Malignant Lesions

- Lentigo Maligna Melanoma
- Acral Lentiginous Melanoma
- Superficial Spreading Melanoma
- Nodular Melanoma
- Amelanotic Melanoma
- Ocular Melanoma
<table>
<thead>
<tr>
<th>Type of melanoma</th>
<th>Frequency (%)</th>
<th>Site</th>
<th>Radial growth</th>
<th>Special features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Superficial spreading melanoma</td>
<td>60–70</td>
<td>Any site, preference for lower extremities (female), trunk (male)</td>
<td>Yes</td>
<td>More pagetoid, less solar elastosis</td>
</tr>
<tr>
<td>Nodular melanoma</td>
<td>15–30</td>
<td>Any site, preference for trunk, head, neck</td>
<td>No</td>
<td>Nodule with vertical growth</td>
</tr>
<tr>
<td>Lentigo maligna melanoma</td>
<td>5–15</td>
<td>Face, especially nose and cheeks</td>
<td>Yes</td>
<td>Slower growth over years on sun-damaged skin</td>
</tr>
<tr>
<td>Acral lentiginous melanoma</td>
<td>5–10</td>
<td>Palms, soles, subungual</td>
<td>Yes</td>
<td>Most common melanoma in patients with darker skin types</td>
</tr>
</tbody>
</table>
Table 114.1 Risk factors for the development of melanoma.

<table>
<thead>
<tr>
<th>RISK FACTORS FOR THE DEVELOPMENT OF MELANOMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Genetic markers (e.g. CDKN2A mutations)</td>
</tr>
<tr>
<td>• Family history of dysplastic nevi or melanoma</td>
</tr>
<tr>
<td>• Ultraviolet irradiation</td>
</tr>
<tr>
<td>• Sunburns during childhood</td>
</tr>
<tr>
<td>• Intermittent burning exposure in unacclimatized fair skin</td>
</tr>
<tr>
<td>• Number (&gt;50) and size (&gt;5 mm) of melanocytic nevi</td>
</tr>
<tr>
<td>• Congenital nevi</td>
</tr>
<tr>
<td>• Number of atypical nevi (&gt;5)</td>
</tr>
<tr>
<td>• Atypical/dysplastic nevus syndrome</td>
</tr>
<tr>
<td>• Personal history of melanoma</td>
</tr>
<tr>
<td>• High socioeconomic status</td>
</tr>
<tr>
<td>• Skin type I, II</td>
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<tr>
<td>• Equatorial latitudes</td>
</tr>
<tr>
<td>• DNA repair defects (e.g. xeroderma pigmentosum)</td>
</tr>
<tr>
<td>• Immunosuppression</td>
</tr>
</tbody>
</table>

Malignant Melanoma

- malignancy of melanocytes and nevus cells
- most commonly begins in a preexisting melanocytic nevus
- most commonly occurs on back in men, and lower extremities in women
- fastest growing cancer in the United States
- Expected up to affect 1 in 30 individuals born in the year 2015
Lentigo Maligna Melanoma

- usually irregular-shaped, flat, pigmented lesion on solar damaged skin
- likely present for a number of years progressing from Lentigo Maligna
- advanced lesions develop papular or nodular component representing downward growth
Acral Lentiginous Melanoma

- most common form of melanoma in African Americans, Asians and Hispanics
- appear as brown or black macules arising on glaborous skin
- represents about 2-3% of melanomas
- not all acral lesions are Acral Lentiginous Melanomas
Superficial Spreading Melanoma

- most common form of melanoma in Caucasians
- slow growing brown or black macular lesion with irregular border
- may have both a macular or papular component
- represents about 70% of melanomas
Nodular Melanoma

• usually brown or black papule that slowly and frequently ulcerates
• more commonly occurs DeNovo
• more aggressive
• represents approximately 15-30% of melanoma
NEW MELANOMA RX. TREATMENTS

