treatment was categorized as primary therapy (n = 11, 50%), adjuvant RT (n = 5, 22.7%), or treatment of recurrence (n = 6, 27.3%). Of those patients who received primary RT, one died of an unrelated cause at 32 months. One patient was alive with distant disease (AWD) at last follow-up. One elderly patient was unable to tolerate her RT and ultimately died of disease (DOD). Concurrent paclitaxel/RT was prescribed for one patient who eventually developed both local and distant disease. The remaining seven patients who received definitive RT achieved local control but developed distant metastases and ultimately expired. Five patients were treated with adjuvant RT after surgical excision. One remains without evidence of disease (NED), and one recurred locally as well as distantly. The remaining three patients who received adjuvant RT achieved local control but failed distantly. Finally, six patients were treated with RT in the recurrent setting. Three had brain metastases and received whole-brain RT; they all went on to die of disease. Three received RT for pelvic recurrences. In two cases, local control was achieved; however, one of the two developed liver metastasis and died of disease. The third patient had a local recurrence after preoperative RT and subsequent resection. She remains AWD on systemic treatment. The median follow-up for the study group was 27.3 months (range: 6.7–88.3). Ultimately, 17 of the 22 patients (77.3%) were diagnosed with distant metastasis. Seventeen patients (77.3%) died of disease, one (4.5%) died of an unrelated cause, three (13.6%) are AWD, and one patient (4.5%) remains NED.

CONCLUSIONS: Radiation therapy may aid in the local control of vulvovaginal melanoma. However, the majority of patients develop distant metastasis and ultimately die of disease.

(P029) Contouring Atlas of Cranial Nerves IX–XII for Head and Neck Cancer

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PURPOSE: Radiation-induced cranial nerve palsy (RICNP) involving the lower cranial nerves (CNs) is a rare but serious complication of head and neck radiotherapy (RT). Recommendations for delineating the lower CNs on RT planning studies do not exist. Here, we develop a standardized methodology for contouring CNs IX–XII.

METHODS: Using anatomic texts, radiologic data, and guidance from experts in head and neck anatomy, we developed step-by-step instructions for delineating CNs IX–XII on computed tomography (CT) imaging. These structures were then contoured on five consecutive patients who underwent definitive RT for locally advanced head and neck cancer (LAHNC). RT doses delivered to the lower CNs were calculated.

RESULTS: We successfully developed a contouring atlas for CNs IX–XII. The median total dose to the planning target volume (PTV) was 70 Gy (range: 66–70 Gy). The median volumes of CNs (IX–XI) and (XII) were 10 cc (range: 8–12 cc) and 8 cc (range: 7–10 cc), respectively. The median V50, V60, V66, and V70 of the CN (IX–XI) and (XII) volumes were (85, 77, 71, 65) and (88, 80, 74, 64), respectively. The median maximal dose to CNs (IX–XI) and (XII) was 72 Gy (range: 66–77) and 71 Gy (range: 64–78), respectively.
CONCLUSIONS: We have generated simple instructions for delineating the lower CNs on RT planning imaging. Further analyses to explore the relationship between lower CN dosing and the risk of RICNP are recommended to establish a limiting dose for these organs at risk.

(P030) Intraoperative High-Dose-Rate P-32 Brachytherapy for Superficial Ophthalmic Malignancies

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PURPOSE: Malignancies occurring near the eye are often effectively managed with radiation therapy. However, the sensitivity and small size of the eye often limit treatment options with teletherapy. For this reason, we have employed a novel brachytherapy technique for superficial ophthalmic malignancies in recent years. This study was conducted to assess the outcome of treatment with this modality.

MATERIALS AND METHODS: With permission of the institutional review board, medical records of patients treated with RIC-100 (R.I. Consultants, Hudson, NH) polymer-bound silicone-coated 32P brachytherapy for superficial ophthalmic malignancies were reviewed. Demographic, comorbidity, cancer, and treatment-related factors were recorded. Visual acuity, intraocular pressure, grade > 2 adverse events (defined and graded per the Common Terminology Criteria for Adverse Events, version 4.0), and tumor control in the treated eyes were noted.

RESULTS: Five patients (two women, three men) underwent six courses of 32P ophthalmic brachytherapy. Median age was 63 years (range: 51–80 years). Median Adult Comorbidity Evaluation-27 score was 1 (range: 1–2). Three patients had squamous cell carcinoma of the conjunctiva, one patient had sebaceous carcinoma of the eyelid, and one patient had bilateral treatment of an atypical T-cell proliferation. Four of five patients (80%) had recurrent cancer, which had failed a median of 1 prior therapy (range: 1–3), including surgical excision, topical chemotherapy, and immunotherapy. No patients had evidence of regional or distant metastases at presentation for brachytherapy. Doses were prescribed to 1 mm from the surface of the applicator and ranged from 5 to 17 Gy (median 15 Gy), at dose rates of 0.325–0.770 Gy/minute (median 0.450 Gy/minute), from 32P sources with activities of 1.35–6.00 mCi (median 5.60 mCi), using custom-designed applicators 1.0–6.7 cm2 (median 4.5). With a median follow-up of 17 months, one patient (who had sebaceous carcinoma) developed an extensive biopsy-confirmed local recurrence 4 months after brachytherapy, which required salvage exenteration. No patient developed regional or distant recurrence or has died since brachytherapy. One grade 4 corneal ulcer occurred 1 month after brachytherapy (in the patient receiving 17 Gy), and one grade 3 cataract occurred 30 months after brachytherapy (in a patient receiving 15 Gy). Visual acuity > 20/200 was preserved in five of six treated eyes. Glaucoma was not noted in any of the treated eyes.

CONCLUSIONS: Intraoperative high-dose-rate 32P brachytherapy is feasible for superficial ophthalmic malignancies. We have not noted severe complications with doses of ≤ 15 Gy. Further study of a larger group of patients will be necessary to validate these preliminary findings.

(P031) Factors Affecting Timing of Adjuvant Radiotherapy (RT) Following Transoral Robotic Surgery (TORS) for Head and Neck Squamous Cell Carcinoma (HNSCC)

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PURPOSE: Overall treatment package time (total days from surgery to radiotherapy [RT] completion) > 100 days and surgery to start of RT > 42 days postoperatively have been shown to have a deleterious effect on the efficacy of postoperative treatment of head and neck squamous cell carcinoma (HNSCC). Given the minimally invasive nature of transoral robotic surgery (TORS), one may expect decreased postoperative recovery times, allowing for earlier initiation of adjuvant RT, thereby shortening total treatment duration. Myriad factors, including physician referral patterns, dental clearance, insurance approval, clinic scheduling, and patient compliance, can potentially delay the timely initiation of adjuvant RT. We set out to quantify the timing of various steps required to complete adjuvant RT to identify areas for future quality improvements in our department.

METHODS: We performed a retrospective systems-based analysis of all patients treated with TORS and adjuvant RT +/−chemotherapy at Mount Sinai Hospital (MSH) for HNSCC from April 2007 to June 2012, quantifying the timing of key intervals in scheduling, planning, and initiating adjuvant RT. Statistical analyses were performed using SPSS to determine the impact of those factors on the timely initiation of adjuvant RT. Patients’ charts were reviewed to identify any factors contributing to these delays.
RESULTS: A total of 33 patients received adjuvant RT at MSH after TORS for HNSCC. Two cohorts were identified based on time to start of RT: 12 patients began RT > 6 weeks and 21 began < 6 weeks postoperatively. Results are presented in the Table. Mean treatment package time and mean time from surgery to RT consultation were significantly shorter in the cohort starting RT < 6 weeks after TORS ($P < .001$ and $P = .007$, respectively). There were no significant differences between the cohorts regarding time from RT consultation to simulation, simulation to start of RT, number of patients seen preoperatively (23.8% vs 25%, $P = .939$), or number of patients receiving chemotherapy (57.1% vs 66.7%, $P = .59$). Length of hospitalization after TORS was similar between cohorts.

CONCLUSION: Patients undergoing TORS are able to initiate and complete adjuvant RT in a timely manner compared with other series reporting on adjuvant RT following traditional surgery for HNSCC. Minimizing delays between surgery and initial RT consultation is shown to positively impact overall treatment package time following TORS. Several key intervals have also been identified within our department to streamline our institutional process and shorten overall treatment package time. Whether further reductions in overall treatment times will further improve outcomes in the adjuvant setting will be the subject of future investigations.

(P032) High-Dose-Rate Brachytherapy of Basal Cell Carcinoma of Facial Skin in Elderly Patients

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PURPOSE/OBJECTIVES: Skin basal cell carcinoma is frequent in sun-exposed areas, such as the skin of the face, and in advanced age, for which a conservative treatment can be a valid option. The aim of this study is to retrospectively evaluate the effectiveness, toxicity, and aesthetic outcome of a conservative treatment, high-dose-rate brachythrapy, in older patients (> 75 years) with basal cell carcinoma of the face with clinical stage T1–T2 N0, according to TNM staging classification (7th edition, 2010 American Joint Committee on Cancer), judged to be inoperable because of comorbiditiy or possible bad aesthetic outcome.

MATERIALS AND METHODS: From January 2011 to October 2012, four patients older than 75 years (median age 88 years,
range: 79–97) with six biopsy-proven basal cell carcinomas of the face were consecutively treated with contact high-dose-rate (HDR) brachytherapy in our department. Two lesions had relapsed after previous surgical excision. Two neoplasms were localized to the nose, and two were at the frontal and temporal areas each. All patients were given a personalized thermoplastic mask with 6-Fr plastic catheter vectors for 192Ir source remote after loading and a 2-mm lead eyeshield. The treatment consisted of daily fractions, 5 days for 1 week, of 2.5–3.5 Gy (median dose 3 Gy) HDR brachytherapy, up to a total dose of 32.5–55 Gy (median dose 46.75 Gy). Median biological equivalent dose, according to the treatment length, was 54.8 Gy (range: 33.4–56.7 Gy). The therapy in the older patient was stopped at 32.5 Gy because of nasal septum bleeding. All patients showed acute moist desquamation in the treated area, which improved after the treatment term. Follow-up consisted of periodic clinical evaluations of disease outcome and aesthetic results.

RESULTS: After a median follow-up of 19 months, no local relapse was detected. All patients are alive and disease-free. Aesthetics were very good except in one patient, who was affected by a chronic actinic skin ulcer (biopsy-proven), about 1.5 cm in maximum diameter, after brachytherapy of a basal cell carcinoma borne on a cutaneous burn scar.

CONCLUSIONS: In elderly patients (> 75 years) affected by facial skin basal cell carcinoma, HDR brachytherapy could be a valid alternative treatment to surgery, according to safety, oncologic outcomes, and aesthetic results.

(P033) Antimicrobial Properties of a Calcium Phosphate Mouth Rinse for Patients Receiving Radiation Therapy
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INTRODUCTION: Xerostomia during and following head and neck irradiation greatly impacts the quality of life in patients. Oral and esophageal infections are more common, since the normal balance of flora in the mouth is altered; consequently, bacterial and fungal organisms flourish.[1] Studies have shown that patients submitted to radiation therapy have a higher number of microbial species, including Streptococcus mutans and Candida albicans. An in vitro time-kill study (ASTM E 2315-03 [2008] NG3694, Assessment of Antimicrobial Activity Using a Time-Kill Procedure) was undertaken to assess the antimicrobial properties of a calcium phosphate rinse (NeutraSal®) when challenged against the aforementioned bacteria and fungi. NeutraSal contains sodium, calcium, phosphate, and bicarbonate ions.

MATERIALS AND METHODS: Stock cultures of the microorganisms were grown in BHI agar at ambient temperature for 72 hours and used to challenge the test substance. NeutraSal, with the standard dose of one packet, was dissolved in purified water (30 mL) and aliquoted (10 mL). One hundred microliters of the test microorganism substance was added to the test substance and allowed to stay in contact for 10 and 20 minutes. At the end of each exposure time, a measured amount of test substance-challenge suspension was harvested and neutralized. Harvested test substances were diluted and plated according to standard microbiological techniques.

RESULTS: Immediate reductions from the initial populations for each challenge microorganism were calculated. NeutraSal demonstrated a significant reduction from baseline against C albicans at all reported time frames. This was a 67.9% reduction at 10 minutes and 53.67% at 20 minutes. The antimicrobial efficacy against S mutans was more modest, showing reductions of 25.67% and 24.67% at 10 and 20 minutes, respectively.

CONCLUSIONS: The results of the study indicate that NeutraSal has antimicrobial activity against both C albicans and S mutans as opposed to normal saline. NeutraSal may be used safely as part of an oral hygiene program that helps alleviate xerostomia in patients undergoing radiotherapy while possibly reducing possible oral infections due to antimicrobial activity.

