Innovating the Delivery of Radiation Therapy

Thomas Bortfeld

Massachusetts General Hospital
Department of Radiation Oncology
Division of Radiation Biophysics
tbortfeld@mgh.harvard.edu

MASSACHUSETTS GENERAL HOSPITAL

HARVARD MEDICAL SCHOOL

Innovating the Delivery of Radiation Therapy

Two Examples:

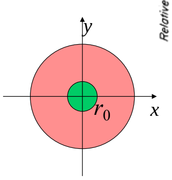
1. **IMRT**
2. Protons

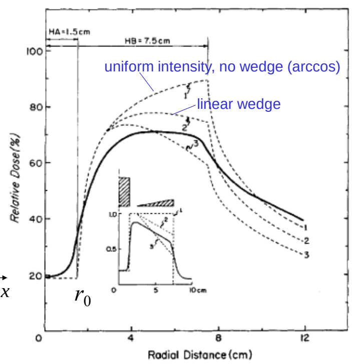
MASSACHUSETTS GENERAL HOSPITAL

Physics Division

IMRT precursor
Need for intensity modulation

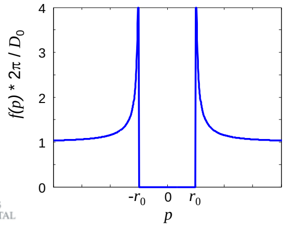
Rawlinson & Cunningham Radiology 102, 1972





The idea of inverse planning was born

$$f(p) = \begin{cases} \frac{D_0}{2\pi} \frac{|p|}{\sqrt{p^2 - r_0^2}} & \text{if } |p| \geq r_0 \\ 0 & \text{otherwise.} \end{cases}$$



MASSACHUSETTS GENERAL HOSPITAL

Physics Division

Birth of IMRT: 1982

Phys. Med. Biol., 1982, Vol. 27, No. 10, 1221–1229. Printed in Great Britain

Solution of an integral equation encountered in rotation therapy

A Brahme†, J-E Roos‡ and I Lax§

§ Department of Hospital Physics, Karolinska Sjukhuset, Box 60204, S-104 01 Stockholm, Sweden

‡ Department of Mathematics, University of Stockholm, Box 6701, S-113 85 Stockholm, Sweden

§ Department of Hospital Physics, Karolinska Sjukhuset, Box 60204, S-104 01 Stockholm, Sweden

Received 30 March 1981, in final form 4 December 1981

Abstract. An integral equation relating the lateral absorbed dose profile of a photon beam to the resultant absorbed dose distribution during single-turn rotating-beam therapy has been set up and solved for the case of a cylindrical phantom with the axis of rotation coinciding with the axis of symmetry of the cylinder. In the first approximation the results obtained are also valid when the axis of rotation is somewhat off-centred, even in a phantom that deviates from circular symmetry, provided the rotation is performed in both clockwise and counter clockwise directions. The calculated dose profiles indicate that improved dose uniformity can be achieved using a new type of non-linear wedge-shaped filter, which can easily be designed using the derived general analytic solution to the integral equation.

Rotation Therapy: Dramatic news in Geneva! October 20th 1992

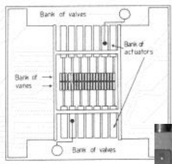
– the World's 1st truly IMRT delivery equipment. First treatment in March 1994 at Baylor. Slice-based Rotation IMRT dominated IMRT clinical practice from 1994-1997. Then (astonishingly) it lost this lead.

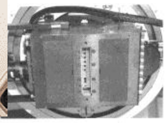
Mark Carol, NOMOS CEO at 12th ICCR Conference 1997 [on roller blades]

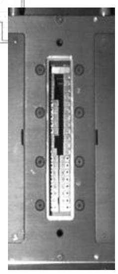
Slide: Steve Webb

1992 Carol first showed the NOMOS MIMiC and associated PEACOCKPLAN planning system CORVUS.

The NOMOS MIMiC







NCI funding “IMRT” (source: NIH Reporter)