<table>
<thead>
<tr>
<th>Therapeutic Landscape</th>
<th>vemurafenib</th>
<th>trametinib</th>
<th>dabrafenib + trametinib combo</th>
</tr>
</thead>
<tbody>
<tr>
<td>ipilimumab</td>
<td></td>
<td>dabrafenib</td>
<td>pembrolizumab</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Date</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>March 2011</td>
<td>ipilimumab</td>
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<tr>
<td>August 2011</td>
<td>vemurafenib</td>
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<tr>
<td>May 2013</td>
<td>trametinib</td>
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<tr>
<td>January 2014</td>
<td>dabrafenib + trametinib combo</td>
</tr>
<tr>
<td>September 2014</td>
<td>pembrolizumab</td>
</tr>
</tbody>
</table>
Initial Presentation
Breslow 1.05 clear wide excision with sentinel node
2 months follow-up
• During melanoma evaluation, patient developed shortness of breath
  • Was hospitalized
  • Diagnosed with pneumonia
  • Diagnosed with CML and CLL
• Treated with nilotinib (Tasigna)
Vemurafenib

- **Zelboraf**, manufactured by Genentech
- FDA approved in August 2011 for the treatment of metastatic melanoma with a BRAFV600E mutation
- Inhibitor of the serine-threonine protein kinase BRAF that is mutated in approximately 40-60% of melanomas
  - 90% of BRAF mutations are V600E
- 960 mg pill taken twice daily, continue until disease progression or toxicity
- Pricing: 240 mg (120): $6,510.48
- **MOA:**
  - BRAF is a protein kinase within the RAS-RAF signaling pathway, a type of MAP kinase pathway that regulates the expression of genes that encode proteins involved in cellular control functions, including cellular proliferation and survival
  - BRAF mutations -> activation of BRAF protein -> promotes overactive signaling and cellular proliferation
  - Vemurafenib binds to mutated BRAF and renders the oncogenic protein inactive
- Cobas 4800 BRAF V600 mutation test
Vemurafenib

- Monitoring parameters
  - Baseline LFTs, Alk phos, bilirubin and monthly during treatment
  - Baseline electrolytes and after dosage modification
  - Baseline EKG, 2 weeks after initiation, monthly for 3 months, then every 3 months
  - Dermatology evaluation at baseline, then every 2 months

- Cutaneous adverse reactions
  - Rash (36%)
  - Alopecia (30%)
  - Photosensitivity (30%)
  - Squamous Cell Cancers (SCC) (16%)
  - Median induction time of 8 weeks from initiation of therapy
  - Pruritus (22%)
  - Papillomas (20%)
  - Hyperkeratosis (20%)
  - Xerosis (16%)
Vemurafenib

• Warnings
  • Cutaneous SCC, new primary melanomas
  • QT prolongation
  • Dermatologic toxicity: Stevens Johnson and Toxic Epidermal Necrolysis have been reported
  • Hepatotoxicity – elevated LFTs,
  • Ocular toxicity – uveitis, iritis, photophobia
  • Photosensitivity – patient should wear broad spectrum sunscreen

• Clinical efficacy (Vemurafenib vs Dacarbazine)
  • Helped patients live longer: 56% reduction in the death from any cause
  • Helped to shrink tumors: 48% of patients vs 5% with Dacarbazine
  • Increased progression free survival by 4 months compared to Dacarbazine
After start of vemurafenib
Dabrafenib

- *Tafinlar*, manufactured by Glaxo-Smith-Kline
- FDA approved on May 29, 2013 for the treatment of unresectable or metastatic melanoma with a BRAF V600E mutation
- 150 mg pill taken BID until disease progression or toxicity occurs
- MOA: same as Vemurafenib
- Monitoring parameters
  - Serum glucose, CBC
  - Dermatology exam every 2 months during treatment
- Clinically shown to increase progression free survival of 5 months compared to 2 months with Dacarbazine
- MC adverse reactions: hyperkeratosis, headache, pyrexia, arthralgia, papilloma, alopecia, hyperglycemia
- Warnings and precautions
  - Dabrafenib results in an increased incidence of SCC (11%), KA (7%), melanoma (2%)
  - If given to wild type BRAF -> amplifies melanoma growth
  - G6PD deficiency-> Dabrafenib may cause a hemolytic anemia
Trametenib

