EPISCLERAL EYE PLAQUES FOR TREATMENT OF INTRA-OCULAR MALIGNANCIES AND BENIGN DISEASES

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Goal

• To present the Procedures involved in the Eye Plaque Treatments of
  – Intraocular Malignant Tumors
  – Benign Diseases
Introduction

• Normal Eye Anatomy
• Intra-ocular Malignancies in Eye
• Episceral Eye Plaques
Eye Anatomy

• Outer Layer
  – Sclera
  – Cornea

• Middle Layer - Uvea
  – Choroid
  – Ciliary Body
  – Iris

• Inner Layer
  – Retina
Intra-ocular Malignant Tumors

• Uveal Melanoma
  – Choroidal Melanoma
  – Ciliary Body Melanoma
• Retinoblastoma
• Retinal Detachment
Choroidal Melanoma

- limbus
- ora
- equator
- foveola
- lens
- apex
- optic nerve
- base
- eye plaque
- choroidal melanoma
Choroidal Melanoma

- **Tumor Base:**
  all pigmented areas of tumor adjacent to the underlying sclera
- **Sclera Thickness:**
  1 mm
- **Interior Sclera:**
  center of tumor base at 1mm from the exterior surface of sclera
- **Apical Height:**
  distance between interior sclera and tumor apex
Macular Degeneration

• Benign ophthalmic condition characterized by
  – progressive destruction and
  – dysfunction
  of the macula (central retina )

• Age-related macular degeneration is the leading cause of blindness in the United States.
# Episcleral Eye Plaque

<table>
<thead>
<tr>
<th>Radionuclides</th>
<th>Physical forms</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-125</td>
<td>Multiple loose seeds assembled in a gold substrate</td>
</tr>
<tr>
<td>Pd-103</td>
<td></td>
</tr>
<tr>
<td>Ru-106</td>
<td>Prefabricated plaques</td>
</tr>
<tr>
<td>Co-60</td>
<td></td>
</tr>
<tr>
<td>Sr-90</td>
<td></td>
</tr>
</tbody>
</table>
60Co Eye Plaques

- 1930’s
- Early Designs, CKA series
- Prefabricated Plaques
- Within the tumor, dose distributions are very similar to I-125 Plaques of comparable diameters
- Delivers higher doses to critical normal structures
- Loosing popularity due to higher energy
- Issue of personnel protection
$^{106}$Ru Eye Plaques

- Prefabricated Plaques
- 16 Different Sizes
- Dose distributions have been calculated and measured
- Popular in Europe
- Available from Bebig, Germany
90Sr Eye Applicator

• Used more frequently for treating Pterygium (Next lecture)
• Used for treatment of shallow tumors
• Prefabricated applicators
$^{125}$I Eye Plaques

- Started in the early 1970’s
- Gold foils made by dental labs serve as substrates
- $^{125}$I seeds (model 6711) were glued onto the concave side of a selected substrate
- Gaining acceptance
- COMS group formed based on the early experience with $^{125}$I Eye Plaques
$^{103}$Pd Eye Plaques

- After $^{103}$Pd seeds became available
- 1990’s
- $^{103}$Pd seeds (model 200, Theraseed) were glued onto the concave side of a selected substrate
- The substrate can be of
  - COMS design (gold backing alone, no silastic)
  - Non-COMS design
- Prefabricated plaques under investigation
Roles of Professionals

• After an ophthalmologist makes the diagnosis of intra-ocular melanoma or benign disease, he/she refers the patient to radiation oncologist for consultation.

• When eye plaque treatment is chosen as the treatment modality, the physicist participates in and organizes
  – treatment planning tasks
  – quality assurance of treatment delivery
  – radiation safety procedures
Collaborative Ocular Melanoma Study (COMS)

- COMS was started by National Eye Institute in the mid 1980’s
- Patients with medium size tumors between 2.5 and 10 mm in apical height, and 16 mm or less in basal diameter, were randomized between
  - Enucleation (Eye removal)
  - I-125 eye plaque treatment
Medium Size Tumors

- **Apical height:** 2.5 to 10 mm
- **Basal diameter:** 16 mm or less

- **Randomization Arms**
  - Enucleation
  - I-125 eye plaque treatment
COMS findings (2001)

• The survival rates are comparable for patients with medium size tumors treated with
  – Enucleation (Eye removal)
  – I-125 eye plaque treatment