Reference

(P034) Dysphagia and Dose to Swallowing-Related Organs in Patients Receiving Induction Chemotherapy (IC) Followed by Concurrent Chemoradiation Therapy (CCRT) for Locally Advanced Squamous Cell Carcinoma of the Head and Neck (LASCCHN)
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PURPOSE: Concurrent chemoradiation therapy (CCRT) for locally advanced squamous cell carcinoma of the head and neck (LASCCHN) is associated with acute and chronic pharyngeal toxicity, often necessitating placement of a PEG tube. Studies have demonstrated associations between dysphagia rates and radiation dose to swallowing-related organs. At Mount Sinai Hospital (MSH), use of induction chemotherapy (IC) for selected patients has been shown to decrease tumor size. We have begun to decrease target vol-
umes for these patients, perhaps reducing radiation exposure to swallowing-related organs. We evaluated the relationship between dysphagia and pharyngeal constrictor/proximal esophagus dose in patients with LASCCHN receiving IC followed by CCRT.

**MATERIALS AND METHODS:** This was a retrospective study analyzing the records of 25 patients with LASCCHN stages III (n = 6), IVa (n = 16), IVb (n = 1), and IVc (n = 2) of the oropharynx (n = 14), nasopharynx (n = 4), larynx (n = 4), and hypopharynx (n = 3) who received IC at MSH with either a docetaxel/cisplatin/5-fluorouracil or paclitaxel/carboplatin regimen followed by 70 Gy via IMRT with concurrent chemotherapy. Dysphagia was assessed by PEG tube duration and weight loss during treatment. Swallowing-related organs, including the superior (SPC), middle (MPC), inferior (IPC), and total pharyngeal constrictor (TPC) and proximal esophagus (PE), were contoured retrospectively, and the dose-volume histogram (DVH) was used to calculate mean dose, maximum dose, V50, and structure volume.

**RESULTS:** Of 25 patients analyzed, 21 had treatment-related PEG tubes placed prophylactically (n = 10) or expectantly during treatment (n = 11). After a median follow-up time of 11 months, the overall median PEG duration was 4 months, with medians of 4 months for prophylactic and 5 months for expectant PEGs. Seven patients (33%) required a PEG for ≥ 6 months, and two (10%) required a PEG for ≥ 12 months. Overall median weight loss during treatment was 17 lbs—11 lbs for prophylactic and 21 lbs for expectant PEGs. Dose characteristics for individual and aggregated structures are found in the Table. On univariate analysis, patients with PEG duration of > 6 months, compared to those with PEG duration < 6 months, had significant increases in PE mean dose (55.8 Gy vs 51.9 Gy, P = .029), V50 (97.6% vs 62.6%, P = .033), IPC V50 (86.6% vs 55.7%, P = .009), and MPC V50 (98.0% vs 87.2%, P = .046).

**CONCLUSIONS:** The duration of PEG tube required in our study cohort was consistent with historical data. There was a direct dose-response relationship with increasing dose to swallowing-related organs, particularly the PE and IPC, resulting in higher rates of PEG use at ≥ 6 months post-RT. Further studies are warranted to directly compare IC followed by CCRT to definitive CCRT to determine if IC can decrease the dose to swallowing-related organs and, in turn, decrease pharyngeal toxicity.

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**(P035) Level V Nodal Coverage During IMRT Planning for Patients With Oropharyngeal Cancer: Clinical Validation and Dosimetric Significance of Consensus Recommendations**

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**PURPOSE:** The impact of level V cervical nodal coverage with the use of intensity-modulated radiation therapy (IMRT) in oropharyngeal cancer (OPC) has not been rigorously evaluated in studies of patterns of failure. Consensus guidelines have recommended selective exclusion of level V from the nodal clinical target volume (CTV). We aim to validate this consensus recommendation by reviewing our clinical experience and, in addition, assess its dosimetric impact.

**MATERIALS AND METHODS:** After IRB approval, 112 OPC patients with nodal stage N0 through N2b treated with IMRT between 2001 and 2010 were identified. Coverage of
ipsilateral and contralateral level V in the original IMRT plan was reviewed and compared with the clinical outcomes. In six randomly chosen patients, three new sets of IMRT plans were generated to compare radiation doses to normal tissue by exclusion of contralateral or bilateral level V from the CTVs. Kaplan-Meier estimates of recurrence-free survival (RFS) and overall survival (OS) were calculated. Log-rank tests (univariate analysis), chi-square (for categorical variables), and paired t test (for means) were used for comparison between different cohorts.

RESULTS: The median patient age was 57 years. The primary tumor site was the base of tongue in 56 (50%), tonsil in 52 (47%), and soft palate in 4 (3%) patients. The stage distribution was T1/T2 (79%), T3/T4 (21%), N0/N1 (30%), and N2a–b (73%). In the original IMRT plan, contralateral level V was excluded from the CTVs in 60 (53%) patients, while bilateral level V was excluded in 35 patients (31%). For the entire cohort, estimated 5-year primary, regional, and distant RFS rates were 92%, 97%, and 93%, respectively. The 5-year and 10-year RFS rates were 86%, while the OS rates were 76% and 69%, respectively. Site of first failure was primary (50%), regional (14%), and distant (36%). There were no failures in nodal level V. No significant differences were noted in RFS or OS between the patient cohorts based on contralateral or bilateral level V exclusion. In the dosimetric study, a highly significant reduction in dose to unspecified normal tissue was noted by excluding contralateral level V (see Table). Similarly significant reductions were also noted when excluding bilateral level V.

CONCLUSIONS: We suggest that exclusion of contralateral level V in IMRT planning for OPC patients is reasonable in well-selected patients with early-nodal-stage (up to N2b) disease. Careful exclusion of ipsilateral level V may also be considered in those with node-negative neck or limited nodal (N1/early N2a) involvement. Careful IMRT planning to maintain high cure rates while limiting late normal tissue effects is important in the era of increasing survival in OPC.

(P036) Thoracic Irradiation Using Proton Therapy and Chemotherapy in Limited-Stage Small-Cell Lung Cancer? An Early Experience at UFPTI

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BACKGROUND: There are no known reported studies using proton therapy in the treatment of limited-stage small-cell lung cancer (SCLC). Concurrent chemoradiotherapy (CRT) is the current standard of care; however, conventional x-ray therapy (XRT) is associated with high toxicity rates, particularly acute grade 3+ esophagitis and pneumonitis. Proton therapy can reduce radiation dose to normal tissue and therefore theoretically reduce toxicity. We present the first known series of SCLC patients treated with proton therapy.

MATERIALS AND METHODS: The study was approved by the University of Florida Institutional Review Board (IRB). The outcomes of six patients treated with proton therapy and chemotherapy were assessed: five were treated concurrently and 1 was treated sequentially. Five patients received 60 to 74 CGE at 2 Gy per fraction, and one patient received 45 CGE in 30 fractions twice daily. Elective nodal irradiation was delivered to between 46 and 60 CGE. All six patients received prophylactic cranial irradiation, and cisplatin and etoposide were used for induction and/or concurrent chemotherapy.

RESULTS: Median follow-up was 12.0 months. One-year overall and progression-free survival rates were 83% and 66%, respectively. There were no cases of acute grade 3+ esophagitis or acute grade 2+ pneumonitis, and no other acute grade 3+ nonhematological toxicities were seen. One patient with a history of pulmonary fibrosis and atrial fibrillation developed worsening symptoms 4 months after treatment, requiring oxygen. CT scan performed at this time showed no evidence of radiation pneumonitis. Three patients died (see Table)—two of progressive disease (having developed distant metastases in sites that were initially suspicious on pretreatment imaging) and one after a fall; the latter patient was disease-free at the 40-month follow-up. Another patient recurred and is alive, while two patients remain disease-free at 12 months of follow-up.

CONCLUSION: In this small series of SCLC patients treated with proton therapy with radical intent, treatment was well tolerated. There were no cases of acute grade 3+ esophagitis or grade 2+ pneumonitis, and no significant detriment in treatment outcome was observed. Proton therapy merits further investigation as a method of reducing toxicity in patients with SCLC.

(P037) Biopsy-Proven Radiation Changes in PET-AVID Lung Lesions Following Stereotactic Body Radiation Therapy: Case Report

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We present two separate but similar cases of non–small-cell lung cancer (NSCLC) patients who were each treated with stereotactic body radiation therapy (SBRT) for solitary lung lesions. PET scans performed for routine follow-up in these asymptomatic patients several months following completion of radiation revealed FDG avidity in the previously treated regions. Radiologic assessment commented on the possibility of residual tumor versus tumor recurrence versus radiation changes. Subsequent biopsies performed on both patients confirmed benign radiation-induced effects.
Post-SBRT radiological changes are commonly seen on follow-up imaging and can cause diagnostic dilemmas. It has been shown that within 6 months of treatment, approximately half of all lesions are associated with radiological abnormalities, with nearly all lesions showing some level of imaging abnormality after 3 years. Theoretically, FDG-PET allows differentiation of metabolically active tumors from inactive fibrosis after radiation therapy. However, the radiobiology of the relatively large fraction sizes in SBRT differs greatly from standard treatment fractions, both with respect to tumor and normal tissue response. It follows, then, that PET findings following SBRT may differ significantly from PET findings after conventional radiation therapy. As evidenced by the independent cases we present, PET has its limitations, specifically frequent false-positive uptake of FDG soon after the completion of radiation therapy.

Ideally, post-SBRT PET avidity would decrease in cases of treatment success. Although available data remain extremely limited, studies have shown that persistent hypermetabolic uptake, even several years following SBRT, may not always represent recurrent disease. Possible explanations for this activity include normal tissue with unresolved postradiation metabolic changes and metabolically active but reproductively dead tumor cells. As SBRT continues to be highly touted as a proven alternative to radical surgery for lung cancer patients, a thorough understanding of posttreatment PET response in anticipation of local failures is becoming increasingly vital. It must be kept in mind that CT-guided biopsies are not benign procedures, and until a more extensive prospective analysis of the optimal evaluation of treatment effect using PET is performed, it would behoove us to keep in mind the ideal time frame for this radiologic study and that once out of this range, false positives are not uncommon.

(P038) Clinical Outcomes for Thoracic SBRT: Does 4DCT Planning Improve the Therapeutic Ratio?

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PURPOSE: Four-dimensional computed tomography (4DCT) is increasingly used in treatment planning for thoracic stereotactic body radiotherapy (SBRT) to allow creation of an internal target volume (ITV). Dosimetric comparisons of 4DCT-based planning to a free breathing approach suggest superior target coverage, but clinical data comparing these methods are lacking. We hypothesize that use of 4DCT planning will improve local control and reduce toxicity as compared to use of free breathing CT (FBCT).

MATERIALS AND METHODS: Between February 2007 and August 2012, 64 consecutive patients underwent SBRT for early-stage non–small-cell lung cancer to 69 lesions. Seven patients had ≤ 2 months to follow-up available, leaving 57 evaluable patients with 60 treated tumors. The first 28 lesions were simulated with FBCT, and the subsequent 32 were simulated with 4DCT. All patients underwent abdominal compression with fluoroscopy to limit diaphragmatic excursion to ≤ 1 cm. For patients simulated with an FBCT, eccentric PTV margins of 1.0 cm in the craniocaudal directions and 0.5 cm circumferentially were added, while a 5-mm PTV was added in all directions to the ITV identified by maximum intensity projection following 4DCT simulation. Target dose ranged from 40 to 60 Gy in 3–8 fractions. Patient charts were retrospectively reviewed for disease control, survival, and acute and late toxicities. Treatment plans and dose volume histograms were retrieved and reviewed. Toxicities were scored with the Common Terminology Criteria for Adverse Events (CTCAE v4.0). Differences for in-lobes control (ILC), locoregional control (ipsilateral lung and mediastinum) (LRC), and overall survival (OS) were compared by log-rank method.

RESULTS: At a median follow-up of 9 months, no significant differences were identified for 1-year estimate of ILC (67% vs 89%, P = .62), LRC (64% vs 85%, P = .99), or OS (68% vs 89%, P = .18) between the two planning approaches. The median GTV was similar between the two groups (2.88 vs 4.22 cc, P = .34), with a trend toward a larger PTV without 4DCT (18.88 vs 36.07 cc, P = .08). No significant differences were identified between the two groups in mean lung dose, V20, V30, or V5. Grade 1–2 pneumonitis was identified in three patients (9%) planned with 4DCT and four patients (14%) planned with FBCT. One case of grade 4 skin toxicity developed in a patient planned by FBCT. No other grade ≥ 3 toxicity was identified.

