Physics Aspects of Clinical Trials: AAPM Task Group 113

Jean M. Moran, Ph.D.

The University of Michigan
Department of Radiation Oncology

Outline

- Motivation
- Goal and scope of AAPM Task Group 113
- IGRT/IMRT examples
  - Immobilization
  - Localization
  - RTOG Head and Neck Phantom
- Challenges

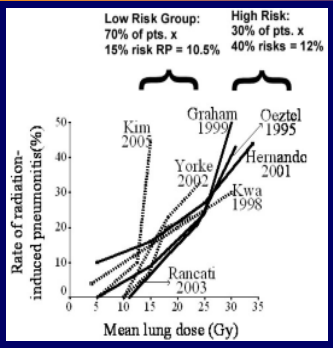
Motivation

- The role of physics QA for clinical trials is to assure consistency in each part of the treatment planning and delivery process.
- The Advanced Technology Consortium is composed of organizations which provide QA services as well as some trial and benchmark design.
- However, there are no standard guidelines for the physics aspects of clinical trials or benchmarks for clinical trials.

Multi-institutional Clinical Trials

- There are multiple cooperative groups in the US
  - Pediatric Oncology Group
  - Southwestern Oncology Group
  - Radiation Therapy Oncology Group
  - Children's Oncology Group
  - Sponsored by the NIH/NCI
- Each cooperative group may work with a different QA organization
- Physics issues are not always explicitly included in the trial design
  - Imaging
  - Homogeneous vs. heterogeneous dose calculations
  - Patient setup details

Dose Response Evaluation: Multiple Trials



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Courtesy of Dr. Lawrence Marks, Duke University

"How is a clinical trial carried out?"

…Every doctor or research center that takes part in the trial uses the same protocol. This ensures that patients are treated identically no matter where or if they are receiving treatment, and that information from all the participating centers (if there is more than one) can be combined and compared."

http://www.cancer.gov/clinicaltrials/learning/how-trials-are-done

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TG113: Physics Standards for Clinical Trials

- Designed for:
  - Physicists and others involved in patient planning and treatment for clinical trials:
    - Provide guidance on methods to improve the consistency and quality of data generated for clinical trials involving external beam therapy
  - QA organizations:
    - Provide a resource for organizations which design and conduct clinical trials
    - Information for designing benchmark tests and phantoms
  - Vendors
    - DICOM export capabilities for export and review by QA centers

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Task Group 113

Members

- Robert Dryzmala
- Mike Herman
- Jon Kruse
- Jean Moran (Chair)
- Art Olch
- Mark Oldham
- Jeff Siewerdsen

Liaisons

- James Galvin – RTOG
- Andrea Molineu – RPC
- Jatinder Palta – RCET, TG100
- James Purdy – ITC
- Marcia Urie – QARC

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Areas of Report

- Patient immobilization
  - Site-specific issues
  - Types: masks, frames
- Image acquisition for volume definition
  - Multiple imaging modalities
  - Use of patient immobilization for all imaging studies
- Treatment guidance
  - EPIDs, cone beam CT, RF markers
  - Validation of margins for trial design

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Areas of Report

- Treatment planning systems
  - 3D treatment planning systems
  - Heterogeneity corrections
  - Calculation grid sizes
- Treatment delivery
  - Participation in RPC TLD program
  - Dosimetric factors: e.g. rounded leaf tip, transmission, delivery technique
- Credentialing for clinical trials
  - Facility questionnaire, dry run
  - Phantom measurements

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Example: Prostate – Litzenberg et al.

- 3 Gold bbs implanted in prostate
- Evaluated prostate position with portal imaging
  - 6 patients prone
  - 4 patients supine

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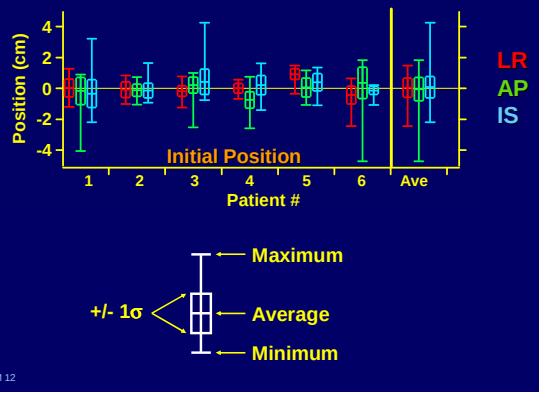
Prone Positioning Results