• Eye Plaque Treatment is Effective.
Pre-treatment Tumor Localization

- Ophthalmoscopy
  - Fundus Photography
- Ultrasound A-scan and B-scan Images
- CT Scan Images (optional?)
- MRI Scan Images (optional?)
- Correlation of Localization Modalities
Ophthalmoscopy

- Direct Wide Angle
- Indirect Narrow Angle

- Optic Disc Diameter (DD) about 1.5 mm
- Distance between two interest points on eye retina
  - estimated in multiples of DD
Fundus Diagram Drawing

• Tumor Dimensions and Location
• Tumor Base
  – Longitudinal Dimension in a Meridian
  – Transverse Dimension across the Meridians
• Critical Normal Structures
  – Optic Nerve
  – Optic Disc
  – Macula
  – Foveola
Fundus Diagram Drawing

temporal

7mm

5mm

10mm

9mm

nasal

R
Guidelines of Radiological Physics Center (RPC)

• Selection of plaque size
  – longest tumor base diameter in mm plus 4 to 6 mm

• COMS standard plaques
  – 10, 12, 14, 16, 18, 20 and 22 mm in diameter
  – gold plaque with silastic seed carrier insert

• Dummy plaques
  – 12, 14, 16, 18 and 20 mm in diameter
  – silver rim, acrylic in center

• Seed activity: 0.5 to 5 mCi
COMS Dose Prescription

• Prescription dose
  – 100 “old” Gy (85 “new” Gy based on the TG43)
  – delivered in 5 to 12 consecutive days

• Prescription dose rate
  – between 0.5 and 1.25 Gy/hr.

• Prescription point
  – 5 mm from tumor base center (interior sclera) for a tumor with height 5 mm or less,
  – tumor apex point for height over 5 mm
Clinical Interest Points for Point Dose Calculation and Reporting

- tumor apex
- 5 mm depth from interior sclera (if different from apex)
- tumor base center (interior sclera)
- center of optic disc
- center of lens
- opposite retina (22 mm from interior sclera)
- foveola (center of macula)
Critical Normal Structures

- sclera
- macula
- optic nerve
- optic disc
- retina
- lens
## COMS Standard Eye Plaques

<table>
<thead>
<tr>
<th>Diameter (mm)</th>
<th># Seed Slots</th>
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<tbody>
<tr>
<td>10</td>
<td>5</td>
</tr>
<tr>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>14</td>
<td>13</td>
</tr>
<tr>
<td>16</td>
<td>13</td>
</tr>
<tr>
<td>18</td>
<td>21</td>
</tr>
<tr>
<td>20</td>
<td>24</td>
</tr>
<tr>
<td>22</td>
<td>21</td>
</tr>
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</table>
### COMS Standard Eye Plaques

<table>
<thead>
<tr>
<th>Gold Plaque</th>
<th>Silastic Insert</th>
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<tbody>
<tr>
<td>Gold</td>
<td>Carbon</td>
</tr>
<tr>
<td>77%</td>
<td>25%</td>
</tr>
<tr>
<td>Silver</td>
<td>Hydrogen</td>
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<tr>
<td>14%</td>
<td>6%</td>
</tr>
<tr>
<td>Copper</td>
<td>Oxygen</td>
</tr>
<tr>
<td>8%</td>
<td>29%</td>
</tr>
<tr>
<td>Palladium</td>
<td>Silicon</td>
</tr>
<tr>
<td>1%</td>
<td>40%</td>
</tr>
<tr>
<td></td>
<td>Platinum</td>
</tr>
<tr>
<td></td>
<td>0.005%</td>
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</table>
COMS Standard Eye Plaques
COMS Standard Eye Plaques
14 mm COMS Eye Plaque

(a)

(b)
Seed Trough Diagrams

12 mm Plaque

18 mm Plaque

16 mm Plaque

20 mm Plaque
Smallest and Largest Eye Plaques

10 mm  22 mm

Courtesy Dr. Mark Rivard
The COMS design plaques

- Circular
- Notched
- Available from Trachsel Dental Studio, Inc., Minnesota
- Designed to accommodate loose seeds
- Only models 6711 and 6702 I-125 seed were used for COMS protocol cases
- Usable for all new models of I-125 and Pd-103 seeds
Notched Eye Plaques

Courtesy Dr. Mark Rivard
Non-COMS Plaques

- Customized Plaques for loose seeds
  - Elongated
  - With indented seed slots
  - With notch
  - Stamped gold foil
- COMS Gold Backing with Dense Packing of Seeds fixed with jet acrylic or silicone glue (without using Silastic Insert)
- Prefabricated Plaques under development
Ru-106 Eye Plaques