CONCLUSION: 4DCT allows precise delineation of an ITV encompassing the range of tumor motion during the respiratory cycle and allows use of a small PTV (0.5 in all directions at our center). However, in our practice, addition of an eccentric PTV to a free-breathing GTV provides similar tumor control without added toxicity. Although limited by modest patient numbers and limited follow-up, our experience suggests that further data to justify the added cost of 4DCT technology are warranted before routine implementation as a standard of care.
(P039) Adaptive Replanning for Lung Cancer: Can We Rely on Autocontouring?

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PURPOSE/OBJECTIVES: Adaptive replanning has the potential to achieve more accurate tumor targeting as well as clinically significant sparing of normal tissue. A major obstacle is the time involved, particularly in recontouring. Autocontouring offers a potential solution; however, accuracy is of utmost importance. This study examines the role of adaptive therapy for non–small-cell lung cancer, assessing changes in primary lung gross tumor volume (GTV) over the course of treatment as well as the accuracy of autocontouring software. To compare the agreement of manually versus autocontoured GTVs, we used the DICE coefficient, a measurement of spatial overlap, with values ranging from 0 to 1, with 1 indicating perfect overlap.

MATERIALS AND METHODS: We selected patients with non–small-cell lung cancer who were treated with definitive chemoradiotherapy to a total dose of 60–70 Gy in whom distinct peripheral primary lung tumors could be identified, as autocontouring is not generally possible in lesions adjacent to the hilum/mediastinum, with at least weekly cone beam CT (CBCT) imaging during treatment. From a pool of approximately 40 chemoradiotherapy patients, 10 met the criteria above. The primary tumor GTV was contoured on all CBCTs manually; nodal volumes were not assessed. The MIM software package was utilized for GTV autocontouring on CBCTs. The planning CT was fused rigidly to each CBCT, providing a starting point for deformable fusion, allowing automatically generated GTVs for each CBCT to be compared to the original planning CT as well as the manually defined GTVs employing the DICE metric.

RESULTS: The average ratio of the volume of the GTV on the planning CT to the manually contoured GTV on the Day 1 CBCT was 1.34 (range: 0.72–1.56), indicating that the CBCT tended to overestimate the GTV. The average DICE coefficient comparing manual and autocontoured GTVs on the CBCTs was 0.68 (range: 0.38–0.86), with the highest DICE found in cases where the GTV was surrounded completely by lung parenchyma, as well as in larger GTVs (see Figure). Over the course of therapy, the GTV volume decreased by an average of 48.18% when manually contoured (range: 18.31%–69.15%) vs 38.74% when autocontoured (range: 2.13%–55.65%). The CBCT did not image the entire lung, precluding assessment of DVH parameters; however, the percentage of total lung volume occupied by GTV decreased by an average of 3.31% (range: 0.04%–13.35%) using manual contouring versus 2.76% (range: 0.007%–12.84%) using autocontouring.

CONCLUSIONS: All tumors demonstrated GTV reduction during the course of therapy, suggesting a potential role for adaptive therapy in lung cancer. Although the sample size precludes rigorous statistical analysis, autocontouring with MIM is generally more accurate for GTVs surrounded by normal lung parenchyma, as well as for larger GTVs. While the subset of patients with these characteristics is relatively small, it is these patients in whom adaptive therapy is more likely to impact the DVH and thus potentially provide clinical benefit. Future study should focus on refining the subset of patients in whom autocontouring is accurate and in assessing the ability of autocontouring on CBCT to generate DVH parameters to clue clinicians when replanning might be considered.

(P040) Outcomes of Hypofractionated Radiation Therapy in Poor-Risk Non–Small-Cell Lung Cancer Patients and Validation of RTOG 0213

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PURPOSE/OBJECTIVES: Although combination chemotherapy (ChT) and radiation therapy (RT) is standard of
care for locally advanced non–small-cell lung cancer patients (NSCLC), multiple comorbidities often preclude delivery of concurrent or sequential ChT/RT. There is no current standard for optimal treatment of these poor-risk patients. We report our institutional experience using hypofractionated RT for NSCLC patients and compared them to RTOG 0213, a prospective poor-risk trial involving celecoxib only as a systemic agent.

**MATERIALS AND METHODS:** We retrospectively reviewed all NSCLC patients treated on an IRB-approved registry at our institution with 45 Gy in 15 fractions between April 1996 and September 2012. Fifty-seven consecutive patients were identified. Median age was 73 years (range: 38–91). Median KPS was 80 (range: 50–100). Twenty-six patients had baseline weight loss of equal to or greater than 5% in 3 months (46%). Patient stages were: stage I, 5 patients (9%); stage II, 3 patients (5%); stage IIIA, 9 patients (16%); stage IIIB, 15 patients (26%); stage IV, 20 patients (35%); and recurrent disease, 5 patients (9%). The median Charlson comorbidity index score was 1 (range: 0–7). Twenty-five patients met the criteria for RTOG 0213, which were stages IIIB, IIIA or IIIB; Zubrod performance equal to or greater than 2; and weight loss greater than 5% in 3 months. Median survival times were calculated using Kaplan-Meier analysis.

**RESULTS:** Fifty-three patients completed planned RT (93%). Median follow-up was 4 months (range: 0.3–166.6). Median survival for all patients was 6.7 months. Stage III patients had a median survival time of 7.8 months, and stage IV patients had a median survival of 5.3 months. Thirty-one patients (61%) experienced progression, including local failure in 18 patients (32%) and distant failure in 23 patients (40%). Most common first sites of distant metastasis after RT were bone (35%) and brain (30%). Four patients had grade 3 esophageal toxicity (7%), consisting of three patients hospitalized for esophagitis and one patient hospitalized for esophageal stricture. Of 48 patients with potential for long-term follow-up, 5 patients (10%) were alive beyond 2 years. Patients eligible for RTOG 0213 had a median survival (MS) of 7.8 months (10 months reported in RTOG 0213). Progression-free survival at 1 year was 24% for this cohort (33.3% reported in RTOG 0213).

**CONCLUSIONS:** Durable local control, the primary goal for this population, was achieved with acceptable rates of esophageal toxicity and modest median survival times. Of eligible patients, similar results are seen in our series compared with RTOG 0213. A small subset of patients were alive beyond 2 years. Hypofractionated RT is an appropriate form of fractionation in this fragile patient population, and selection criteria for patients most likely to benefit from this regimen remain under investigation.

**(P041) Role of Combined Treatment With Molecular Targeted Therapy and Radiation in Synovial Sarcoma**

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**PURPOSE/OBJECTIVES:** There are no established curative options for inoperable and metastatic synovial sarcoma. We report an effective combination of molecular targeted agents and radiation therapy.

**MATERIALS AND METHODS:** Triple therapy with a combination of sorafenib (Nexavar), nelfinavir (Viracept), and sirolimus (Rapamune) was used to treat metastatic synovial sarcoma in a patient with multiple metastatic lesions. Subsequently, cetuximab (Erbitux) was added, and palliative radiation was given concurrently for treatment of large metastatic lung nodules.

**RESULTS:** An objective clinical and radiological response with a significant decrease in size of the tumor lesions was noted (see Table). A novel combination of a multikinase inhibitor, an AKT inhibitor, and an mTOR inhibitor resulted in disease stabilization. Complete disappearance of mult-

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<th>Table P041</th>
<th>Tumor Response Following Molecular Targeted Therapy and Radiation Therapy</th>
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<td><strong>Tumor Location</strong></td>
<td><strong>Tumor Type</strong></td>
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<tr>
<td>Lung upper lobe</td>
<td>Metastatic</td>
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<td>Chest wall</td>
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<td>Subcarinal mass</td>
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multiple smaller lesions was achieved with this systemic therapy combination, and partial to complete reduction in size of larger tumor masses was achieved with the addition of cetuximab—an EGFR inhibitor—and localized external beam radiation therapy.

CONCLUSIONS: The combination of multiple molecular targeted agents demonstrates a strong synergistic effect with localized radiation therapy and results in marked shrinkage of the tumor mass. We report the radiosensitizing effect of multiagent target therapy. This approach has clinical significance for downsizing large unresectable synovial sarcoma with neoadjuvant use. For metastatic synovial sarcoma, this treatment may allow better disease control. This combined therapy can be extended further to a range of other sarcoma subtypes.

(P042) Reirradiation of Spinal Metastasis With Stereotactic Body Radiosurgery

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OBJECTIVES: Stereotactic body radiotherapy for previously irradiated progressive spinal metastases is a viable option in well-selected patients. The authors examine a series of spinal metastases reirradiated with stereotactic body radiosurgery (SBRT).

METHODS: Using our institutional database, we collected data from 253 cases of SBRT for spinal metastasis, of which there were 49 cases that were reirradiated using SBRT between 2007 and 2011 with data available, including dose per fraction, total dose of both treatment courses, and appropriate follow-up. Spinal magnetic resonance imaging (MRI) was performed before treatment initiation and patients had either CT or MRI at regular follow-up intervals to evaluate for disease progression. The National Cancer Institute Common Toxicity Criteria, version 3.0 were used to evaluate toxicity. The patients were immobilized in typical supine full-supported fashion with a vacuum bag system. The planning and treatment component was conducted, with the majority of the plans categorized as forward planned, static field, static aperture with reserved comparison to IMRT, and VMAT when necessary. A small-field biased superposition/convolution algorithm was used for planning, and delivery was executed with a 6-MV beam with a 4-mm MLC. A robotic couch was used for daily repositioning and stereotactic treatment alignment.

RESULTS: The mean and median intervals between initial radiotherapy and SBRT reirradiation were 15.9 months and 13 months, respectively (range: 1–52). Mean and median follow-up periods were 16.6 months and 13 months, respectively (range: 1–60). None of the patients experienced myelitis, progression of fracture, or a new fracture. Radiographic local control was 81%. Of the sites treated for pain palliation, 79% reported improvement and 45% remained pain-free. Toxicity was limited to grade 1 dysphagia in three patients and grade 1 dermatitis in two patients. The cumulative reirradiation doses for the SBRT ranged from 15 to 24 Gy given in 1 to 4 treatment fractions with one treatment per week.

CONCLUSION: Reirradiation for progressive spinal metastases with stereotactic body radiosurgery results in symptomatic improvement and increased local control with minimal toxicity. However, it is prudent to propose the collection of prospective data from a greater number of patients receiving reirradiation to assess the safety of reirradiation using SBRT.

(P043) Long-Term Institutional Results of I-125 Plaque Brachytherapy for Uveal Melanoma

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INTRODUCTION: Plaque brachytherapy is a commonly utilized treatment for uveal melanomas. Treatment delivery is complex, however, and specific recommendations exist for appropriate treatment delivery. In addition, results of long-term follow-up data greater than 10 years are limited. The purpose of this study was to review our institutional experience with plaque brachytherapy and evaluate long-term results of treatment.

METHODS: Our institution was retrospectively reviewed from 1996 to 2011, and all patients who underwent plaque brachytherapy for uveal melanoma were included. Data were collected regarding patient and treatment characteristics, and long-term follow-up data were reviewed regarding local control, distant metastases, and side effects from treatment. Kaplan-Meier analysis was performed to evaluate local control (LC), freedom from distant metastases (FDM), freedom from progression (FFP; ie, lack of local failure or distant metastases), and overall survival (OS). Univariate analysis was performed by log-rank analysis to identify treatment characteristics impacting failure-free survival (FFS). Statistical significance of treatment factors affecting side-effect rates was determined by unpaired t-test.
**RESULTS:** Between April 1996 and November 2011, a total of 108 patients underwent plaque brachytherapy; 85% of tumors were in the Collaborative Ocular Melanoma Study (COMS) medium size category. I-125 plaques were utilized in all cases. Local control at 10 years was 94%. FDM, FFP, and OS rates at 10 years were 89%, 83%, and 79%, respectively. Of the local and distant failures, only one distant failure occurred after the first 60 months. On univariate analysis, COMS classification, tumor stage, equatorial position, ciliary body involvement, tumor height, and plaque margin were not found to have a prognostic impact on FFP. The treatment was well tolerated, with radiation retinopathy and cataracts being the most common effects of treatment, occurring in 25% and 24% of patients, respectively. Clinically useful vision (> 20/200) was maintained in 78% of patients. There was a statistically significant association between lens dose received and both cataract development and glaucoma development ($P = .05$ and $P = .04$, respectively). There were no other statistically significant tumor variables identified that predicted for treatment side effects.

**CONCLUSIONS:** Long-term follow-up of patients receiving plaque brachytherapy for ocular melanoma demonstrates excellent outcomes, with almost no local or distant failures after the first 5 years. In addition, it is well tolerated and should remain a standard of care for medium-sized tumors.