Title	Type	PI	Year
EFFICIENT GENERATION OF OPTIMAL MULTIBEAM IMRT PLANS	R43	LEVINE, ROBERT Y	1999
AUTOMATED VERIFICATION SYSTEM FOR CONFORMAL RTP AND IMRT	R43	MARYANSKI, MAREK J	1999
MONTE CARLO TOOLS FOR IMRT	R01	MA, CHANG-MING CHARLIE	2001
IMRT FOR GYNECOLOGICAL MALIGNANCIES	R01	LOW, DANIEL A	2002
PHYSICAL; RADIOBIOLOGICAL; AND CLINICAL ASPECTS OF IMRT	R01	MOHAN, RADHE	2003
IMRT IN THE TREATMENT OF NODE-POSITIVE BREAST CANCER	R21	PIERCE, LORI J	2003
OPTIMIZED IMRT INCORPORATING BEAM DELIVERY	R01	SIEBERS, JEFFREY V	2004
4-D IMRT: IMAGING; PLANNING AND DELIVERY	R01	KEALL, PAUL J	2006
LUNG TRAJECTORY MAPPING FOR IMRT	R01	LOW, DANIEL A	2006
IMRT GUIDED BY MAGNETIC RESONANCE SPECTROSCOPIC IMAGING	R01	XING, LEI	2006
IMAGE-GUIDED IMRT FOR INTER-FRACTIONAL CHANGES	R01	MOHAN, RADHE	2008
HYPOFRACTIONATED IMRT FOR LOCALIZED PROSTATE CANCER	R01	RITTER, MARK A	2008
MULTIATTRIBUTE DECISION THEORY FOR IMRT PLAN SELECTION	R01	PHILLIPS, MARK H.	2009
IMAGE-GUIDED ADAPTIVE IMRT FOR HEAD AND NECK CANCER	R21	SCHWARTZ, DAVID LOUIS	2009

MASSACHUSETTS GENERAL HOSPITAL

Physics Division

NCI funding “IMRT” (source: NIH Reporter)

Title	Type	PI	Year
IMRT DOSE OPTIMIZATION	R01	XING, LEI	2009
INDIVIDUALIZING IMRT TREATMENT IN BRAIN AND HEAD/NECK CA	P01	EISBRUCH, AVRAHAM EISBRUCH	2010
OROPHARYNGEAL FUNCTION AFTER RADIOTHERAPY WITH IMRT	R01	LOGEMANN, JERILYN A	2010
MULTI-CRITERIA IMRT OPTIMIZATION	R01	BORTFELD, THOMAS R.	2011
IMAGE-GUIDED IMRT AND BRACHYTHERAPY FOR PELVIC TUMORS	P01	WILLIAMSON, JEFFREY F	2011
ACCURATE TARGET DELINEATION AND MOTION TRACKING TO IMPROVE IMRT EFFECTIVENESS	K25	WU, XIAODONG	2011
CARDIAC SPARING WHOLE LUNG IMRT IN CHILDREN AND YOUNG ADULTS WITH LUNG METASTASES	R21	KALAPURAKAL, JOHN ANDREW	2012
IMAGE-GUIDED BONE MARROW-SPARING IMRT FOR CERVICAL CANCER	R21	MELL, LOREN K.	2012
4D IMRT: STEREOTACTIC BODY RADIOTHERAPY FOR LUNG CANCER	R01	KEALL, PAUL J	2013
REDUCED-ORDER CONSTRAINED OPTIMIZATION FOR RAPID IMRT AND VMAT TREATMENT PLANNING	R01	RADKE, RICHARD J	2013
ASSESSMENT OF EFFECTIVENESS OF IMPT VS. IMRT THROUGH PHASE II RANDOMIZED CLINICAL TRIALS	U19	MINSKY, BRUCE D.	2014