Courtesy Bebig. Germany
Fundus Photo of an Eye with Choroidal Melanoma
Ultrasound A Scan

transducer
sound beam

transducer
sound beam
Ultrasound A Scan

Anterior Surface Peak
Tumor Peak
Choroidal Peak
Scleral Peak

Courtesy Hilaris et al
Ultrasound B Scan

transducer

sound beam
Ultrasound B Scan

Courtesy Hilaris et al
Magnetic Resonance Imaging (MRI) Scan Images

Sagittal

Pre-Op

Post-Implant

Coronal

Courtesy Houdek (1989)
## Comparison of Modalities

<table>
<thead>
<tr>
<th></th>
<th>Basal Diameter</th>
<th>Apical Height</th>
<th>Retinal Detachment</th>
<th>Specificity</th>
<th>Extra-ocular Extension</th>
<th>3-d</th>
<th>Plaque Imaging</th>
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<tbody>
<tr>
<td>Fundoscopy</td>
<td>W</td>
<td>X</td>
<td>?</td>
<td>?</td>
<td>X</td>
<td>X</td>
<td>X</td>
</tr>
<tr>
<td>US A-Scan</td>
<td>X</td>
<td>W</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>X</td>
<td>?</td>
</tr>
<tr>
<td>CT Scan</td>
<td>W</td>
<td>W</td>
<td>V</td>
<td>V</td>
<td>W</td>
<td>W</td>
<td>X</td>
</tr>
<tr>
<td>MRI Scan</td>
<td>W</td>
<td>W</td>
<td>V</td>
<td>W</td>
<td>W</td>
<td>W</td>
<td>W</td>
</tr>
<tr>
<td>Pathology</td>
<td>V</td>
<td>V</td>
<td>V</td>
<td>W</td>
<td>W</td>
<td>2-d</td>
<td>N/A</td>
</tr>
</tbody>
</table>
Fundus Diagram Drawing

- **R** (Right Eye):
  - 12: Limbus
  - 11: Optic Disc
  - 10: Nasal
  - 9: Temporal
  - 8: Macula
  - 7: Nasal
  - 6: Temporal
  - 5: Optic Disc
  - 4: Nasal
  - 3: Temporal
  - 2: Macula
  - 1: Optic Disc

- **L** (Left Eye):
  - 12: Limbus
  - 11: Optic Disc
  - 10: Nasal
  - 9: Temporal
  - 8: Macula
  - 7: Nasal
  - 6: Temporal
  - 5: Optic Disc
  - 4: Nasal
  - 3: Temporal
  - 2: Macula
  - 1: Optic Disc

Key:
- **R:** Right
- **L:** Left
- **temporal:** Temporal
- **nasal:** Nasal
- **limbus:** Limbus
- **foveola:** Foveola
- **optic disc:** Optic Disc
- **equator:** Equator
Fundus Diagram Drawing

temporal

7mm

5mm

7mm

9mm

10mm

5mm

R

nasal
Fundus Diagram Drawings

(a) Temporal 11 12 1 R Nasal
   10 2
   9
   8 7 6 5
   7mm 5mm 9mm 10mm

(b) Nasal 11 12 L Temporal
   10 2
   13mm 14mm
   12mm 10mm
Cross-sectional Diagrams

(a) temporal

14mm plaque

optic disc

optic nerve

limbus

ora

equator

(b) superior

16mm plaque

optic disc

optic nerve

limbus

ora

equator

inferior
3D Perspective,
Plaque over Posterior Tumor
3D Perspective,
Plaque over Anterior Tumor
Dosimetry for Eye Plaques

• Major challenge
  – Steep dose gradient, high spatial resolution
  – Tumor dimension and location
  – Plaque placement relative to tumor location

• COMS protocol and guidelines

• RPC guidelines

• Continuing development and improvement
COMS/RPC Dosimetry Requirement

- $^{125}$I seed
  - Model 6711
  - Model 6702
- COMS standard plaque design
- Point source approximation
- Ignore heterogeneity correction
- Doses to interest points
Dosimetry for Eye Plaques

• Previous “Apparent” Dosimetry for 6711 seed with point source approximation (Ling, 1983)
• Revised “Real” dosimetry for 6711 seed (1994)
• TG43 recommended parameters for line source approximation in homogeneous water (1995)
• In 1995, COMS adopted the revision of the dose rate constant for 6711 seed, based on TG43 recommendation, but still insisted on using point source approximation for protocol cases.
I-125 seed, model 6711