**PURPOSE:** To report epidemiology, treatment, and outcomes for an international cohort of patients with extraskeletal osteosarcoma (ESOS), a rare yet aggressive disease mostly summarized only in case reports or series.

**PATIENTS AND METHODS:** Through the Rare Cancer Network, retrospective data on patients with ESOS were collected. Local institutional review board approval was obtained for each hospital. Patient characteristics, multimodality treatment information, and survival status were retrieved. Data were anonymized and sent to one investigator for data analysis. Univariate and multivariate analyses were performed to elucidate prognostic factors for overall and nonmetastatic disease-free survival.

**RESULTS:** Thirty-seven patients in four health care institutions were identified with a median age of 55 years (quartiles: 48–70 years); 21 patients (57%) were male. Twenty-eight (76%) patients were from a single institution. Thirty-one (86%) patients had high-grade (3/4) tumors: 33 (89%) were soft tissue (retroperitoneum, pelvis, and extremities) and 4 (11%) were in organs (2 hard palates, 1 ethmoid sinus, and 1 breast). Seven (19%) tumors were < 5 cm, 15 (42%) were 5 to 10 cm, and 14 (39%) were greater than 10 cm. Most patients (27 [73%]) had stage III disease; 4 (11%) had metastases at initial presentation. Fourteen (38%) patients received neoadjuvant chemotherapy or chemoradiation. Of 28 (85%) who underwent surgery, 21 (75%) had free margins achieved and 15 (41%) subsequently received adjuvant chemotherapy. I-MAP or MAP (ifosfamide, mitomycin/methotrexate, doxorubicin, and cisplatin) combination chemotherapies were most common choices upfront; gemcitabine appeared effective as a second-line chemotherapy regimen. The median prescribed radiation dose was 50.4 Gy (range: 40–70 Gy). At median follow-up of 45 months (quartiles: 15.6–88.9 months), 20 (55%) patients were alive and 13 (43%) were disease-free. The median overall survival (OS) has not been reached yet; 75% and 60% of patients were alive at 26 and 54 months, respectively. Excluding patients with initially metastatic disease, 65% and 57% remained disease-free and alive at 20 and 40 months, respectively. Univariate analysis showed that OS was related to stage IV ($P < .001$; hazard ratio [HR] = 24.15), no surgery ($P < .001$; HR = 16.67), primary size > 10 cm ($P = .002$; HR = 4.83), and age ($P = .002$; HR = 1.06). In the multivariate analysis, stage IV ($P < .001$; HR = 26.76) and primary size > 10 cm ($P = .005$; HR = 5.05) were prognostic for OS. For patients
without metastases, univariate analysis showed that poorer disease-free survival (DFS) was related to primary size > 10 cm ($P = .003; HR = 4.72$), pathologic size > 10 cm ($P = .03; HR = 3.54$), local recurrence ($P = .003; HR = 5.95$), and age ($P < .001; HR = 1.09$). In multivariate analysis for DFS, primary size > 10 cm ($P = .01; HR = 5.10$) and age ($P < .001; HR = 1.10$) remained significant.

**CONCLUSION:** The survival outcome in this cohort of patients with extraskeletal osteosarcoma was similar to those reported in osteogenic sarcomas. Multimodality approach remains standard in patients with localized disease, although the indications for neoadjuvant therapy are less clear in ESOS. Larger tumor size and old age were prognostic for poorer disease-free survival.

**P045 Application of IQ Scripts to Automate and Improve the Overall Efficiency of Workflow in a Radiation Oncology Department**

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**INTRODUCTION:** IQ scripts are customizable tools in MOSAIQ used to automate workflow and improve work efficiency, treatment, and patient safety. These scripts are triggered on the completion of a quality checklist (QCL) item or on the generation of an observation order. Both of them can produce another QCL item and assessment that implement the workflow in an automated fashion. In this study, we identified areas where IQ scripts could be applied and measured parameters to assess their efficacy.

**MATERIALS AND METHODS:** More than 200 such scripts were programmed in the IQ engine to manage the workflow by selecting the QCL procedure or order that would trigger the next QCL item or assessment. Each QCL item was given a responsible staff or location. Indices used to quantify improvement pertained to safety, efficiency, and policy requirements. The parameters that were used were (1) the time taken to complete physics chart checks, (2) the number of charts that missed physics checks within the required time frame, and (3) the availability of requests and alerts for obtaining critical information before a patient receives care. Situations with a need for critical information included (1) presence of a pacemaker, (2) previous radiation, (3) need for pregnancy screening, and (4) special needs. A sample of 60 charts for patients treated in 2009 was selected for analysis prior to implementation of the paper-free environment. Postimplementation data were obtained from the date of implementation of the paper-free environment.

**RESULTS:** The time taken to complete the initial physics chart check was significantly reduced with the application of IQ scripts from completion before the third fraction to before the second fraction ($P < .05$, policy requires checks before the third fraction). The percentage of patients that received initial chart checks after the treatment of 3 or more fractions was reduced from 0.6% to 0.0% ($P < .05$). The number of charts that received final checks after 7 days of treatment completion was reduced from 10% to 0% ($P < .05$, policy requires checks within 7 days). Automated QCLs sent through IQ scripts for critical situations always made the necessary information available to physicians, nursing, therapists, and medical physicists. This improved patient treatment safety. Since the QCLs and assessments...
were programmed, their completion automatically generated the assessment to use and the task to perform, improving accuracy of the workflow. The decrease in the need to manually append QCL items as well as the ability to send out multiple QCLs simultaneously to different groups reduced manual input, potential errors, and bottlenecks. This enabled tasks to be performed in parallel, thus improving overall efficiency.

CONCLUSION: With the application of IQ scripts and QCLs, our department observed a significant reduction in the time required to complete tasks pertaining to policy requirements and in the number of missed chart checks. Development of event- and process-driven IQ scripts that are more closely matched to process completion rather than QCL completion will further eliminate manual input and streamline workflow.

(P046) Early-Stage Non–Small-Cell Lung Cancer Treated with Stereotactic Body Radiotherapy in Patients With Fibrotic Interstitial Pulmonary Disease

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BACKGROUND: Fibrotic interstitial lung diseases (FILDs) are a group of chronic, restrictive pulmonary syndromes, including idiopathic pulmonary fibrosis (IPF), characterized by deposition of collagen in the pulmonary interstitium with a resultant progressive decline in pulmonary function. The tenuous pulmonary status of patients with concurrent lung cancer and FILD often precludes their ability to undergo surgical resection. Current evidence suggests that clinical outcomes for stereotactic body radiotherapy (SBRT) in early-stage non–small-cell lung cancer (NSCLC) are approximately equivalent to surgical outcomes. Accordingly, SBRT may represent the preferred treatment modality for patients with concurrent NSCLC and FILD.

METHODS: Four male patients (median age 75 years) with underlying FILD were treated with SBRT for stage I NSCLC. Two patients had IPF, one had probable IPF, and the fourth had asbestosis. Patients underwent 4D computed tomography (CT) simulation, the entire respiratory volume was contoured and expanded by 7 mm, and patients were treated during free breathing on a linear accelerator with an arc-based technique in 3 to 5 fractions. SBRT dose ranged from 40 to 54 Gy (biologically effective dose range: 80–151.2 Gy).

RESULTS: With a median follow-up of 6.4 months, local control was 100%. Median percent predicted pre- and posttreatment forced vital capacities (FVCs) were 62% (range: 35%–66%) and 48% (range: 31%–73%), respectively. Median percent predicted pre- and posttreatment corrected diffusion capacities of the lung for carbon monoxide (DLCO) were 41% (range: 25%–53%) and 30% (range: 18%–45%), respectively. All patients saw a decline in corrected DLCO, and three patients saw a decline in FVC post-SBRT. The patient who experienced an increase in FVC post-SBRT (66% to >73%) would ultimately have a gradual decline in FVC expected of patients with FILD; however, he experienced no acute increase in oxygen requirement or pulmonary symptoms. Despite a decrease in FVC and DLCO, a second patient would also have no increase in oxygen requirement or pulmonary symptoms. The remaining two patients had significant morbidity with sustained increases in oxygen requirement and marked increases in diffuse ground-glass opacities by CT following SBRT. One of these patients developed a pulmonary embolus and died 2.2 months after treatment, while the other was hospitalized for altered mental status, thought to be secondary to increasing steroid requirement. In total, three of the four patients are currently living.

CONCLUSIONS: SBRT is an acceptable and potentially curative treatment modality in this high-risk population. In our series, two patients were symptomatically and objectively stable following SBRT, while two patients experienced a more pronounced decline by objective pulmonary function testing and by symptoms. Given the high mortality of untreated NSCLC, SBRT should be considered in patients with FILD with borderline pulmonary function.

(P047) Radiation Safety Considerations in Proton Aperture Disposal

Priscilla K. Walker, BS, Andrew C. Edwards, Indra J. Das, PhD, FACR, Peter A.S. Johnstone, MD, FACP; Indiana University Health Proton Therapy Center; Indiana University Cyclotron Operations; Department of Radiation Oncology, Indiana University School of Medicine

OBJECTIVE: Most proton radiotherapy (PRT) using either passive scattering or uniform scanning requires beam shaping by customized brass apertures for each field. Due to proton interactions, these apertures become radioactive and could pose safety issues and radiation hazards. A mechanism is required for each proton center to manage the used radioactive apertures.
METHODS: The records of Indiana University Cyclotron Operations (IUCO) and IU Health Proton Therapy Center (IUHPTC) were screened to describe used aperture disposal policies. Close to 2,000 patient-specific devices per year are used that require proper guidelines for disposal. Processes for storage and waste recovery are outlined to minimize safety risk.

RESULTS: IUCO practice has been to store these apertures for at least 4 months in a secure place to allow for safe transfer to recycling contractors. Over 150 apertures are utilized each month at IUHPTC. They require decay in two staged secure locations, including at least 4 months in a separate building, at which point half are ready for disposal. At 6 months, 20% to 30% of apertures require further storage.

CONCLUSIONS: Brass apertures require additional storage after a course of PRT to allow decay to acceptable levels. This requires significant space and manpower and should be considered in the design process for new clinical facilities. More widespread adoption of pencil beam or spot scanning nozzles may obviate this issue, as apertures will no longer be necessary.

(P048) Target Volume Heterogeneity Index: A Potentially Valuable Metric in Prostate Cancer Treatment Planning

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PURPOSE/OBJECTIVES: Heterogeneity index (HI) has been described in the literature as a tool for evaluating dose gradients within a planning target volume (PTV). HI may be expressed as D1/D95, where D1 and D95 equal the dose encompassing 1% and 95% of the target volume, respectively. The purpose of this study is to evaluate the effect of target volume dose heterogeneity on dose received by local organs at risk in the treatment of low- and intermediate-risk prostate cancer.

MATERIALS AND METHODS: Treatment plans were reviewed for 157 patients with low- or intermediate-risk prostate cancer treated with dose-escalated radiation therapy from June 2007 to February 2012. Patients treated in the postoperative setting or receiving pelvic nodal irradiation were excluded. Patients were treated with either standard intensity-modulated radiation therapy (IMRT) using seven or eight fields or 2-arc volumetric modulated arc therapy (VMAT). All patients had daily image guidance. PTV HI (D1/D95) and dose-volume histogram (DVH) data at eight dose levels for rectum and bladder were recorded. Patients were categorized into two groups (low HI or high HI) with respect to median index score. A two-tailed t-test was used to test for differences in dose received by the rectum and bladder for the two groups. The data were then fit using a linear regression model to evaluate the predictive value of HI for dose received by the rectum and bladder.

RESULTS: For the 157 plans evaluated, the mean PTV volume was 164 cc and the mean prescription dose was 7,833 cGy. Median HI was 1.04 (range: 1.0–1.08). Low HI (≤ 1.04) was found to correlate with significantly lower rectal V50 (P = .02), V55 (P = .01), V60 (P = .01), V65 (P = .01), and V70 (P = .01). There was no significant correlation with dose received by the bladder. HI was similar for patients treated with standard IMRT and VMAT (P = .85).

CONCLUSIONS: Target volume HI ≤ 1.04 is associated with more favorable rectal doses at clinically relevant doses. We believe HI may serve as a valuable metric in prostate cancer treatment planning. Further work is needed to correlate these dosimetric findings with clinical outcomes.