- **Mekinist**, manufactured by Glaxo-Smith-Kline
- FDA approved on May 29, 2013 for the treatment of unresectable or metastatic melanoma with a BRAF V600E or V600K mutation
- Not indicated for patients who have had previous BRAF therapy
- 2mg po qday until disease progression or toxicity
- **MOA**
  - Reversibly and selectively inhibits mitogen-activated extracellular kinase (MEK) 1 and 2 activation and kinase
  - MEK is a downstream effector of BRAF
  - Mutant BRAF -> activation of the BRAF and MEK pathways
  - Trametinib inhibits MEK -> decreased cellular proliferation, cell cycle arrest, increased apoptosis
- Clinically shown to increase progression free survival by 4.8 months compared to 1.5 months with Dacarbazine
- **MC adverse reactions**: rash, diarrhea, lymphedema
- **Warnings**: Cardiomyopathy, dermatological toxicity (rash), ocular (retinal pigment epithelial detachments), interstitial lung disease, pneumonitis
- **Monitoring parameters**
  - CBC and LFTs at baseline and periodically
  - Assess LVEF by ECHO at baseline, 1 month after initiation, then every 2-3 months
  - Regular dermatology and ophthalmology exams
Melanoma Vaccine

• Currently in clinical trials
  • June 2013 (Journal of Clinical Investigations) – Washington University, St Louis
    • Systemic administration of Interleukin 12p70
      • Promoted a T cell response against the melanoma
    • 6 of 7 patients with metastatic melanoma responded favorably
    • Slowed tumor growth in 3 of 7 patients
    • “personalized immunotherapy”- taking a patient’s own dendritic cells and using them to increase production of IL-12p70 -> stimulates a robust immune response against the melanoma
    • Still years away from a mass production secondary to toxicities
Amelanotic Melanoma

• considered a nonpigment producing variant of nodular melanoma
• may be confused with benign or less aggressive malignant tumors
Risk Factors

- individuals with fair complexion (burn easy and never tan)
- individuals with numerous atypical nevi or large congenital melanocytic nevi
- previous history or family history of melanoma
Biopsy

• Any lesion with suspicion of melanoma, change of size, shape, color, or border should be biopsied.
• Biopsy will not risk metastasis.
• Consider future treatment when doing biopsy and take narrow margins
• Punch or incisional biopsy of the darkest area or excise in its entirety
Staging

- Clark’s Level
- Breslow Depth
- American Joint Commission on Cancer
Clark’s Level

- system used to describe depth of invasion
- shown to correspond well with 5 year survival rates
- Level I-tumor cells in epidermis only (melanoma in situ)
- Level II-tumor cells extend from epidermis into, but do not fill, papillary dermis
- Level III-tumor cells extend form epidermis into and fill papillary dermis
- Level IV-tumor cells extend into reticular dermis
- Level V-tumor cells extend through the dermis into underlying subcutaneous fat
Breslow Depth

• a more precise assessment of level of invasion
• measured from granular layer to the point of deepest invasion of tumor cells
• more easily reproducible and objective then Clark’s Levels
COMPARISON OF SURVIVAL CURVES IN FOUR STAGES OF MELANOMA

Proportion surviving

Survival (years)

Stage I (n=9175)
Stage II (n=5739)
Stage III (n=1528)
Stage IV (n=1158)

Prognosis

• Once metastasis occurs, survival drops dramatically.
• In addition to tumor thickness, a number of other clinical and histologic factors affect prognosis.
• Lesions on scalp, hands and feet have a poorer prognosis.
• Males have a poorer prognosis at all stages.
• Vertical growth phase has increased metastatic potential.
Treatment

• excision
• elective lymph node dissection
• chemotherapy
• immunotherapy
• investigational
Excision

• Wide, local, excision remains the standard of care for primary melanoma, and it’s felt to remove any occult foci.
• The long axis of the excision should be oriented toward the regional draining lymph nodes.
• Width of excision is based on depth of melanoma
• Depth of resection to muscle fascia
• For acral or subungual, disarticulation proximal to tumor
Surgical Margins

- Fusiform or elliptical excision is the workhorse procedure
  - Orient specimen excision with its longest axis along skin tension lines with a 3:1 ratio of length to width and a 30 degree angle at each pole and orientated toward lymph node drainage when possible
  - Proper undermining reduces wound tension and creates wound edge eversion
  - Surgical excision should be to underlying fasical plane
  - Because of the importance of the risk of bad outcomes this should be done by individuals with proper training

- Melanoma surgical margins
  - In situ
    - 5-9 mm border of clinically normal skin
  - <2mm Breslow depth
    - 1cm border of clinically normal skin
  - >2mm
    - 2-3cm margin
SENTINAL LYMPH NODE BIOPSY