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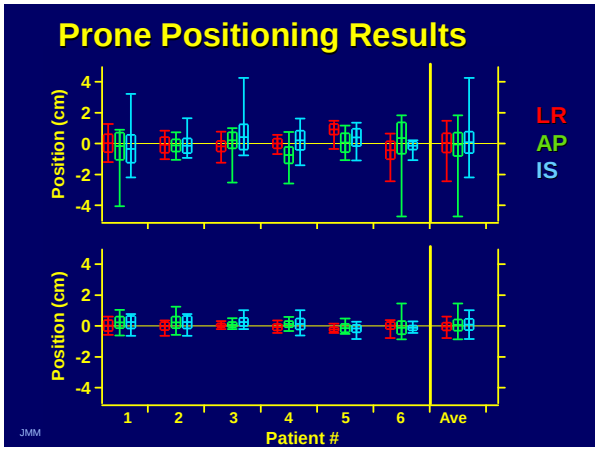

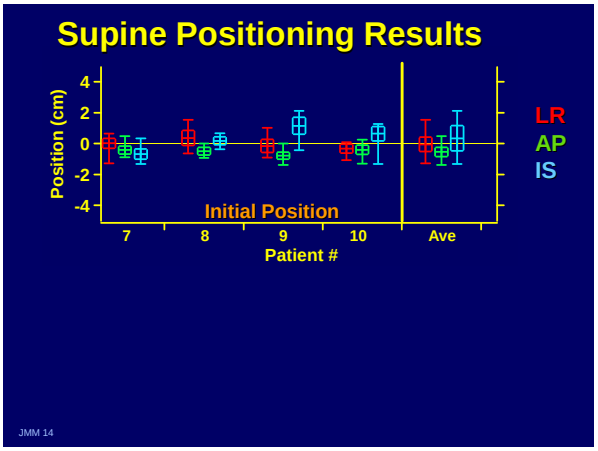

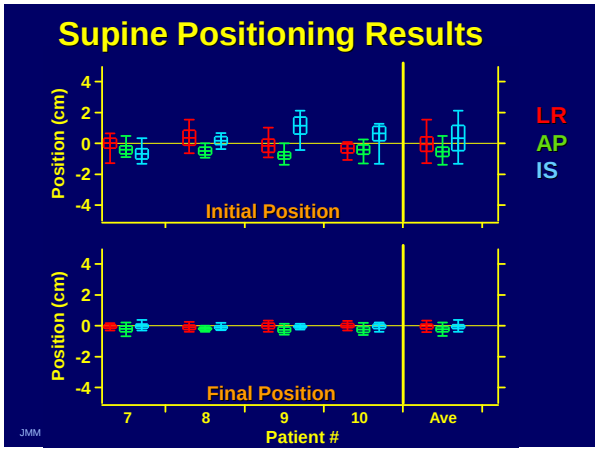

Treatment Guidance

- Image guidance methods
  - Cameras
  - RF beacons
  - kV fluoroscopic imaging
  - MV cine loops
- Type of intervention depends on the frequency of the event
  - Real-time evaluation is needed to address intra-fraction motion
  - Fiducials

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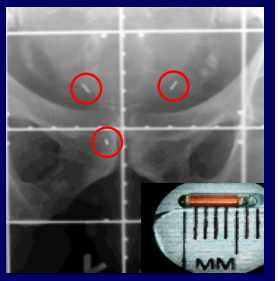
Example: Treatment Guidance

- 3 transponders
- Implanted transrectally under ultrasound guidance
- 10 minute procedure
- Consistent with gold marker implant effects
- Good positional stability over 8 weeks (σ_{ave} = 0.8 mm)



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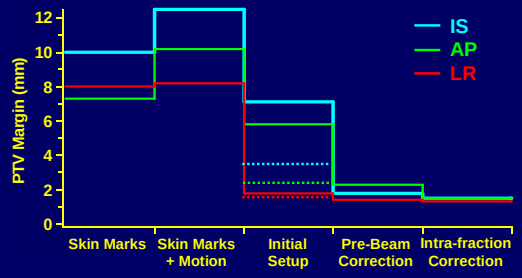
Slide courtesy of Litzenberg

Results



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Litzenberg Int J Radiat Oncol Biol Phys 2006

Credentialing for Clinical Trials

- Facility questionnaire
  - Information about department, equipment and software used for patient care
- Dry run
  - Hard copy or electronic submission of a treatment plan that intends to meet the guidelines of the protocol
- Additional testing depends on the trial and QA organization
- Examples:
  - Image fusion benchmark
  - Head and Neck phantom irradiation