(P049) Validation of a Novel Superior Vena Cava Syndrome Identification, Classification, and Management Algorithm

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INTRODUCTION: Superior vena cava (SVC) syndrome results from compromised venous return due to extrinsic compression of the great vessels, obstruction from an intramural thrombus, and/or secondary to an indwelling catheter. SVC can escalate into a life-threatening condition. The Yale classification system and management algorithm is based upon patient presentation and tumor characteristics and was devised as a starting point towards evidence-based multidisciplinary treatment and to allow comparison of results from different institutions. The Yale classification system does not address respiratory symptoms that may precede vascular compromise (facial, neck, or extremity edema), nor does it address nononcologic causes of SVC. We hypothesized that this classification system and management algorithm was limited in scope and may exclude clinical parameters, patient populations, and gender differences, which could lead to earlier identi-
fication of SVC syndrome from a broader range of causes. Our specific aim was to validate the Yale classification algorithm and develop a comprehensive model for SVC identification.

METHODS: Retrospective data from Oregon Health and Science University patients diagnosed with ICD-9 code 459.2, compression of vein, between 2008 and 2011 were collected. Patient demographics, vital signs, physical examination findings, radiographic studies, tumor characteristics, hospitalization records, and outcomes were collected and analyzed. Student t- and chi-squared tests were utilized to assess significant differences in clinical presentation between men and women \( (P \leq .05) \).

RESULTS: The study population consisted of 207 patients; 157 were removed due to compression of a vessel other than the SVC. Women \( (n = 23) \) were older than men \( (n = 27) \) (48 years, standard deviation [SD] = 24 yrs vs 55 years, SD = 18 years, respectively; \( P = .02 \)). There was no difference between the two groups with respect to length of hospitalization; duration of ICU stay; or admission heart rate, blood pressure, or respiratory rate. Dyspnea, facial edema, and cough were the most common physical examination findings. Thirty patients presented with SVC syndrome secondary to a malignancy. Treatment courses often mirrored the Yale classification system and management algorithm. Patients who presented with cough or dyspnea secondary to a malignancy, without facial, neck, or extremity edema \( (n = 7) \), did not meet the required criteria and were not candidates for a classification. SVC syndrome secondary to iatrogenic causes—postprocedure fibrotic stricture \( (n = 5) \) or an indwelling catheter-related thrombus \( (n = 11) \)—also could not be classified.

CONCLUSION: The Yale classification system and management algorithm was applicable to patients with a malignancy. It was limited in scope and did not account for patients presenting with respiratory symptoms prior to the onset of those associated with vascular compromise (facial, neck, or extremity edema), and nononcologic causes were not addressed. A new classification system that accounts for the escalation of symptoms due to mass effect on surrounding tissues and a new management algorithm incorporating their respective treatments were devised.

(P050) Predictors and Trends in Academic Career Selection Among Radiation Oncology Residents: A National Survey of Radiation Oncology Program Directors

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PURPOSE: Given the changing dynamic of the United States health care system, along with the increasing demand for radiation therapy services, academic radiation oncology departments and radiation oncology residency programs have been forced to adapt to increasing clinical volumes. The effect of these changes on the decision choice of residents to become academic radiation oncologists is unknown. The purpose of this study was to identify trends in the proportion of radiation oncology residents pursuing academic careers and possible program characteristics that may affect resident career choices.

METHODS: A survey was sent to 83 radiation oncology residency program directors within the United States regarding residents who graduated between the years 2001 and 2011. The survey contained questions regarding the
number of residents who pursued an academic position following graduation, research time during residency, and number of residents per class. Additionally, data regarding the major hospital for each residency program were obtained through publically available data from US News and World Report. A logistic regression model was built to test predictors of resident career choice.

RESULTS: Of the 83 radiation oncology programs contacted, 15 (18.0%) completed the survey, representing approximately 26% of radiation oncology residency graduates from 2001 to 2011. Data regarding career choice and gender were obtained for 306 residency graduates from 2001 to 2011. A total of 144 (47%) residents initially chose academic careers following graduation; 45% of male graduates and 49% of female graduates initially chose academics. The percentage of residency graduates who pursued academics increased slightly over the study period (35% in 2001 vs 48.5% in 2011). Logistic regression analysis found that residents from programs with more research months during residency (odds ratio [OR], 1.02; \( P = .041 \)), more residents per class (OR, 1.35; \( P = .005 \)), and an affiliation with an NIH cancer center (OR, 1.39; \( P = .036 \)) were more likely pursue academic careers. Conversely, residents who trained at hospitals with large clinical volumes (as measured by annual discharges) were less likely to pursue academic careers following graduation (OR, 0.98; \( P = .005 \)).

CONCLUSIONS: Over the last decade, there has been a relative increase in the proportion of radiation oncology residents who have chosen academic careers following graduation. The choice to pursue academic radiation oncology does not seem to be related to gender but rather characteristics of the residency program and hospital where a resident is trained.

(P051) Definitive Treatment of Leptomeningeal Spinal Metastases in Children

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OBJECTIVE: Unique to children, the existence of leptomeningeal spinal metastases (LSMs) does not confer a uniformly grave prognosis. Although the tolerance of spinal cord to radiation therapy (RT) is of significant concern in these cases, the chemosensitivity and radiosensitivity of these lesions argue for an aggressive approach where possible.

MATERIALS AND METHODS: The records of the Indiana University Health Proton Therapy Center were reviewed for patients undergoing proton beam therapy (PBT) with curative intent for LSMs between June 1, 2004 and July 15, 2012. Patients with microscopic disease only on lumbar puncture (M1) were not included. Details of the therapy, including dose, field sizes, associated toxicity, and outcomes, were collated.

RESULTS: A total of 22 children received therapy as described in this era, with a median age of 5 years (range: 1.1–17.1). Most had medulloblastoma (n = 9), followed by atypical teratoid rhabdoid tumor (ATRT; n = 4) and ependymoma and primitive neuroectodermal tumor (n = 3 each). Five lesions (23%) were chemorecurrent, though no patient had prior radiation to the spine. Median follow-up was 8 months (range: 1.2–32.9); one patient was lost to follow-up after his last treatment. Of 14 patients with well-defined LSMs (22 lesions), local control was achieved in 17 lesions (77%) in 12 patients, with a median lesion dose of 37.8 Gy (range: 21.6–54 Gy). Seven patients with chemorecurrent disease or diffuse cord/cauda seeding (“sugar coating”) did poorly, with local control only achieved in three patients. Actuarial 12-month overall survival was 72% for the entire cohort. The most frequently encountered toxicity of therapy was grade 1 skin erythema.

CONCLUSIONS: This is the largest reported series of LSMs treated with RT with definitive intent and the only data from the proton environment. Durable response is possible for these children in over 75% of cases. Significant toxicity was infrequent using proton radiotherapy and these fractionation schemes.

(P052) Lymph Node Management in 255 Patients With Paratesticular Rhabdomyosarcoma: A Population-Based Analysis

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INTRODUCTION: Paratesticular rhabdomyosarcoma (PTRMS) is the most common primary solid tumor arising from the mesenchymal tissue of the testis. Traditionally, retroperitoneal lymph node dissection is not recommended for children < 10 years of age due to morbidity of the procedure, lack of survival benefit, and low risk of retroperitoneal nodal involvement. We analyzed the patient and tumor characteristics of PTRMS as well as survival outcomes associated with lymph node dissection status.
MATERIALS AND METHODS: A total of 255 cases of PTRMS were identified from the patient data reported by the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute (1973–2009).

RESULTS: Among patients > 10 years of age (n = 173), lymph node dissection improved 5-year overall survival (OS) from 64% to 86% ($P = .019$. Conversely, patients < 10 years of age fared extremely well, regardless of lymph node dissection status; the 5-year OS was 100% and 97% for patients with and without lymph node dissection, respectively ($P = .31$). The yield of lymph node dissection was approximately 20% or higher when < 12 lymph nodes were removed. The incidence of lymph node involvement was also higher in older patients (40%) compared with younger patients (8%). Radiation therapy improved overall survival in patients with lymph node involvement (5-year OS 90% with radiation vs 36% without radiation, $P < .0001$).

CONCLUSION: Lymph node dissection is recommended in patients aged > 10 years. Dissection of 12 or more lymph nodes did not increase yield of nodal positivity. Radiation is beneficial in patients with node-positive disease.

(P053) Management of Disseminated Choroid Plexus Papilloma: A Case Study

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BACKGROUND: Choroid plexus papillomas are exceedingly rare, accounting for 0.5% of adult and 1% to 3% of pediatric intracranial neoplasms. Symptoms are usually secondary to hydrocephalus due to overproduction of cerebrospinal fluid (CSF), blockage of CSF flow, or hemorrhage. While roughly 25% of cases are malignant, central nervous system dissemination can occur despite benign histopathology. Surgery is the standard of care for primary lesions; yet, the optimal management of disseminated disease remains unknown. Few patients are reported in the literature, and experience with radiation therapy for the management of choroid plexus papilloma is extremely limited.

METHODS: A 31-year-old female with a history of recurrent choroid plexus papilloma that was first diagnosed and resected in 2002 was found to have widespread central nervous system (CNS) dissemination 8 years later and underwent resection and adjuvant radiation therapy. The patient received craniospinal irradiation (CSI) to 39.6 Gy, followed by boosts to areas of disease, including the surgical bed to 54 Gy, the thoracic region to 45 Gy, and the thecal sac region to 48.6 Gy.

RESULTS: Two years after completing radiation therapy, the patient remains free of evidence of disease progression according to follow-up imaging. The patient reports no problems with memory or cognition and denies headache, nausea, or vision changes. She reports good energy levels and has returned to work.

CONCLUSIONS: Optimal management of disseminated choroid plexus papilloma has not been established, but our approach of surgical resection with adjuvant radiotherapy appears to have controlled recurrent disease with minimal toxicity or complications at 2 years of follow-up. Further research is necessary to determine the best strategy for combating this rare and vexing disease.

(P054) Proton Therapy for the Treatment of Childhood Craniopharyngiomas: Cyst Dynamics and Initial Outcomes

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PURPOSE/OBJECTIVES: Cystic changes are frequently encountered during or immediately after radiation therapy (RT) in patients with craniopharyngiomas. This necessitates changes in therapy and may potentially affect long-term outcomes. We evaluated our early experience for changes in cyst size and early outcomes in pediatric patients treated with proton beam therapy (PBT).

MATERIALS AND METHODS: Pediatric patients with craniopharyngiomas treated with PBT at UT MD Anderson between 2007 and 2012 were identified and retrospectively reviewed. Patient demographics were complied along with treatment details, tumor characteristics, and toxicities. Categorical data were analyzed using Fisher’s exact test. Overall survival (OS) from end of RT to death or last follow-up was calculated. Progression was subcategorized as growth of the solid component versus postradiation cystic change. Kaplan-Meier method was used to calculate progression-free survival (PFS) and OS.

RESULTS: Nineteen patients met the criteria for evaluation with a median follow-up of 31.8 months (range: 5.3–65.6). Median age was 9.7 years (range: 4.5–17.9), and median
tumor size at presentation was 4.5 cm (range: 1.1–7.8). Fifteen patients underwent at least one surgical intervention (four gross total resections, eight subtotal resections, three biopsies/fenestrations) prior to RT. PT was delivered most often as adjuvant, postoperative therapy (n = 8) but also for recurrent disease (n = 7). Median RT dose was 50.4 Gy (RBE [relative biological effectiveness]) (range: 50.40–54) delivered in 1.8-Gy (RBE) fractions using passive scattering proton therapy (n = 17) or scanning beam therapy (n = 2). Reimaging during RT to evaluate for potential cystic changes was performed at variable intervals (including weekly and zero to three times during treatment) at the discretion of the treating physician. Five patients experienced cyst growth during RT, while six patients experienced shrinkage. Of the five patients experiencing cyst growth, two patients required cyst decompression during RT and one required replanning. Four patients experienced cyst growth within 3 months following RT, three of whom were transient. Additionally, four patients experienced slow cyst growth in long-term follow-up, with three requiring decompression. Median time to cyst growth was 24.1 months (range: 16.2–33.3). One patient had progression of nodular enhancement requiring surgical resection; pathology demonstrated viable disease with brain invasion. For the entire cohort, 5-year OS was 93%, 5-year PFS was 91%, and median survival has not been reached. The single death was attributed to significant electrolyte abnormalities secondary to preradiation, surgically induced diabetes insipidus. In follow-up, eight patients had panhypopituitarism, and 17 patients required at least one hormonal replacement during or posttreatment. Two of the eight patients were new post-RT deficiencies and not associated with endocrine deficiency at presentation or postoperatively. Two patients were diagnosed with potential radiation-associated vasculopathy.

CONCLUSIONS: Craniopharyngiomas, while benign, are associated with long-term morbidity both from the disease itself and the treatment. During proton therapy, the evaluation of cyst dynamics is important to ensure adequate coverage. Initial evidence suggests that, similar to photon therapy, cystic changes following radiation are common.