- Helpful in treatment and prognosis for mid-level melanoma
SENTINAL NODE BIOPSY

• Any melanoma >2.0 without palpable nodes should have THE OPTION for SNB
• Some feel any breslow >1.0 should have SNB
• SNB does NOT improve prognosis/survival
• If SNB is positive then regional node dissection is indicated
• SNB requires specific training and equipment
HOW TO BIOPSY
Shave vs. Punch Biopsy

- Depends on the disease process involved
- What size punch???
Size of the punch biopsy

- 3 vs 4mm biopsy
- 3mm punch: $1.5 \times 1.5 = 2.25$ mm
- 4mm punch: $2 \times 2 = 4$ mm

So a 4mm punch gives me almost twice as much tissue as a 3mm punch biopsy.
Shave biopsy
Objectives: tissue processing

• Explain the process of tissue fixation and processing
• Explain standard H&E staining as well as immunohistochemistry
• Describe the workflow once the biopsy reaches the lab
Tissue fixation

• Organic tissue undergoes decay after it is removed (biopsy) from the body through 2 mechanisms
• Enzymatic activities continue after the blood supply is disrupted, and these processes break down the cells (autolysis)
• Bacteria can proliferate and degrade the tissue as well (putrefaction)
Tissue fixation

• Organic tissue undergoes decay after it is removed (biopsy) from the body through 2 mechanisms
• Enzymatic activities continue after the blood supply is disrupted, and these processes break down the cells (autolysis)
• Bacteria can proliferate and degrade the tissue as well (putrefaction)
Fixation

- The goal of tissue fixation is to stop autolysis and possible putrefaction.
- Soluble tissue elements must be made insoluble so they are not lost in processing.
- Another function is to maintain the relationship of cells with their extracellular material.
- Fixatives enhance refractive indexes between tissue elements.
- Staining is enhanced by fixation as well.
Fixatives

• Fixatives can be chemical or physical
• The physical means of fixation involve heat or desiccation
• Heat is frequently used to enhance chemical fixation during processing (microwave processors)
Chemical fixatives

• Kills bacteria, penetrates tissue, and hardens it to some extent
• Stabilizes proteins
• Can act as a mordant to enhance tissue staining
• Can mask antigens for immunohistochemical staining
Examples of chemical fixatives

- Formaldehyde
- Glutaraldehyde
- Methanol/ethanol
- Acetone
- Acetic acid
- Glyoxal
- Mercuric chloride
- Osmium tetraoxide
- Picric acid
- Potassium dichromate
- Zinc salts
Formaldehyde

• Introduced in 1893 as a type of tissue fixative
• 10% formalin is the most commonly used fixative, and is actually around 4% formaldehyde
• Penetrates tissue quickly, although complete fixation is slow
• It reacts with the amino group on side chains of amino acids, forming methylene bridges that link proteins together
Tissue fixatives

• If tissue is not properly fixed, the resulting processing will not work well and the end product is suboptimal histology.
• The appropriate ratio of fixative to tissue is at least 10:1.
• Consider this when you cram a large excision into a bottle intended for a biopsy.
Tissue Processing

The three steps include dehydration, clearing, and infiltration.

Automated processors existed at least 50 years ago, while "processing" of tissue has occurred for at least 100 years.

The end goal is to have tissue that can be embedded into a medium that can be sectioned into thin (5 microns for standard histology) sections.
Clearing

- The purpose of the clearing agent is to remove the alcohol/dehydrating agent before infiltration.
- Xylene is most commonly used.
- Rapidly displaces alcohol and is miscible with paraffin.
- Other agents include benzene, toluene, limonene, acetone, and alkanes (nonirritating compared to xylene).
Infiltration

• The purpose is to support the tissue so the relationships of the structures are maintained (intra and extracellular)

• Most common medium is paraffin wax

• Other types include celloidin, carbowax, and hard plastics (epoxy resins)
Paraffin Wax

• Inert mix of hydrocarbons derived from petroleum
• Tends to be mixed with additives to change the melting point, hardness, and enable ribbons of tissue to be cut
• Special staining can be done easily
• Enhanced infiltration done with vacuum
Once processing is complete, the tissue is embedded in a molten paraffin "block" and cooled. This is done at a table that has molten paraffin as well as hot and cold plates. The embedding of the tissue correctly allows eventual histologic assessment on properly oriented tissue.
Sectioning

