


Michael Goitein's Impact on The Evolution of Proton Therapy

THE UNIVERSITY OF TEXAS MD Anderson Cancer Center
Making Cancer History®

Radhe Mohan, PhD

Michael Goitein Memorial Symposium: Milestones in Treatment Planning, Biophysical Modeling, and Delivery of Proton Therapy
AAPM Annual Meeting 2017, Denver Colorado

Michael Goitein

A Pioneer → Ahead of His Time

Michael Goitein – Major Contributions of Relevance to Protons Therapy

- CT reconstruction algorithms
- Introduction of CT into radiation oncology
- 3D conformal radiotherapy
- Beams-eye view
- Consideration of uncertainties in treatment planning
- Dose-volume histograms quantitative plan evaluation
- Compensator design to conform the distal proton beam edge to target volume
- Smearing of proton beam compensators to account for uncertainties introduced by misalignment with anatomy
- Understanding the impact of tissue heterogeneities on the degradation of distal edges of a proton beams
- Biophysical modeling of tumor control and normal tissue complication probabilities
- …

Beyond the Specifics …

- Recognized critical issues, articulated them and found solutions
  - 3D nature of the disease and planning for it using 3D CT
  - Uncertainties in all aspects of radiotherapy
  - Biology matters
  - Translating protons into clinical practice effectively
- Laid the foundation for future developments

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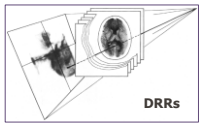
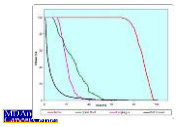
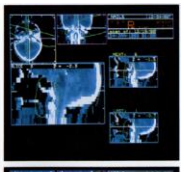
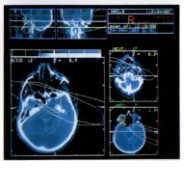
Three-Dimensional Conformal Radiotherapy

- 3D CRT Concepts and their Translation









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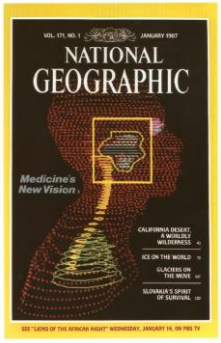
Three Dimensional Treatment Planning

The NCI contract on the Evaluation of 3D Treatment Planning for Photons (1983-1987)

Goitein – the intellectual driving force
An inspiration

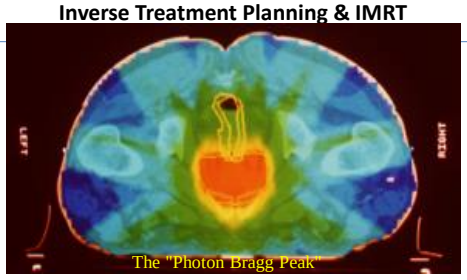
3D RTP at MSKCC
Propelled by the NCI Contract



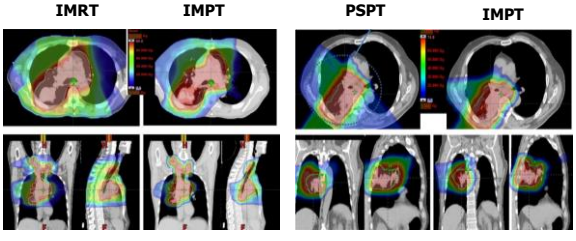
Impact on the Evolution of the Field – Three Dimensional Treatment Planning for Protons →

3D Photons → IMRT → IMPT

Inverse Treatment Planning & IMRT



Mohan, R., et al., Radiother. Oncol. 32, 232-248 (1994)



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Uncertainties

If there's one thing that's certain in life

It's uncertainty

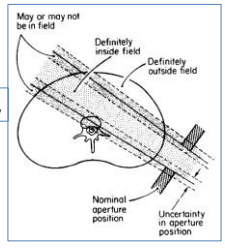
"(Almost) Everything is Uncertain"

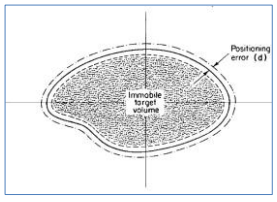
- **Diagnosis**
- **Imaging**
- **Delineation of Volumes of Interest**
- **Prescription**
- **Development of a plan of treatment**
- **Patient handling (e.g., patient immobilization and/or positioning, patient and organ motion)**
- **Treatment delivery**
- **Treatment response assessment**

Goitein: Radiation Oncology: A Physicist's-Eye View

A technique for estimating uncertainty in dose at a point

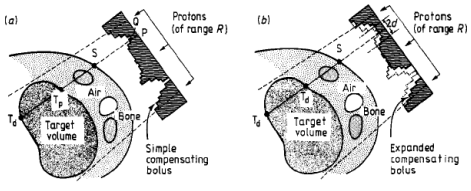
Zones of Uncertainty





Goitein Calculation of the uncertainty in the dose delivered during radiation therapy, Med Phys 1984

Compensator Smearing to Account for Misalignment & Lateral Scattering to Ensure Target Coverage for PSPT



Perhaps the earliest attempt to improve robustness of dose distributions in the face of uncertainties

Managing Uncertainties

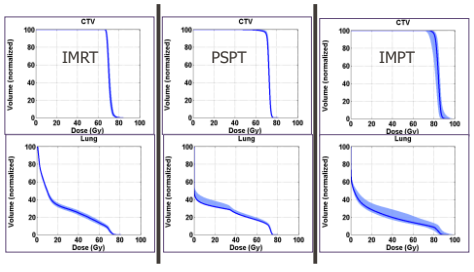
Urie, et al Phys. Med. Biol., 1983.