(P055) Outpatient Management of Vascular Access Devices in Children Receiving Radiotherapy: Complications and Morbidity

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OBJECTIVE: When treating children with cancer, long-term venous access is critical. This is especially true in the context of children receiving daily radiation therapy under general anesthesia. We have previously reported a 0.074% risk of complications in over 4,040 pediatric treatments under general anesthesia in our outpatient facility. Here, we present our experience with venous catheter access techniques in children receiving daily proton RT.

MATERIALS AND METHODS: After institutional review board approval, we reviewed our center’s records between September 9, 2004 and October 23, 2012 with respect to complications and morbidity of indwelling catheters in our pediatric patients.

RESULTS: Vascular access devices included 110 indwelling ports (PACs), 34 PICCs, and 34 central lines (CVCs) in 170 patients. Median catheter life was 43 days (range: 1–86 days), with a total of 7,169 total catheter-days. A total of 110 indwelling catheters experienced a 14% complication rate, including negative blood return (7.4%) and infection (4.6%). Complication rates for PICCs and central lines were 38% and 21%, respectively (P = .007). The most frequent complications for PICC lines were no blood return (11.8%) and infection and occlusion (8.8% each). Frequent complications of central lines were breakage (8.8%) and infection (8.8%). Access device replacement rates were 3.6% for PACs, 14.7% for PICCs, and 8.8% for CVCs.

CONCLUSION: In the outpatient delivery of radiation therapy to children, indwelling ports provide greater convenience, less likelihood of infection or complication, and greater durability than PICC placement or central lines.

(P056) Does the Degree of Resection Affect Locoregional Control in Children Receiving 24 Gy to the Primary Site for High-Risk Neuroblastoma?

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PURPOSE: Locoregional relapse is a significant cause of treatment failure in children with high-risk neuroblastoma. In a Memorial Sloan-Kettering Cancer Center study utilizing 21 Gy radiotherapy (RT) to the primary site, patients who had surgical subtotal resections (STRs) had inferior locoregional control compared with those who had undergone gross total resections (GTRs). More recently, a German trial showed excellent locoregional control in children who had STRs but received 36 Gy to
the primary site. In the current Children’s Oncology Group (COG) protocol for high-risk neuroblastoma (ANBL0532), a dose of 21.6 Gy is delivered to patients who underwent a GTR, while 36 Gy is delivered to patients with a subtotal resection. At our institution, since 2006, we have delivered 24 Gy to the primary site regardless of the degree of resection. We have now conducted a retrospective review to compare the rates of locoregional relapse in patients after GTR and STR followed by 24 Gy.

METHODS: From January 2006 to June 2011, 26 patients with high-risk neuroblastoma were treated at one radiation therapy department. All patients received induction therapy with 5 cycles of chemotherapy and surgical resection. They were then treated with 24 Gy in 12 fractions to the primary site and MIBG-avid distant metastatic sites that were documented at the end of induction chemotherapy. The clinical target volume for primary site RT was the postinduction, presurgical volume with a 1-cm margin. RT was followed by a single round of high-dose chemotherapy with autologous stem cell rescue and maintenance therapy using cis-retinoic acid. The degree of resection and sites of recurrence were determined utilizing postoperative and surveillance CT-MRI and MIBG scans.

RESULTS: There were 12 boys and 14 girls who completed high-risk neuroblastoma treatment during this time, with a median age at RT of 39 months (range: 8–129 months). Primary tumor was located in the abdomen in 24 patients (92.3%). Of the 26 patients identified, 19 patients had a GTR while 7 patients had an STR. With a median follow-up of 37 months (range: 10–77 months), the 3- and 5-year overall survival rates were 67% and 60%, respectively. The 3- and 5-year locoregional control rate was 87%. Three of the 19 patients with a GTR had a radiographic locoregional recurrence, while none of the seven patients who underwent an STR had locoregional relapse ($P = .26$). All locoregional recurrences were in the primary site tumor bed; there were no regional node failures. Median time to locoregional recurrence was 12 months.

CONCLUSION: In our experience, the locoregional control rate was not affected by the degree of resection when 24 Gy RT was delivered to the primary site.

(P057) Patient Characteristics and Immobilization Impact Setup Accuracy for Stereotactic Body Radiation Therapy for Upper Lung Tumors

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OBJECTIVES: To compare the impact of pulmonary function, body habitus, and stereotactic body radiation therapy (SBRT) immobilization strategies on setup and reproducibility for upper lung tumors.

METHODS: From 2008 to 2011, the institutional prospective SBRT database was searched for patients with upper lung tumors, defined as an internal tumor volume superior to the T5 vertebra. Two SBRT immobilization strategies were used: full-length BodyFIX (76 tumors) and thermoplastic S-frame (17 tumors). At simulation, free breathing 4-dimensional computed tomography was performed. The patient’s pulmonary function test, height, and weight were recorded. For each treatment, patients were first set up to isocenter with in-room lasers and skin tattoos. Subsequent shifts from initial couch position were made with cone beam CT (CBCT) to correct for tumor position. Accounting for setup uncertainties, the institutional tolerance of 3-dimensional CBCT-based shifts for treatment was 2, 2, and 4 mm; shifts exceeding these limits required reimaging. Couch shifts were analyzed as square root of sum of squares in all directions. Kaplan-Meier analysis, Wilcoxon rank sum test, Fisher exact test, and t-test were used for nonpaired comparisons between subgroups. A multistep, multivariate linear regression model was performed.

Boxplots for First Fraction (F1), First Shift Errors With Bodyfix Versus S-Frame ($P < .001$).
RESULTS: For the 88 patients identified, the median follow-up was 8.7 months; the median age was 71.8 years. Sixty-eight patients (77%) were past or current smokers, and 59 (67%) had clinically significant chronic obstructive pulmonary disease (COPD). No statistical interaction between S-frame and BodyFIX was found except for body surface area, which slightly favored patients who had S-frame ($P = .03$). Eighty-eight patients with 93 upper lung tumors (21 central and 72 peripheral) were identified; 64 tumors were non–small-cell lung cancer (54 primary and 10 recurrent) and 29 were metastatic from other sites. Lesion sizes were < 1 cm (15%), 1.1 to 2 cm (50%), 2.1 to 3 cm (25%), and > 3 cm (11%). Seventeen tumors were immobilized with S-frame, and 76 were immobilized with BodyFIX. Dose schemes were 48 Gy/four fractions (28%), 50 Gy/five fractions (24%), and 54 Gy/three fractions (46%). All shifts from first fractions were statistically better with S-frame than with BodyFIX. Correction by first-couch shifts was usually successful; second-couch shifts were similarly small, regardless of immobilizing device. For all patients, the 2- and 3-year local control (LC) rates were 94% and 81%, respectively; the median has not been reached yet. LC was not different for patients immobilized with S-frame versus BodyFIX (log-rank $P = .70$). There was no difference in LC by patient age, PFT function, body habitus, or COPD or smoking status, though tumors > 2 cm had poorer LC (log-rank $P < .006$). Multivariate modeling confirmed that body habitus and immobilization device impacted couch shift errors, which in turn were correctable during SBRT setup for treatment of upper lung tumors.

CONCLUSIONS: For upper lung tumors treated with SBRT, initial setup was more consistent with S-frame immobilization than with BodyFIX, resulting in fewer CBCTs in our clinical practice. Patients with obese habitus and poor lung function had more SBRT setup uncertainty; however, their outcome and probability for local tumor control remained excellent.

(P058) Photon Tomotherapy Is an Alternative to Proton Beams for Selected Brain and Head and Neck Tumors

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PURPOSE: For selected tumor sites in the brain and head and neck regions, we compared the quality of treatment plans generated using passively scattered protons with those using photon helical tomotherapy. Plan quality metrics included tumor dose uniformity and conformity, as well as a composite equivalent uniform dose (EUD) among tumors and organs at risk (OARs). We identified instances in which tomotherapy may be preferable to proton therapy.

MATERIALS AND METHODS: Plans were created for eight cases, four of which featured both a primary and a boost target volume. Among the disease sites considered were posterior fossa (two cases), orbit (two cases), parameningeal tumor, nasopharynx, suprachiasm, and a case of whole-ventricle irradiation. All patients were originally planned and treated using helical tomotherapy (TomoTherapy, Accuray Inc). Proton plans were generated using a commercial planning system (XiO, v4.62, Elekta) with a passively scattered proton beam model featuring a maximum range of 32 g/cm² (225 MeV), range modulation in 0.5-g/cm² increments, and Lucite range compensators with a milling tool diameter of 4.8 mm. All proton plans were limited to two beams per target volume except for the nasopharynx case, which used four non-coplanar beams, and the whole-ventricle case, which used three coplanar beams. Plan quality was compared using dose volume parameters, including uniformity index (UI) (the ratio of the minimum doses covering 5% and 95% of the target volume); conformity index (CI) (the ratio of the target volume to the volume encompassed by the prescribed dose); and an EUD-based plan quality index, fEUD (composite value calculated using EUDs for all targets and OARs; a larger fEUD indicates higher plan quality).
**RESULTS:** For 11 of 12 targets, the UI improved for the proton plan; on average, the UI was 1.05 for protons versus 1.08 for tomotherapy. For 8 of 12 targets, the tomotherapy plan exhibited a more favorable CI; on average, the CI was approximately 10% higher for tomotherapy than for protons. For proximal OARs, such as the brainstem for posterior fossa and the optic nerves for the orbit and nasopharynx, tomotherapy yielded a lower maximum dose. For the posterior fossa, this was attributed to a higher CI from tomotherapy. For distal OARs, such as the eyes and pituitary for the posterior fossa and the contralateral eye and inner ear for the orbit, the maximum dose was much lower for proton plans; this was attributed to the choice of beam directions. Near-total avoidance for distal OARs provided by protons led to improved fEUD over the tomotherapy plans. However, if the distal OARs were excluded from the fEUD calculation, the fEUDs for the tomotherapy and proton plans were similar.

**CONCLUSIONS:** The target dose homogeneity and avoidance of dose to distal OARs are generally more favorable from passively scattered proton planning than from tomotherapy. For disease sites where distal OAR sparing is critical, proton therapy is preferable. However, target dose conformity and proximal OAR sparing are more favorable with tomotherapy planning, and the EUD-based plan quality is comparable to that of protons. In such cases, photon intensity-modulated radiation therapy (IMRT) techniques, such as tomotherapy, may be preferable to protons.

**Optimizing Gamma Knife Quality Control: Output Factor and 3D Gamma Analysis Using Presage Dosimeters**

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**PURPOSES/OBJECTIVES:** Measuring small collimator output factors for Gamma Knife is notoriously difficult, due to the compact dose distribution, steep dose gradients, detector volume averaging affects, and precise detector positioning. High-resolution three-dimensional (3D) dosimeters can overcome many of these challenges. The purposes of this study were to: (1) test the accuracy of PRESAGE polymer dosimeters in measuring the 4-mm Gamma Knife output factor and (2) test the feasibility of using 3D gamma analysis on Gamma Knife dose distributions.

**MATERIALS AND METHODS:** An anthropomorphic CyberKnife stereotactic head phantom was outfitted with a Gamma Knife treatment halo for irradiation in a Gamma Knife Perfexion treatment machine. A water-equivalent plastic insert was machined to hold a tall cylindrical PRESAGE dosimeter (60-mm diameter and 90-mm height) (Heuris Pharma, Skillman, NJ) in the skull compartment of the phantom. One 4-mm shot and one 16-mm shot (4 Gy at 50%) were delivered to the dosimeter axis, spaced by 45 mm. The PRESAGE dosimeter was read using the Duke Medium Optical Scanning System (DMOS). PRESAGE data were measured in 0.5-mm x 0.5-mm x 0.5-mm voxels via an optical CT technique. Peak shot dose was measured by averaging the dose centered on each shot in a series of different spherical pixel volumes and extrapolating this curve back to a theoretical zero-sized detector. This unique ability of 3D dosimetry systems helps avoid detector volume averaging issues inherent in diode and ion chamber detectors. The 4-mm output factor was calculated, taking the ratio of the 4-mm peak dose to 16-mm peak dose and assuming zero timing errors. The 3D gamma analysis was calculated over a 29-mm x 38-mm x 58-mm rectangular volume surrounding the two shots. 3D gamma analysis was computed using CERR (Washington University, Deasy et al).