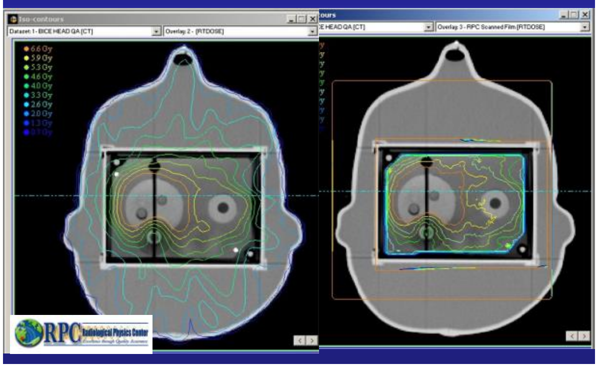
Total: $26.5 Million

MASSACHUSETTS GENERAL HOSPITAL

Physics Division

Scan, Plan, Treat a phantom

Plan vs. Treatment

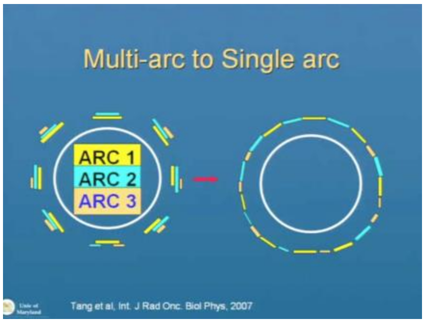


Phantom Results

Phantom	H&N	Prostate	Thorax	Liver
Irradiations	217	58	28	4
Pass	135	35	14	2
Fail	52	12	4	-
Under analysis or at institution	12	11	4	2
Unevaluable	12	6	4	1
Year introduced	2001	2004	2004	2005

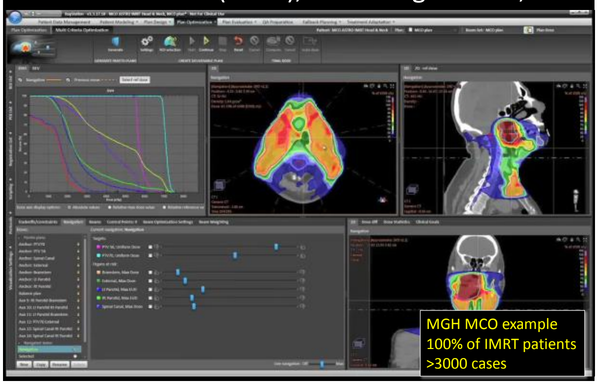
* 34% of institutions failed on the first attempt

IMAT -> VMAT?



IMAT: Cedric Yu, PMB 1995
NCI funding 2001

Improvements in IMRT planning
multi-criteria (MCO), knowledge based, …



Innovating the Delivery of Radiation Therapy

<u>Two Examples:</u>

1. IMRT
2. **Protons**

MASSACHUSETTS GENERAL HOSPITAL

Physics Division

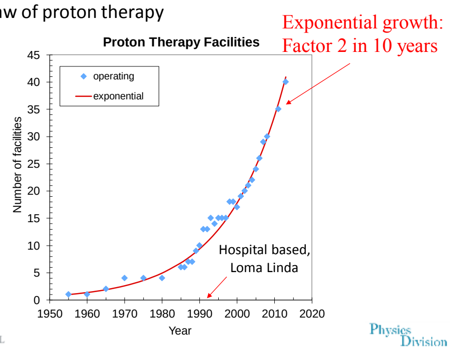
Early history of proton therapy

1946 – Robert R. Wilson (Harvard) article on proton therapy
1954 – first patient treatment at Berkeley
1957 – first patient at Uppsala, Sweden
1961 – first patient at MGH / Harvard Cyclotron Laboratory (HCL)



History of proton therapy

Moore's law of proton therapy



- "The proton therapy operation at HCL would have closed almost certainly by the mid 1970s without the active and large program initiated by MGH and support from NIH."
  - Herman Suit and Michael Goitein

NCI funding “proton therapy” (source: NIH Reporter)

Title	Type	PI	Year
RADIOGRAPHIC AID TO PROTON THERAPY	R43	MARTIN, RONALD L	1991
PROTON THERAPY RESEARCH AND TREATMENT CENTER	C06	GOITEIN, MICHAEL	1995
PROTON RADIATION THERAPY RESEARCH	P01	SUIT, HERMAN D.	1998
CONSTRUCTION OF PROTON THERAPY CENTER	C06	CAMERON, JOHN M	2002
PROTON RADIATION THERAPY RESEARCH	P01	LOEFFLER, JAY STEVEN	2004
PROTON PUMP INHIBITOR THERAPY	M01	KIM, KAREN E	2005
RADIATION HARD X-RAY DETECTOR FOR IMAGE-GUIDED PROTON BEAM CANCER THERAPY	R43	SBROCKEY, NICK M.	2009
FAST PET DOSIMETRY FOR PROTON THERAPY	R43	WEINBERG, IRVING	2009
HIGH SENSITIVITY MOBILE PET FOR BRAIN IMAGING AND PROTON THERAPY MONITORING	S10	EL FAKHRI, GEORGES	2010
IN-ROOM PET MONITORING OF PROTON THERAPY	R21	EL FAKHRI, GEORGES	2011
A COMPACT DOSE DELIVERY SYSTEM FOR PROTON RADIATION THERAPY	R44	CAMERON, JOHN M	2012

