Introduction and Overview:
Determination, Minimization and Communication of Uncertainties in Radiation Therapy

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Disclosures

• None ... except I am involved with ...
“Uncertainty”: Wikipedia

• “A term used in subtly different ways in a number of fields including philosophy, physics, statistics, economics, finance, insurance, psychology, sociology, engineering, and information science.”

• “It applies to predictions of future events, to physical measurements that are already made, or to the unknown.”

• “Uncertainty arises in partially observable and/or stochastic environments, as well as due to ignorance and/or indolence.”


Stages in Radiation Treatment Process

Uncertainties occur at every stage of the treatment process!

Uncertainties in Radiation Therapy

• Scientific Uncertainty

• Human Uncertainty
Scientific Uncertainty

- Medical Physicists’ task
  - Minimize uncertainties in radiation treatment
    - Dose uncertainties
      - Calibration
      - Machine commissioning
      - Treatment planning computer commissioning
      - Dose delivery
    - Geometric uncertainties
      - Imaging uncertainties
      - Determination of patient anatomy
      - Determination of patient-beam geometry

Human Uncertainty

- Decision making
  - Diagnosis
  - Patient staging
- Target volume definition
- Normal tissue definition

Factors involved in volumetric uncertainty in target volume delineation

Uncertainties

- New technologies ... IMRT, IGRT, 4-D
  - Purpose
    - Minimize toxicity and maximize tumor dose
    - ... allows for dose escalation
    - ... allows for increases in dose/fraction
- Further clinical gain with new technologies
  - May be limited by uncertainties in various stages of treatment process

History ... Accuracy

- 1970s-1980s: 2-D RT era
  - ICRU Report 24
  - “... need for an accuracy of ±5% the in the delivery of an absorbed dose to a target volume ...”
- 1980s-1990s: 3-D CRT era
  - 3.5% (1 σ) at specification point and 5% at other points in PTV for combined Type A and B uncertainties ... this required accuracy cannot always be achieved even for simple geometries.
  - Dutreix, Brahme, Mijnheer, Wambersie

Issues

- Reports on accuracy requirements mostly written in 2-D to 3-D CRT era
- Emphasis on dose to reference point in the target volume
- Technology has evolved
  - 2-D RT to 3-D CRT to IMRT, IGRT, 4-D & motion management
“Zone of Uncertainty”

Para-aortic nodes – junction

Nominal “Upper bound” Misregistered by 1 cm “Lower bound” Misregistered by 1 cm

“The Role of Uncertainty Analysis in Treatment Planning

M. M. Uziy, Ph.D., M. Gitter, Ph.D., K. Doprka, M.S., J. G. Kuczer, Ph.D., T. LoBasso, Ph.D., R. Moran, Ph.D., J. E. Menninger, M.D., M. Sontag, Ph.D., and J. W. Wong, Ph.D.

University of Pennsylvania School of Medicine and the Fox Chase Cancer Center, Philadelphia, PA 19111. Memorial Sloan-Kettering Cancer Center, New York, NY 10065. Memorial Institute for Radiology, Washington University School of Medicine, St. Louis, MO 63110, and Massachusetts General Hospital, Department of Radiology, Boston, MA 02114 and Harvard Medical School.

"New ways of displaying the uncertainty information are badly needed.”

1991!
2011 AAPM Summer School

Preface

Summer School Program Objectives:
- Provide in-depth understanding of sources of uncertainties in external beam radiotherapy planning and delivery.
- Provide practical guidance in assessing the overall uncertainty of delivered dose to patients treated with different technologies.
- Provide practical guidance on mitigating sources of uncertainties and strategies for dealing with residual uncertainties.
- Emphasize the fact that “What You See Is Not What You Get” (WYSINWyG) and how to deal with it on a patient-by-patient basis.

J. Padula, Ph.D., and T. Rock Mackie, Ph.D.
August 2011

2011 AAPM Summer School Summary

- 27 Chapters
- Considers all aspects of dosimetric uncertainties
  - Each stage of treatment process
  - In individual chapters
- No grand summary
- No specific consensus recommendations other than what is in individual chapters

New IAEA Report

- In press, 2014

Accuracy Requirements and Uncertainties in Radiation Therapy

> 230 pages!
> 600 references!
Objective of IAEA Report

- To provide an “international guidance document on accuracy requirements and uncertainties in radiation therapy in order to reduce these uncertainties to provide safer and more effective patient treatments”.