**RESULTS:** The 4-mm output factor was calculated to be 0.832 ± 0.004 (95% confidence interval). This result was within 2.1% of the manufacturer’s stated 0.815 4-mm output factor. The pass rate on the 3D gamma test was 91.1% using the criteria of a 5% dose difference, 1-mm distance to agreement (DTA), and zero threshold. The pass rate was < 50% when the dose difference was 3%. The results are summarized in the Table.

| Table P059 | Summary of 3D Gamma Analysis Results |
| --- | --- | --- | --- |
| Dose Difference (%) | DTA (mm) | Threshold (% of peak dose) | 3D Gamma Pass Rate |
| 3 | 1 | 0.001 | 29.4% |
| 3 | 2 | 0.001 | 43.2% |
| 5 | 1 | 0.001 | 91.1% |
| 5 | 2 | 0.001 | 95.7% |

**CONCLUSIONS:** PRESAGE/DMOS can accurately measure output factors within a few percentage points of the expected results and avoids the detector positioning and volume averaging challenges of traditional techniques. 3D gamma analysis is a useful tool in measuring the quality of a delivered Gamma Knife plan. A 90% pass rate on a 3D...
gamma test using the criteria of 5% dose difference, 1-mm DTA, and zero threshold shows promise as a future global quality assurance benchmark to allow interinstitutional comparisons and credentialing.

(P060) Electronic Brachytherapy for Treatment of Nonmelanoma Skin Cancers: The University of Arizona Preliminary Experience

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BACKGROUND: Although surgical approaches, including Moh’s chemosurgery, are standard for most nonmelanomatous skin cancers, some patients are not ideal candidates for invasive procedures due to medical comorbidities or functional and cosmetic considerations of lesion location. High-dose-rate electronic brachytherapy (eBT) surface applicators may be a potential alternative treatment modality.

METHODS: Retrospective chart review was performed for patients treated from April 2011 to June 2012. All lesions were pathologically confirmed malignant basal cell or squamous cell carcinoma. A high-dose-rate eBT system (Xoft) utilizing a miniature x-ray source with a maximum energy of 50 KeV was used to deliver a median 2-Gy equivalent dose of 49.7 Gy (α/β = 10; range: 5.2–58.0 Gy/2–29 fractions) to a depth of 0.1–0.3 mm using applicator sizes of 10–50 mm ID. Fraction size ranged from 2 Gy to 5 Gy per fraction, with smaller fraction sizes used on eyelids or when lesions occurred near the canthus. Treatment feasibility, acute toxicity, and cosmetic outcomes were assessed.

RESULTS: Sixteen patients (mean age 74.4 years; range: 56–91 years) with 22 nonmelanoma cutaneous lesions were treated; 13 (59.1%) were T1 lesions, 1 (4.5%) was a T2 lesion, and 8 (36.4%) were recurrent lesions. Lesion locations included the scalp (one, 4.5%), face (nine, 40.9%), nose (seven, 31.8%), extremity (2, 9.1%), ear (1, 4.5%), and eye canthus (2, 9.1%). Acute grade 2–3 radiation skin toxicities occurred during treatment of 13 (59.1%) lesions and were associated with treatment durations lasting > 25 days (P = .03). These toxicities resolved after a mean of 18.4 days ± 4.4, and treatment breaks were necessary in 11 cases, with a mean duration of 10.9 days ± 4.4. Patients ≥ 70 years of age (P = .04) and lesions treated with fraction size 500 cGy (P = .05) had a lower proportion of acute toxicities. At a median follow-up of 4.1 months, all patients were without evidence of disease and with good to excellent cosmetic outcomes.

CONCLUSION: Our early outcomes of eBT for nonmelanomatous skin cancers are encouraging in terms of cosmetic outcome and safety. Fewer acute toxicities were noted in patients aged ≥ 70 years, those who were treated with fraction size ≥ 500 cGy, and those who completed treatment in < 25 days. Longer follow-up is needed to assess local control rates.

(P061) Rapidarc® IGRT for Prostate Cancer: Acute Toxicity

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PURPOSE: To evaluate the acute toxicity and feasibility of image-guided radiotherapy (IGRT) using the Varian RapidArc® delivery technique in the treatment of prostate cancer.

MATERIALS AND METHODS: of 196 patients with clinically localized prostate adenocarcinoma were treated with Varian RapidArc® IGRT between February 2009 and February 2011. IGRT was performed with daily cone beam imaging and three prostate 0.80-mm AnchorMarkers®. The plans were optimized using commercially available software, Eclipse (Varian Medical Services, Palo Alto, CA), using one to two coplanar arcs. All patients were treated with 6-MV photons using a Varian iX linear accelerator.

RESULTS: The mean treatment time was 66 seconds (range: 32.4–118.8), based on 600 MU/min (MU range: 276–1,558, mean 692). The mean patient age was 68.0 years, mean PSA was 9.9 ng/ml, and Gleason score ranged from 6 to 10. The mean prescribed prostate PTV dose was 79.7 Gy (range: 75.6–81 Gy) in 42–45 fractions. The mean rectal dose was 25.9 Gy, and V70 of 3.3%. The mean bladder dose was 27.6 Gy, and V75 of 5.2%. There was no significant change in IPSS; baseline IPSS was 8.8, was 8.3 at 3 months, 8.3 at 6 months, 8.3 at 9 months, and 7.6 at 12 months. An increase in mean RTOG bowel symptom scores occurred at 3 months and normalized at 6 months, with a mean baseline of 0.04, 0.11 at 3 months (P = .02), and 0.07 at 6 months (P = .16). Two patients developed grade 2 toxicity at 3 and 6 months that was resolved at 12 months; there was no grade 3/4 toxicity. The mean baseline Sexual Health Inventory for Men score in hormone-naive patients (n = 177) was 12.9, which decreased to 8.7 at 3 months (P = .2), 8.7 at 6 months (P = .001), 8.1 at 9 months (P = .001), and 8.8 at 12 months. In men with no or mild pretreatment ED (SHIM 17–25) (n = 71), only 19 patients (27%) developed a SHIM score < 17 at the
12-month follow-up. The mean penile bulb dose was 18.1 Gy (range: 3.7–71.9 Gy), with 94% of patients meeting RTOG penile bulb dose constraint (≤ 50% volume receives > 52.5 Gy). In hormone-naive patients (n = 177), the mean initial PSA was 8.8, 1.6 at 3 months, 1.1 at 6 months, 0.9 at 9 months, and 1.0 at 12 months.

CONCLUSION: RapidArc® IGRT for localized prostate cancer using daily cone beam imaging with fiducial alignment is clinically feasible and appears to be well tolerated and initially biochemically effective. The clinical relevance/application of RapidArc® delivery is that it reduces overall treatment times from static IMRT, which may provide a more accurate delivery of radiation and less opportunity for prostate organ motion.

(P062) Predictive Factors for Pneumonitis in Patients Receiving Thoracic Radiation With Helical Tomotherapy

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BACKGROUND AND PURPOSE: It is unknown whether established dose-volume histogram (DVH) parameters predictive of radiation pneumonitis (RP) are applicable to multiple disease sites within the thorax. Larger volumes of lung receiving lower doses are reported to be hazardous in patients with lung and esophageal cancer. In addition, the impact of intensity-modulated radiation therapy (IMRT) on the development of RP remains unexplored. We investigated both clinical and DVH factors associated with RP in a heterogeneous population of patients receiving helical tomotherapy (HT) IMRT, with the hypothesis that lung volumes receiving lower doses are not associated with RP. A secondary goal was to identify novel DVH parameters predictive of RP that could apply to a broader range of patients.

MATERIALS AND METHODS: One hundred patients who received thoracic radiation with HT were included in this retrospective chart review. Patients were ineligible if they received less than 30 Gy or had a follow-up of less than 6 months without an RP event. RP was scored according to the Common Terminology Criteria for Adverse Events (CTCAE) v4.0. An RP grade ≥ 3 was defined as a clinically significant event and was the endpoint used for all statistical analyses. Time to RP was calculated based on radiation start date to the date of last follow-up note, date of death, or the first date that RP was noted in the record. Correlation analyses were performed, and significant clinical and dosimetric factors predictive for grade ≥ 3 RP were assessed using Cox multivariate analysis (MVA).

RESULTS: Fifty-three patients developed RP (grade 1–5); the majority (41%) had grade 1 toxicity. Six patients experienced grade ≥ 3 RP, two of whom had lung cancer and received concurrent chemotherapy. The mean time to RP was 3 months. The sole predictor of RP on MVA was a lung volume receiving a maximum of 20 Gy (VS20) < 1600 cc versus ≥ 1600 cc (hazard ratio [HR] = 18.3; 95% confidence interval [CI] = 3.3–99.2; P < .001). The percentage of lung volume receiving ≥ 5 Gy and the lung volume spared from receiving a maximum of 5 Gy (VSS) were not significant prognostic factors for RP. The RP-free survival at 1 year in patients with VS20 < 1600 cc versus ≥ 1600 cc was 55.6% and 97.7%, respectively (log-rank, P < .001). In a separate MVA including patients without lung cancer (n = 43), VS20 < 1600 cc remained the sole predictor for RP (HR = 16.6; 95% CI = 1.7–159.6; P < .05).

CONCLUSIONS: Higher volumes of lung receiving 5 Gy were not found to be associated with RP. VS20 < 1600 cc was a significant adverse prognostic factor for the development of RP. This is a new dosimetric parameter that can be utilized for treatment planning. Further validation studies are necessary.

(P063) Heart Position and Volume Changes With Deep Inspiration Breath Hold

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PURPOSE/OBJECTIVE: Heart shift and heart volume change with deep inspiration breath hold were analyzed and correlated with heart dosimetry.

MATERIALS AND METHODS: A total of 37 free breathing (FB) and deep inspiration breath hold (DIBH) radiation planning CT scans were obtained at simulation for 35 consecutive left breast cancer patients requiring radiation (breast or chest wall). DIBH was assessed and maintained by the Varian RPM system. Lung and heart volumes were contoured on both the DIBH and FB CT datasets by one physician. A radiation plan in DIBH was designed with a standardized dose of 5,000 cGy in 25 fractions to all treated areas (2, 3, or 4 fields). The FB CT scan was then fused to the treatment planning DIBH CT scan via targeted fusion of the left breast reference volume, with the aid of the left breast skin contour, radiation planning markers, scar marker, and excision cavity or tissue expander. The DIBH radiation treatment plan was superimposed
directly onto the fused FB CT scan for concurrent dosimetric analysis of the same treatment plan for both DIBH and FB situations. For each patient, the magnitude of DIBH was defined as the change in total lung volume (TLV). The centroid (center of mass) of both the DIBH and FB hearts was determined, as was the three-dimensional shift of the centroid evident with DIBH. Multiple heart dosimetric parameters were obtained and compared for both DIBH and FB CT datasets.

RESULTS: The three-dimensional heart centroid shift with DIBH ranged from 1.12 cm to 4.34 cm, with a mean of 2.77 cm. The mean heart centroid shift with DIBH was 0.41 cm medial, 0.26 cm posterior, and 2.68 cm inferior. The mean absolute reduction in heart volume with DIBH was 70.61 cc. This corresponded to a 12% relative reduction in heart volume. With DIBH, there was improvement in all heart dosimetric parameters assessed: mean dose, maximum dose, V5, V10, and V20. For instance, the heart V5 absolute reduction with DIBH ranged from 7.08 cc to 177.48 cc, with a mean reduction of 65.05 cc. Breath hold extent (TLV change) correlated with both heart centroid shift (Pearson r = 0.85) and heart volume reduction (r = 0.57). Heart centroid shift correlated with heart volume reduction (r = 0.61). Improvement in heart dosimetric parameters correlated more strongly with increases in heart shift than decreases in heart volume. For instance, heart V5 absolute reduction correlated more with increases in heart shift (r = 0.81, see Figure) than decreases in heart volume (r = 0.58).

CONCLUSIONS: DIBH resulted in obvious heart centroid shift (most evident in the inferior direction) and a modest decrease in heart volume. Larger magnitude of DIBH predicted greater heart shift and a greater decrease in heart volume. Improvement in heart dosimetry was better predicted by heart shift than by heart volume change. This appears to be the mechanism by which larger breath holds result in greater improvement in heart dosimetry.

(P064) Hematologic Toxicity Is Associated With Mean Vertebral Dose in Adult Medulloblastoma Patients Treated With Craniospinal Irradiation

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PURPOSE: To evaluate the association between vertebral radiation dose and hematologic toxicity in adults with medulloblastoma treated with craniospinal irradiation (CSI).

MATERIALS AND METHODS: Thirty-six adult medulloblastoma patients treated with conventional photon CSI (x-CSI) (n = 18) or proton CSI (p-CSI) (n = 18) at MD Anderson Cancer Center from 2003 to 2011 were retrospectively reviewed. The mean vertebral dose (MVD) was compared with the percent reduction in white blood cells (WBCs), platelets, and hemoglobin at their nadir during CSI and 1 month after completion of radiation therapy (RT). Multivariate linear regression analyzed hematologic toxicity as a function of MVD and modality (x-CSI versus p-CSI). Four p-CSI and four x-CSI patients received concurrent chemotherapy.