(a)

\[ \frac{D r^2}{S} \]

- homogeneous, Ling 1983
- homogeneous, Chiu-Tsao 1990
- plaque, de la Zerda 1994
Isodose Curves
Single model 6711 Seed in 20 mm Plaque

Gold Plaque with Silastic insert
Homogeneous
Heterogeneity Effect

- Influence of Silastic Insert
- Influence of Gold Backing
- Influence of eye-air interface
- Lip Collimation Effect
- Interseed interference effect

- These were all ignored in the COMS protocol cases, for the lack of consensus of such data.
Isodose Curves
Multiple 6711 Seeds in an Eye Plaque

Homogeneous

With lip collimating effect

Courtesy Astrahan
Treatment Planning

• Transferring tumor information based on
  – Fundus Diagram
  – Ultrasound A-Scan and B-Scan Images
  – CT Scan Images (optional?)
  – MRI Images (optional?)

• Plaque Selection

• Seed Model (close to 20 new models up to year 2005)

• Seed Activities and Availability
  – Uniform Loading
  – Differential Loading

• Dose Calculations
Treatment Planning Computer System

• General purpose
  – Adequate for the COMS dose calculation protocol
  – NO heterogeneity correction

• Special purpose
  “Plaque simulator” (PS)
  available from Bebig, Germany
Treatment Planning Computer System

- “Plaque simulator” (PS) by Astrahan at USC
- User can turn on the effect of silastic insert, gold backing and eye-air interface
- Accuracy of PS calculations has been evaluated by Knutsen (2001) and Krintz (2002)
- Newer enhanced version, Astrahan, IJROBP 2005; 61:1227
COMS 12mm Eye Plaque

Dose rate in cGy/h with 1 mCi per seed

Courtesy Astrahan 2005
COMS 20mm Eye Plaque

COMS Protocol  Original PS  Enhanced PS

Dose rate in cGy/h with 1 mCi per seed

Courtesy Astrahan 2005
COMS 20mm Eye Plaque

from interior sclera

Courtesy Astrahan 2005
Depth Dose Curves along the Central Axis

Relative depth dose curves for three different beta-ray sources:

- $^{90}$Sr/$^{90}$Y Planar
- $^{106}$Ru/$^{106}$Rh Planar
- $^{106}$Ru/$^{106}$Rh Concave

Courtesy IAEA
Newer models of Seeds?

- The heterogeneity effects are different for Pd-103 seeds.
- Are the heterogeneity effects determined for model 6711 seed applicable for newer models of I-125 seeds and new design of eye plaques?
- More work needs to be done about these effects.
  - Determination
  - Implementation in Treatment Planning System
Eye Plaque Preparation
Eye Plaques in Lead Container
Sterilization Bag for Gas Sterilization
Operating Room

• Transillumination
  – Marking of Tumor Base Border
• Measure with Caliper
  – Distance from Limbus to Tumor's Anterior Margin
  – Tumor Base Diameter
• Dummy Plaque Suturing
• Active Plaque Suturing
• Transillumination with Sutured Plaque
Transillumination

Scleral Marking

light source
Operating Room

• Intraoperative Ultrasound Scan with Sutured Plaque

• Measure with Caliper
  – Distance from Limbus to Plaque's Anterior Margin
  – Cornea Diameter
Ultrasound Verification of Plaque Placement

Well centered Plaque

Malpositioned Plaque

Courtesy Pavlin (1989)
A posterior tumor plaque edge very close to optic nerve
Operating Room

- Accidentally Contaminated Plaque
- Autoclaving
- Gold plaque and silastic insert would survive occasional autoclaving
- Acrylic insert in silver dummy plaque would melt in high heat
- Push out the acrylic insert before autoclaving silver dummy plaque
Post Implant Sagittal MRI Images

Courtesy Houdek
Removal of Silastic Insert from the Gold Backing
Final Dose Calculations

• 2-d cross-sectional diagram
• Identify
  – Tumor location
  – Plaque location (after sutured in place)
• Dose calculations
• Isodose curve plot
• Critical structure dose estimates
• Reporting and documentation
CONCLUSION

• Procedures involved in the eye plaque treatments of intraocular tumors have been presented.
Eye Plaque Treatment is Effective.

More work needs to be done to refine the modality!!!