IAEA Draft Report

Nine recommendations:
1. Accuracy statement... AAARA, technical & biological...
2. Implement ICRU reports and/or other recognized consensus group recommendations
3. Sample guide of uncertainty estimates for both external beam & brachytherapy
4. Independent dosimetry audit
5. Implement comprehensive QA program
6. Appropriate education and training
7. Uncertainty estimates should be reported in publications
8. Training by vendors on use of technologies
9. Areas for further research

Areas for Further Research ...

- Display of uncertainties as part of the treatment planning process
  - “… Further research is required into practical methods of displaying and using treatment uncertainties as an aid to decision making and as a means of developing robust treatment plans that minimize the impact of uncertainties and provide a maximum therapeutic benefit for the patient.”
Impact of Uncertainties on Plan Optimization

Eugene Wong, 12th ICCR, 1997

- Schematic PTV and critical organ
- Four 6 MV fields with 17 beamlets each
- 68 beamlet weights are varied between 0 and 1 for optimization

Dose deviations (chi-square)

<table>
<thead>
<tr>
<th>Distance [cm]</th>
<th>PTV</th>
<th>OAR</th>
<th>TOTAL</th>
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<tbody>
<tr>
<td>0.1</td>
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<td>0.4</td>
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Optimized: No uncertainties

Optimized: With uncertainties

Dose distributions for ideal and blurred optimized techniques

Optimized: No uncertainties

Optimized: With uncertainties

PTV = Planning target volume
OAR = Organ at risk

Idealized case

Objective function plotted for “ideal” and “blurred”

Ideal yields 4 field technique as optimal

Blurred yields 3 fields with wedges as optimal

Relative beamlet weights

PTV
OAR
TOTAL

-0.2 0 0.2 0.4 0.6 0.8 1 1.2

-0.2 0 0.2 0.4 0.6 0.8 1 1.2

-0.2 0 0.2 0.4 0.6 0.8 1 1.2

-0.2 0 0.2 0.4 0.6 0.8 1 1.2

4 field open, equal beam weights

3 field: open anterior, wedged laterals

4 field open, equal beam weights

3 field: open anterior, wedged laterals
Impact of Uncertainties on Plan Optimization

Eugene Wong, 12th ICCR, 1997

- Conclusions - Technique Optimization
  - Predicted outcome is strongly dependent on uncertainties propagated through treatment process.
  - Optimized plans are affected by uncertainties.
  - Proper optimization requires uncertainty information.

Communicating Uncertainties

- “It’s more than just error bars”
- How do radiation oncologists know about levels of uncertainty in their treatment plans?
  - We tell them ... usually “guestimates”
  - We show them data
    - Commissioning data
    - Published data
      - E.g., inter & intra-physician target volume delineation
      - Audit data of calibrations, TPSs, QA center end-to-end tests
    - In planning process, we ask physician’s preferences
      - If there is a significant uncertainty, do you prefer a higher dose or a lower dose to ...?

This Symposium

- Learning Objectives
  - To review uncertainty determination in the overall radiation treatment process.
  - To consider uncertainty modeling and uncertainty propagation.
  - To highlight the basic ideas and clinical potential of robust optimization procedures to generate optimal treatment plans that are not severely affected by uncertainties.
  - To describe methods of uncertainty communication and display.
This Symposium …

- Introduction & Overview
  - Jake Van Dyk, Professor Emeritus, Western University, London, Canada
- Dose Uncertainty Modeling
  - Jatinder Palta, Professor & Chairman Medical Physics, Radiation Oncology Virginia Commonwealth University, Richmond, VA.
- Robust Optimization Accounting for Uncertainties
  - Thomas Bortfeld, Professor, Francis H Burr Proton Therapy Center, Massachusetts General Hospital, Boston, MA
- Communication of Uncertainties in Radiation Therapy
  - Ben Mijnheer, Dept of Radiation Oncology, Netherlands Cancer Institute, Amsterdam, Netherlands

MORE ON ...

Uncertainty Just Ahead