MASSACHUSETTS GENERAL HOSPITAL

Physics Division

NCI funding “proton therapy” (source: NIH Reporter)

Title	Type	PI	Year
PBEAM: FAST AND EASY MONTE CARLO SYSTEM FOR PROTON THERAPY	R01	PAGANETTI, HARALD	2012
REDUCING RANGE UNCERTAINTIES IN PROTON RADIATION THERAPY	P01	BORTFELD, THOMAS R.	2013
IMPROVING THE THERAPEUTIC RATIO OF PROTON RADIATION THERAPY	P01	DELANEY, THOMAS F	2013
PROTON RADIATION THERAPY RESEARCH	P01	DELANEY, THOMAS F	2013
ACHIEVING 'WHAT-YOU-SEE-IS-WHAT-YOU-GET' IN PROTON THERAPY	P01	DONG, LEI	2013
IGF::OT::IGF LASER-DRIVEN PROTON AND CARBON THERAPY	N43	O'SHEA, FINN	2013
NEUROCOGNITIVE OUTCOMES FOLLOWING PROTON BEAM RADIATION THERAPY FOR TREATMENT OF	K07	KAHALLEY, LISA SCHUM	2014
4D ROBUST OPTIMIZATION IN INTENSITY-MODULATED PROTON THERAPY	K25	LIU, WEI	2014
TOPAS: FAST AND EASY TO USE MONTE CARLO SYSTEM FOR PROTON THERAPY	R01	PAGANETTI, HARALD	2014
A RAPID RESPONSE DETECTOR SYSTEM FOR INTENSITY MODULATED PROTON THERAPY DOSIMETRY	R44	SOLBERG, KEITH	2014

Total: $ 97.7 Million

MASSACHUSETTS GENERAL HOSPITAL

Physics Division

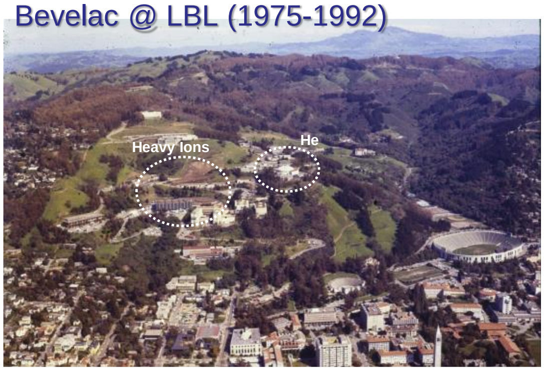
By-products of proton P01

- Dose-volume histograms
- Beam’s eye view
- 3D treatment planning based on CT
- TCP, NTCP modeling
- Equivalent Uniform Dose (EUD)
- Robust optimization
- …

MASSACHUSETTS GENERAL HOSPITAL

Physics Division

Heavier Ions
Bevelac @ LBL (1975-1992)



Courtesy of George TY Chen

Heavier Ions

(Bragg Peak) Clinical Trials at LBNL, 1975–1992

J.R. Castro, MD, UCSF conducted the LBNL clinical trials.