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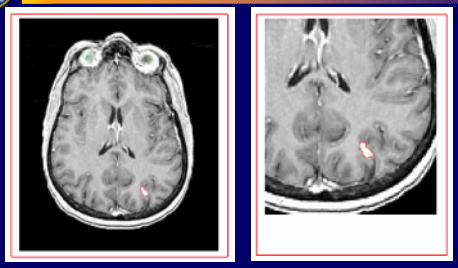
Example: QARC Fusion Benchmark



- Lesion only visible on MR
- CT and MR data are downloaded to the institution
- Institution contours, fuses the data set, and exports the location of the lesion in the CT coordinate system
- Results reviewed by QARC

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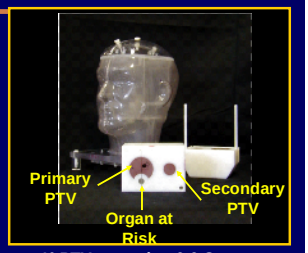
RPC: IMRT H&N Phantom

- Primary PTV
  - 4 cm diameter
  - 4 TLD
- Secondary PTV
  - 2 cm diameter
  - 2 TLD
- Organ at risk
  - 1 cm diameter
  - 2 TLD
- Axial and sagittal radiochromic films



- 1º PTV treated to 6.6 Gy
- 2º PTV treated to 5.4 Gy
- OAR limited to < 4.5 Gy

Designed in collaboration with RTOG; Molineu et al, IJROBP, October 2005

Courtesy of Molineu, RPC

RPC: IMRT H&N Phantom Results

- 163 irradiations were analyzed
- 115 irradiations passed the criteria
  - 28 institutions irradiated multiple times
- 48 irradiations did not pass the criteria
- 128 institutions are represented

Only 68% of institutions passed the criteria on the first irradiation.

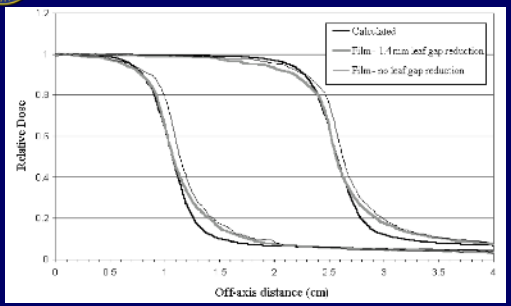
Courtesy of Molineu, RPC

RPC: Explanations for Failures

Explanation	Min # of occurrences
Incorrect output factors in TPS	1
Incorrect PDD in TPS	1
Inadequacies in beam modeling at leaf ends (Cadman, et al; PMB 2002)	14
Not adjusting MU to account for dose differences measured with ion chamber	3
Errors in couch indexing with Peacock system	2
2 mm tolerance on MLC leaf position	1
Setup errors	7
Target malfunction	1

Courtesy of Molineu, RPC

Effect of Leaf Position Offset on IMRT



Cadman et al "Dosimetric considerations for validation of a sequential IMRT Process with a commercial treatment planning system" PMB: 3001-3010 (2002).

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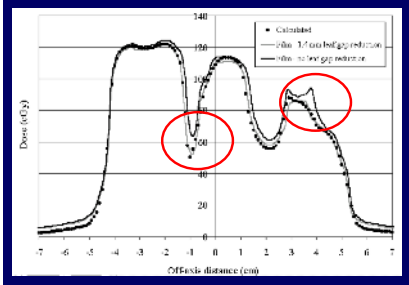
Effect of Leaf Position Offset on IMRT



No leaf offset correction
-3-12% errors

With leaf offset corrected
+/- 5%

Cadman et al "Dosimetric considerations for validation of a sequential IMRT Process with a commercial treatment planning system" PMB: 3001-3010 (2002).

Impact on clinical trials

- There is a clear role for dosimetric verification when complex technologies are being introduced
- RPC phantom found dosimetric errors that would have adversely affected trial results

Challenges for TG113

- What is the question that is being asked in the trial?
  - Is it a radiation question or an evaluation of different chemotherapy regimens?
  - Should standards be different for these different scenarios?

How should new technologies be incorporated into clinical trials?

- We do not want to limit participation in clinical trials, but we do want delivery to be as accurate as possible
  - As well as also representative of how patients will be treated in a variety of hospital settings
- We want to address how to deal with new technologies generally so that the report is not outdated once published
- Focus is on physics issues that affect the consistency of data acquired during clinical trials
  - The report is not meant to address QA in general

Timeline

- Complete outline has been created and reviewed by WG on Clinical Trials and a representative of QAOIS
- We will have a complete rough draft by ASTRO
- The document will include templates to identify physics issues that can be explicitly defined during the design of clinical trials

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