• The blocks are secured in a microtome, and 5 micron sections are cut usually in consecutive “ribbons” of slices.
• They are placed in a water bath to smooth out folds/wrinkles, minimize bubbles, and then gently placed on glass slides.
• There needs to be an adhesive within the bath, or charged slides need to be used, otherwise the tissue will fall off with staining.
• The slides are dried and are ready to be stained.
PATHOLOGY

• ALWAYS USE A DERMATOPATHOLOGIST
• GIVE AS MUCH GOOD INFORMATION AS POSSIABLE
• CALL AND DISCUSS CASE IF IT IS COMPLICATED OR YOU DON’T AGREE WITH RESULTS
• PHOTOGRAPH IS EXTREMELY HELPFUL FOR THE PATHOLOGIST AND REFERAL
• ALWAYS ASSUME THAT A POSITIVE HISTOLOGIC MARGIN WILL COME BACK!
Staining
Staining

• Nuclear staining is done with basic (cationic) dyes. A metal mordant is used to enhance the binding of the dye (aluminum, zinc, iron, magnesium).

• Cytoplasmic staining is done with an anionic dye that attaches to side chains on amino acids in a solution below the isoelectric point of the proteins (pH 6).
Hematoxylin
After staining

- Coverslip, dry and ready for interpretation
- There are several types of mounting media, resinous and aqueous
- Mounting media is necessary for crisp microscopic interpretation
- There are several types of coverslips as well with plastic and glass varieties
- All slides are not equal as well, with varying thickness, width, and length
Immunohistochemistry (IHC)

- Principles of IHC developed in the 1930's
- First IHC demonstrated by Coons in 1942 with immunofluorescence (FITC) demonstrating pneumococcal antigen in tissue with rabbits
- Enzyme tagging developed in late 1960's and avidin-biotin complex (ABC) in 1974
- Monoclonal antibodies developed in mice in 1975
• Revolution of diagnosing disease processes (mainly neoplastic) in the 1980's through today
• Antibodies to various antigens can differentiate tumors of epithelial, melanocytic, lymphoid, neural, vascular, and other supporting tissues (mesenchymal)
IHC
IHC

- Fluorescent/staining tag
- Goat anti-rabbit
- Rabbit anti-A
- Cell
- A
- B
- B
IHC

• There are steps to increase the availability of antigens (such as heat induced epitope retrieval HIER) and there are steps to block nonspecific background staining (blocking reactions).

• There are positive and negative controls to ensure that the stain(s) work and there is little to no background (nonspecific) staining.

• Hematoxylin is commonly used as a counterstain so the tissue cells and architecture can be visualized.
The Lab

- Biopsy is received in the lab and given a unique identifying number and accessioned in the computer program.
- Tissue is measured, inked, sectioned, and placed in a labeled cassette.
- Cassettes held in formalin for nightly processing.
- Tissue embedded in paraffin wax block.
- Block sectioned on microtome and labeled slides are made.
- Slides stained and coverslipped.
- Dried slides matched with correct paperwork and given to pathologist for interpretation.
Treatment

- excision
- elective lymph node dissection
- chemotherapy
- immunotherapy
- investigational
Excision

• Wide, local, excision remains the standard of care for primary melanoma, and it’s felt to remove any occult foci.
• The long axis of the excision should be oriented toward the regional draining lymph nodes.
• width of excision is based on depth of melanoma
• depth of resection to muscle fascia
• for acral or subungual, disarticulation proximal to tumor
SENTINAL LYMPH NODE BIOPSY

• Helpful in treatment and prognosis for mid-level melanoma
SENTINAL NODE BIOPSY

The SNB involves injecting a radioisotope and a visible dye into the original melanoma biopsy site.

After migration of the markers to the regional nodal basin the surgical technique allows the specific node to be evaluated with frozen section.

The nodal evaluation may include histologic evaluation and special studies including PCR.
Elective Lymph Node Dissection

- may be important for improving survival and also for staging patients who should be considered for adjuvant therapy
- based on hypothesis that melanoma cells metastasize from primary site to regional lymph nodes, then to distant sites
Elective Lymph Node Dissection

• Advocates feel that when tumor is thick, survival rates are improved due to removal of clinically, undetectable microscopic metastasis.