RESULTS: The median CSI dose was 30.6 Gy for both p-CSI (range 23.4–36 Gy RBE [relative biological effectiveness]) and x-CSI (range: 23.4–40 Gy). p-CSI patients had significantly lower MVDs than x-CSI patients (median 22.4 Gy RBE versus 32.5 Gy, P < .0001). There was a trend toward a reduction in WBCs, hemoglobin, and platelets with increasing MVD, both at the blood count nadir during RT and at 1 month after RT. This trend was statistically significant for WBCs (Pearson correlation coefficient [r] = –0.37, P = .03) and platelets (r = –0.58, P < .001) at their nadir but not 1 month after RT (WBC: r = –0.37, P = .056; platelets: r = –0.3, P = .13). The association between the percent reduction in hemoglobin and MVD was not significant at the nadir (r = –0.21, P = .22) but became significant 1 month after RT (r = –0.63, P < .001). Hematologic toxicity was not associated with modality (x-CSI versus p-CSI) after differences in MVD were taken into account.

CONCLUSIONS: MVD was significantly associated with acute hematologic toxicity. A dose-dependent reduction in blood counts during RT was observed for WBCs and
platelets; however, the reduction in hemoglobin was not evident until 1 month after RT, likely because of the relatively long half-life of red blood cells. The MVD was significantly lower for patients treated with p-CSI compared with x-CSI. Proton beam RT, or other techniques to decrease MVD, may reduce acute hematologic toxicity in patients requiring CSI.

(P065) Cost-Effectiveness Research and Radiation Oncology: A Systematic Analysis of the Published Literature

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PURPOSE: The continued rise of health care costs in the United States has served as an impetus for increasing interest in the use of cost-effectiveness analysis to aid in improving the value of health care delivery. The high burden and cost of cancer care and the multiple available therapeutic modalities make radiation oncology a field in which cost-effectiveness studies could significantly impact health care costs and patient care. The purpose of this study was to identify and analyze the published cost-effectiveness research that has focused on radiation therapy. We also aimed to better understand the relative proportions of the disease sites that have been studied, the modalities that have been compared, and trends over time.

METHODS: A PubMed search was performed using the terms "cost" and "effectiveness" and "radiation," specifically looking for studies that studied the cost-effectiveness of radiation therapy (RT). Studies were subdivided by disease site, year of publication, country of publication, and comparison modality. Comparison modalities categories were defined as "RT vs RT," "RT vs Chemotherapy," "RT vs Surgery," and "RT vs Observation." Logistic regression models were built to test whether comparison modality categories were related to year of publication and country of publication. To account for society disease burden, publicly available data regarding the prevalence, incidence, person-years life lost, and disability-adjusted life-years were obtained for each disease site from the National Cancer Institute and World Health Organization. The correlation between the number of cost-effectiveness studies and societal disease burden for each disease site was tested using Fisher's exact test.

RESULTS: A total of 704 articles were identified through the PubMed search. Of these studies, 58 met the inclusion criteria for analysis. The most frequent disease sites studied were prostate (22.4%), metastatic disease (17.3%), breast (15.5%), and head and neck (10.3%). Several sites of disease have not had any published cost-effectiveness articles, including skin and nonprostate GU. Radiotherapy was most frequently compared with another radiation modality (53.5%), followed by a comparison with observation (27.6%) and a comparison with surgery (15.5%). A comparison between two radiation modalities was more likely to be published after 2003 (odds ratio [OR] = 1.15; P = .02), while a comparison with observation was more likely to be published before 2003 (OR = 0.85; P = .02). By Fisher's exact test, we found a statistically significant relationship between the proportions of studies for each disease site and prevalence of disease (P < .001). The same relationship was not found when testing incidence (P = .07), disability-adjusted life-years (P = .42), or person-years of life lost (P = .31).

CONCLUSIONS: While the cost of health care in the United States has continued to increase, there are relatively few cost-effectiveness studies focused on radiation therapy. The studies that have been performed have most frequently compared radiation modalities, and the proportions of disease sites that have been studied have been correlated with disease incidence. There is a great need and opportunity for robust cost-effectiveness research in radiation oncology.

(P066) Intensity-Modulated Radiation Therapy for Recurrent Ovarian Cancer Refractory to Chemotherapy

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PURPOSE/OBJECTIVE: Evaluate the local control, survival outcomes, and acute and late toxicity after intensity-modulated radiotherapy (IMRT) for recurrent ovarian cancer refractory to chemotherapy.

MATERIALS AND METHODS: Thirty-three patients were treated with IMRT for recurrent ovarian cancer from January 2006 to July 2012. Patients with brain metastases were excluded. Progression-free survival (PFS) and overall survival (OS) were calculated by the Kaplan-Meier method. Acute (< 28 days) and late (> 28 days) toxicity was retrospectively assessed using the Common Terminology Criteria for Adverse Events (CTCAE) v4.03. Statistical comparisons utilized univariate Cox regression to evaluate the impact of patient characteristics on survival and toxicity.
RESULTS: Median follow-up time was 8.7 months. Median age was 62 years (range: 42–84). The FIGO stage at initial diagnosis was stage I in 7 patients (21.2%), II in 2 patients (6.1%), III in 20 patients (60.6%), and IV in 4 patients (12.1%). Patients received a median of three chemotherapy regimens prior to IMRT (range: 1–12), with 10 (30.3%) of these patients undergoing concurrent chemoradiation. Fifty-five sites were treated in 33 patients to a median dose of 50.4 Gy (range: 39.6–70) with a median dose per fraction of 180 cGy in 28 fractions (range: 160–230 cGy and 22–33 fractions). Thirty-three sites were located within the abdomen or pelvis; 5 sites were located within the thorax; and the remaining 17 sites included cervical lymph nodes (LNs), supraclavicular LNs, inguinal LNs, axillary LNs, internal mammary LNs, two chest wall metastases, and a lateral rectus metastasis. Seven (12.7%) of 55 treated sites had in-field failures; 4 were within the abdomen or pelvis, 1 was within the thorax, and the remaining 2 included the inguinal and axillary LNs. Six of 31 patients had in-field failures with a crude local control rate of 81% and a 1-year actuarial local control rate of 74%. One year PFS and OS rates were 22% and 85%, respectively. Fifteen patients had both a pretreatment and posttreatment PET-CT; six (40%) of these patients had a complete metabolic response posttreatment, while nine (60%) had a partial metabolic response. Acute grade 3 or greater gastrointestinal (GI) toxicities occurred in two (6.3%) patients. Late grade 3 or greater GI toxicities occurred in nine patients (28.1%); six (18.8%) of these toxicities were believed to be secondary to tumor progression and three (9.3%) to radiotherapy. Acute grade 3 or greater hematologic toxicities were identified in seven patients (21.9%). Late grade 3 or greater hematologic toxicities were described in 10 patients (31.3%) of which were associated with cytotoxic chemotherapy and only 1 (3.1%) that was believed to be related to radiotherapy alone. No significant predictors of grade 3 toxicities were found. On univariate analysis, the ratio of pretreatment CA-125 to posttreatment CA-125 was negatively associated with chances of progression but not overall survival \( (P = .043) \).

CONCLUSION: IMRT for recurrent ovarian cancer is associated with excellent local control and limited toxicity. Future studies will be required to determine which patients will benefit most from IMRT and whether alternative techniques such as stereotactic body radiotherapy may be feasible, given the low rates of toxicity reported here.

(P067) The Feasibility of Collecting Patient-Reported Outcomes via an Internet-Based Tool

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PURPOSE/OBJECTIVES: Patient-reported outcomes (PROs) are increasingly being recognized as important but can be difficult to collect accurately. When health care providers attempt to gather PROs through office-based surveys, patient responses may be subject to bias. We sought to determine the feasibility of collecting PROs for survivors of diverse cancers through the use of a voluntary, internet-based tool.

MATERIALS AND METHODS: Patient-reported data were gathered via a convenience sample frame from cancer survivors utilizing a publically available, free internet-based tool for creation of survivorship care plans. Available at www.livestrongcareplan.com and through the OncoLink website, the tool allows survivors to enter data regarding diagnosis, demographics, treatments received, and side effects/late effects experienced and provides them with customized guidelines for future care. Customized questions regarding potential late effects, tailored for diagnosis and treatments, are posed to each user. Answer choices include “yes,” “no,” and “I don’t know” for all questions; some questions are paired with subquestions using recognized PRO scales. Users are asked to complete a satisfaction survey immediately following use and a second survey 1 month later. All data have been maintained anonymously with IRB approval.

RESULTS: More than 15,000 cancer survivors voluntarily used this tool between May 2007 and November 2012, and PRO data are available for 7,603 users. (PRO questions were added in May 2010.) Median age at diagnosis was 48 years (range: 18–93 years); current median age was 52 years (range: 18–93 years). Users were 75% female, 88% Caucasian, 63% college graduates, and 71% US residents. Cancer diagnoses were most commonly breast (42%), followed by blood (12%), genitourinary (11%), and gastrointestinal (10%) disease. On average, users responded to 15–25 questions regarding common late effects after specific surgeries, chemotherapeutics, and radiotherapy techniques. The median time to complete the queries posed by the tool, including PRO questions, was 7 minutes 22 seconds. Overall, 95% of users reported good to excellent satisfaction with their experience using the tool both immediately after use and 1 month later; 63% reported that they plan to share it with their health care team.

CONCLUSIONS: This anonymous tool uses a convenience sample frame to gather patient-reported assessments of...
late effects after cancer treatment. The tool can be completed in less than 10 minutes, and users appear to be highly satisfied with it. Future goals include expansion to greater diversity regarding demographics and cancer diagnosis.

(P068) Early Feasibility and Tolerability Study of a Minimally Invasive Modality for Eye Fixation in CyberKnife Treatment of Choroidal Melanoma

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BACKGROUND: Intraocular melanomas constitute the most common primary ocular malignancy among Caucasians, with the majority of cases occurring in North America and Europe. A variety of radiotherapeutic modalities are available in the management of choroidal melanoma, with the specific treatment being largely dependent on tumor thickness as well as proximity to neighboring critical structures. Episceral plaque brachytherapy has been the most extensively studied modality, with Collaborative Ocular Melanoma Study (COMS) data on patients spanning over 3 decades. Protons and stereotactic radiosurgery have been used for larger tumors and neoplasms adjacent to structures pivotal to the visual pathway. However, these modalities entail invasive procedures for fiducial placement and eye immobilization, respectively. CyberKnife is an attractive frameless alternative to Gamma Knife, but it is technically challenging with respect to developing less invasive eye fixation approaches. We review the methodology and short-term follow-up data on 10 patients with choroidal melanoma who received retrobulbar injection with paralytics immediately prior to simulation and treatment with CyberKnife radiotherapy.

METHODS: Patients who were diagnosed with primary choroidal melanoma had CT-based simulation in the treatment position using a custom-fit Aquaplast mask prior to irradiation. On the day of treatment, patients were subjected to a retrobulbar anesthetic nerve block performed by an ophthalmologist. MRI was done upon achieving effective extraocular muscle paralysis, followed by fusion to previously acquired CT images for immediate planning of target and avoidant structures. A single fraction of external beam radiation to a prescription dose of 20 Gy at 80% isodose was then administered using the CyberKnife system with CT-MRI–fused guidance. The medical records from ophthalmology follow-up visits were then carefully reviewed on all 10 patients to assess for posttreatment changes in visual acuity and radiation-induced side effects.

RESULTS: Ten patients were treated for choroidal melanoma with CyberKnife, with a median follow up of 10 months (range: 3–19 months). Mean tumor thickness was 5.1 ± 1.8 mm (range: 2.8–9.3 mm), and mean largest tumor diameter was 12.5 ± 2.9 mm (range: 8.2–17.6 mm), as measured by A- and B-scan ultrasound during initial evaluation. One patient had improved visual acuity, three patients had worsened visual acuity, and the remainder had stable visual acuity following treatment. Acute local control was achieved in 90% of patients (n = 10). New-onset side effects included excessive lacrimation, blurred vision, and pain. There were no new-onset retinal or macular derangements. Two patients ultimately underwent enucleation during the follow-up period.

CONCLUSION: The preliminary data in this series support the feasibility of performing retrobulbar block as an effective means of ocular immobilization for precise targeting of the gross tumor volume in the treatment of choroidal melanoma with CyberKnife. Furthermore, these results are consistent with prior literature reports that demonstrate CyberKnife external beam radiation to be a promising radiotherapeutic alternative for medium-sized choroidal melanoma tumors.
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