- 1st He patient 6/75
- 1st C patient 5/77
- 1st Ne patient 11/77
- 1st Ar patient 3/79
- 1st Si patient 11/82

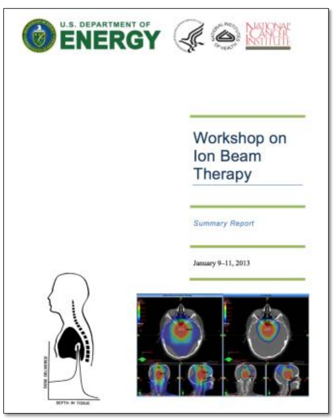
Total patient treated: 1314
1977–1992
- He patients 858
- Heavier ions 456

CA Tobias, LBL UCB
HI Visionary

Courtesy of George TY Chen

Heavier Ions
renewed interest

seed grants

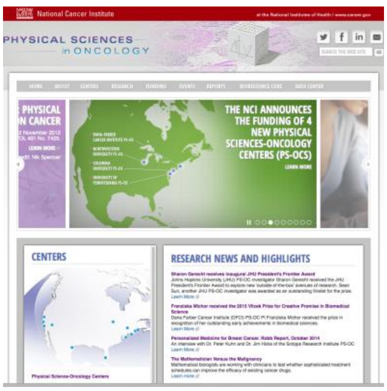


- “If it was up to the ~~NIH~~ Medical Physicists to cure cancer you’d have the best particle beam in the world but not a cancer cure .”
  – Samuel Broder, former NCI director

MASSACHUSETTS GENERAL HOSPITAL

Physics Division

Physical Sciences in Oncology Centers



Relevant NIH Funding Opportunities: The Physical Sciences-Oncology Network (PS-ON) Projects and Centers

PHYSICAL SCIENCES in ONCOLOGY

Network (PS-ON)

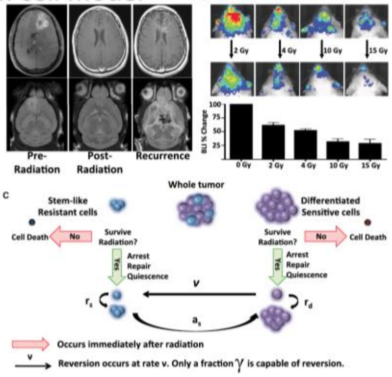
Thematic Areas

The Physical Dynamics of Cancer | Spatial Organization and Cancer

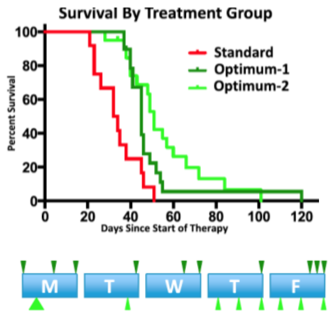
	Project (PAR-15-021)	Center (PAR-14-169)
	PS-OP	PS-OC
Mechanism	U01	U54
Budget	$500K Direct / Yr	$1.5 M Direct / Yr
Letter of Intent Deadline	Oct 14 2015 and 4 additional dates	Oct 14 2015
Application Deadline	Nov 25 2015 and 4 additional dates	Nov 25 2015
Number of Projects	1	2-3
Shared Resource Core	0	0-2
Education & Outreach Unit	0	1

Fractionation optimization for glioblastoma
Stem cell model

Leder et al., Cell 156, 2014

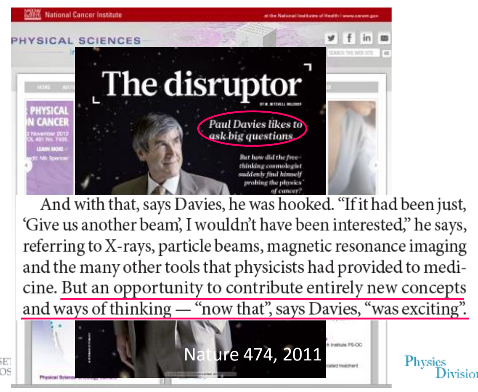


Survival in mouse experiment
10 Gy over 1 week, different fractionation



Leder et al., Cell 156, 2014

Physical Sciences in Oncology Centers



Physics Division

Ask bigger questions!

AAPM WG Future initiative:
"Provocative questions in Med Phys" workshop 2016

MASSACHUSETTS GENERAL HOSPITAL

Physics Division

Summary

Innovating the Delivery of Radiation Therapy

- IMRT: NCI support helped to refine IMRT delivery, and ensured safety and accuracy. However, IMRT would probably be here without NCI support.
- Protons/particles: NCI support has been absolutely crucial.
- We all have to be careful about über-optimizing the "iron lung" of radiation therapy.

MASSACHUSETTS GENERAL HOSPITAL

Physics Division