Impact on the Evolution of the Field –

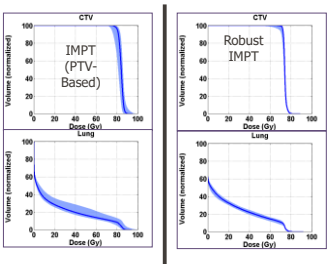
Consideration of Uncertainties in Treatment Plan Design and Evaluation

Introduction of the PTV and ORV Concepts
IGRT
Robustness Evaluation and Robust Optimization
Adaptive Replanning

Robustness Evaluation – DVH Bands
A NSCLC Case



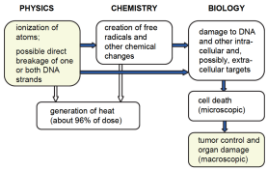
Robust Optimization
A NSCLC Case



Liu, Zhang and Mohan

Biology Matters!

"… dose is only a surrogate for what is clinically important … Our goal is biological."



Biology Matters!

- Factors that modulate radiation dose response
  - The fractionation scheme
  - The inherent radiosensitivity of the tumor and normal tissues
  - Chemotherapy
  - Genetic differences, and so forth
  - …
- Biophysical modeling
  - An "attempt to capture, in a mathematical recipe, that which is in the clinician's head and make it explicit"

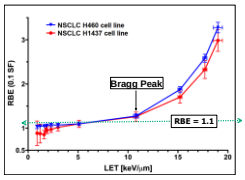
Impact on the Evolution of the Field – Biology Matters!

Improving out understanding of biology of particles

Improving our understanding of response to treatments with photons, protons and heavier particles

Evolution Of Biological Aspects of Protons and Heavier Ions

- Recent and ongoing research to improve understanding of complex nature of biological effects of particles
  - Fixed RBE = 1.1 → Variable RBE
  - IMPT optimization based on new knowledge of biological
  - The dose bath effect ("Compact" proton/particle dose distributions)
  - Immunosuppressive and immunogenic properties of particles

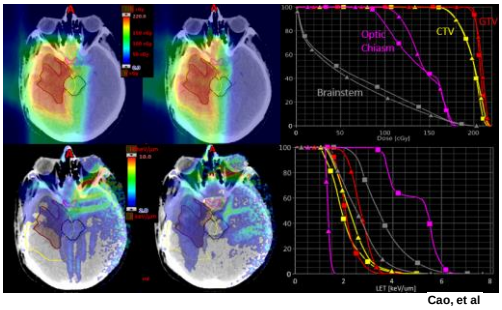


Glioblastoma

1.1Dose Opt. (LET + 1.1Dose) Opt.

RBE=1.1 Dose

LET_d



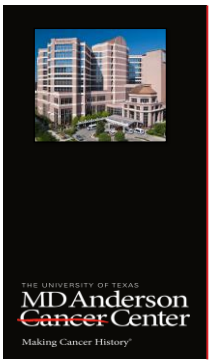
Cao, et al

in my [MG] opinion

- The future of proton beam therapy very much depends on:
  - an understanding of the consequences of the dose bath which x-rays are forced to deliver;
  - or, conversely, the benefit which may accrue from the ability of protons to significantly reduce the dose bath.

Unfortunately, this is an extremely hard problem, and there is little enthusiasm for either pursuing it, or funding research to understand it.

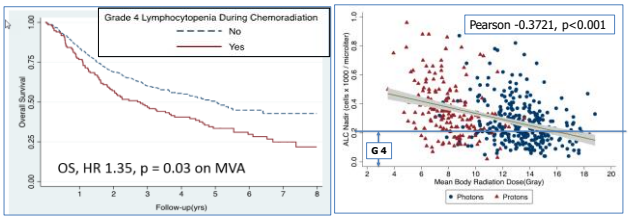
Michael Goitein (Keynote Address) as Advisor on P01 Round Top, TX April, 2007 [24]



Proton Beam Therapy significantly reduces high grade lymphopenia to chemoradiation in esophageal cancer

Steven H. Lin, M.D., Ph.D.
Associate Professor
Thoracic Radiation Oncology
MD Anderson Cancer Center

Clinical Outcomes in Patients with G4 Lymphopenia (ALC Nadir)



A couple of Words of Wisdom from MG

- **"From time to time, the imminent death of radiation oncology is announced, often by advocates of some treatment modality (immunology, gene therapy, and so forth) which is competing for research funds or for 'market share.' …these obituaries are premature."**
- **"Please, resist the ever increasing pressure to be constrained by purely economic considerations. There is no lack of people worrying about finances and figuring out how to cut costs (and corners). Let yourself be an advocate for the patient."**

Goitein: Radiation Oncology: A Physicist's-Eye View ("Afterword")

From a letter of support for the award of ASTRO Gold Medal to Michael Goitein

Undoubtedly, his intellectual and scientific capabilities are far above that of his peers.

A visionary who has advanced the field of medical physics immensely

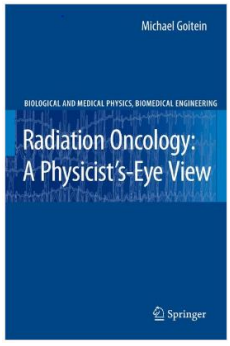
Amazing depth and breadth of understanding of a vast array of subjects

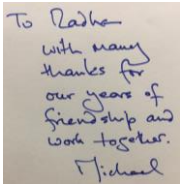
Incisive ability to analyze the strengths and weaknesses of solutions to problems

An eagerness to attempt the extraordinary and not be deterred by what others might consider to be impossible

Unconventional thinker, thought provocateur

Extraordinarily articulate and lucid communicator with a great knack for making even the most complex concepts appear simple





The Fields of Radiation Physics and Radiation Oncology Owe a Debt of Gratitude to Michael Goitein

His larger than life influence on our field will be felt for many decades to come

RIP Michael

We Miss You!