• Recent randomized study supports hypothesis and showed that patients 60 years or younger with intermediate, non-ulcerative tumors may benefit from elective lymph node dissection.
Elective Lymph Node Dissection

• If the sentinel node is positive then a regional node dissection is indicated
• If histology is neg. and PCR is positive is a source of debate and current study
• Recent randomized study supports hypothesis and showed that patients 60 years or younger with intermediate, non-ulcerative tumors may benefit from elective lymph node dissection.
Chemotherapy

- used in treatment of metastatic melanoma
- no cure, remission rates only about 20%
- Dacarbazine—response rate around 20% with duration averaging less than 6 months
- Cisplatin—somewhat effective, but has significant toxicities
- Nitrosoureas—[Carmustine, Lomustine, Semustine] overall response rate of 13-18%
- Vinblastine, Vincristine and Taxol similarly respond only 12-15%
Table 114.14 Treatment options for metastatic melanoma. *Should be performed as part of controlled studies.

<table>
<thead>
<tr>
<th>Metastatic site (TNM)</th>
<th>Treatment choice</th>
</tr>
</thead>
<tbody>
<tr>
<td>In-transit metastasis (TxN2cM0)</td>
<td>1st: &lt;5 surgery, &gt;5: extremity perfusion*</td>
</tr>
<tr>
<td></td>
<td>2nd: radiotherapy, CO₂ laser ablation, intrallesional IL-2</td>
</tr>
<tr>
<td></td>
<td>3rd: systemic therapy</td>
</tr>
<tr>
<td>Brain metastasis (TxNxM3)</td>
<td>1st: surgery</td>
</tr>
<tr>
<td>Single</td>
<td>2nd: stereotactic radiosurgery</td>
</tr>
<tr>
<td>Multiple</td>
<td>1st: radiotherapy</td>
</tr>
<tr>
<td></td>
<td>2nd: systemic therapy</td>
</tr>
<tr>
<td>Lung metastasis (TxNxM2)</td>
<td>1st: surgery</td>
</tr>
<tr>
<td>Single</td>
<td>1st: systemic therapy</td>
</tr>
<tr>
<td>Multiple</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal metastasis (TxNxM3)</td>
<td>1st: surgery</td>
</tr>
<tr>
<td>Single</td>
<td>1st: surgical therapy</td>
</tr>
<tr>
<td>Multiple</td>
<td></td>
</tr>
<tr>
<td>Skin, soft tissue metastasis (TxNxM1)</td>
<td>1st: surgery</td>
</tr>
<tr>
<td>Single</td>
<td>1st: systemic therapy</td>
</tr>
<tr>
<td>Multiple</td>
<td></td>
</tr>
<tr>
<td>Painful bone metastasis (TxNxM3)</td>
<td>1st: radiotherapy</td>
</tr>
<tr>
<td>Disseminated metastasis (TxNxM3)</td>
<td>1st: systemic therapy +/− surgery, radiotherapy of symptomatic metastasis</td>
</tr>
</tbody>
</table>
Immunotherapy

- Intron A - Interferon Alfa-2b
- response rate of 15-20%
- overall survival increase 9%
- higher response rate, variously reported 40-50% range with combination with Decarbazine, Cysplatin and Tamoxifen
- very few respond with liver or visceral metastasis
Investigational Treatments

• genetic modification of tumor infiltrating lymphocytes to make them more effective at killing tumor cells
• modify tumor cells so they produce immunostimulating cytokines which attract and stimulate an immune response
• in-situ genetic modification of tumor cells slowly produce non-self HLA antigens, the immune system then rejects the tumor similar to organ transplant
Follow-Up

- Patients are encouraged to perform regular self body exams and minimize sun exposure.
- Routine evaluations consisting of complete cutaneous exams and thorough evaluations of lymph nodes must be done regularly.
- Patients are seen every three months during the first year, every four months during the second year, every six months during years three through five, and then yearly.
- Lab testing and chest x-rays are performed on an annual basis.
What’s New

- reverse transcriptase polymerase chain reaction
- positron emission tomography
Reverse Transcriptase Polymerase Chain Reaction

- experimental test used to detect circulating melanoma cells in peripheral blood
- found to correlate well with stage of disease and may help identify patients who will eventually develop disease
Positron Emission Tomography

- uses a glucose analog coupled to a positron emitter capable of identifying clinically undetectable lymph node and visceral metastasis
RESEARCH AT KCOM

• Dr.s Cox and Bear
• Early diagnosis and current treatment
• Evaluate all skin lax.
• Evaluate family members
• Have patients protect themselves from solar damage
• THE END