Innovating the Delivery of Radiation Therapy

Two Examples:
1. IMRT
2. Protons

IMRT precursor
Need for intensity modulation

Rawlinson & Cunningham Radiology 102, 1972
The idea of inverse planning was born

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

Birth of IMRT: 1982


Solution of an integral equation encountered in rotation therapy

A. Broström†, J-E. Rosén and I. Larj†
†Department of Medical Physics, Karolinska Institute, RO-06204 Stockholm, Sweden
‡Department of Mathematics, University of Stockholm, BOX 680, S-113 83 Stockholm.
§Department of Hospital Physics, Karolinska Institute, RO-06204 S-144 85 Stockholm, Sweden

Received 30 March 1981; in final form 4 December 1981

Abstract. An integral equation arising in the theory of inverse planning of a radiation beam to the optimum desired dose distribution in a two-dimensional planar problem is solved. The solution is used to determine the beam shape on 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-centered; i.e., in a finite cylinder. The solution is expressed in terms of elliptical cylinders and the parameters of the ellipse are obtained using a new kind of ray matrix method. The result is then used to determine the shape of the beam on the surface of the cylinder and on the centerline of the cylinder. The solution is obtained using the method of inverse planning and the results are illustrated using a new kind of ray matrix method.

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


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.

### NCI funding “IMRT” (source: NIH Reporter)

<table>
<thead>
<tr>
<th>Title</th>
<th>Type</th>
<th>PI</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>EFFICIENT GENERATION OF OPTIMAL MULTIBEAM IMRT PLANS</td>
<td>R1</td>
<td>LEVY, ROBERT Y.</td>
<td>1999</td>
</tr>
<tr>
<td>AUTOMATED VERIFICATION SYSTEM FOR CONFORMAL RT AND IMRT</td>
<td>R1</td>
<td>KAYHANI, MANSOOR</td>
<td>1999</td>
</tr>
<tr>
<td>NOMOS CURVED TIGHTS FOR IMRT</td>
<td>R21</td>
<td>CHANG, MINH Q.</td>
<td>2001</td>
</tr>
<tr>
<td>IMRT FOR GYNECOLOGICAL MALE GENITALIANS</td>
<td>R01</td>
<td>LOW, DANIEL A.</td>
<td>2002</td>
</tr>
<tr>
<td>PHYSICAL, RADIOBIOLOGICAL, AND CLINICAL ASPECTS OF IMRT</td>
<td>R01</td>
<td>SCHMIDT, RASHE A.</td>
<td>2003</td>
</tr>
<tr>
<td>IMRT IN THE TREATMENT OF NODE-POSITIVE BREAST CANCER</td>
<td>R01</td>
<td>PEREZ, LORI J.</td>
<td>2003</td>
</tr>
<tr>
<td>OPTIMIZED IMRT INCOPTERATING GLASS AND DELIVERY</td>
<td>R01</td>
<td>SEIBERT, JEFFREY V.</td>
<td>2004</td>
</tr>
<tr>
<td>6D IMRT: MEASURING, PLANNING, AND DELIVERY</td>
<td>R01</td>
<td>DIAZ, PAUL J.</td>
<td>2006</td>
</tr>
<tr>
<td>LUNG TRAJECTORY MAPPING FOR IMRT</td>
<td>R01</td>
<td>LOW, DANIEL A.</td>
<td>2006</td>
</tr>
<tr>
<td>IMRT GUIDED BY MAGNETIC RESONANCE SPECTROSCOPIC IMAGING</td>
<td>R01</td>
<td>XING, LEI</td>
<td>2006</td>
</tr>
<tr>
<td>RINGS-GUIDED IMRT FOR INTER-TRUCTIONAL ENAMAGES</td>
<td>R01</td>
<td>BOYER, RASHE A.</td>
<td>2008</td>
</tr>
<tr>
<td>HIPPOET/NOET/NOET IMRT FOR LOCALIZED PROSTATE CANCER</td>
<td>R01</td>
<td>RITTER, MARK A.</td>
<td>2008</td>
</tr>
<tr>
<td>MULTIATTRIBUTE DECISION THRESHOLD FOR IMRT PLAN SELECTION</td>
<td>R01</td>
<td>PHILLIPS, MARK A.</td>
<td>2009</td>
</tr>
<tr>
<td>RINGS-GUIDED ADAPTIVE IMRT FOR HEAD AND NECK CANCER</td>
<td>R21</td>
<td>SCHWARTZ, DAVID L.</td>
<td>2009</td>
</tr>
</tbody>
</table>

**Total:** $26.5 Million
Scan, Plan, Treat a phantom

Plan vs. Treatment

Phantom Results

<table>
<thead>
<tr>
<th>Phantom Results</th>
<th>H&amp;N</th>
<th>Prostate</th>
<th>Thorax</th>
<th>Liver</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irradiations</td>
<td>217</td>
<td>58</td>
<td>28</td>
<td>4</td>
</tr>
<tr>
<td>Pass</td>
<td>135</td>
<td>35</td>
<td>14</td>
<td>2</td>
</tr>
<tr>
<td>Fail</td>
<td>52</td>
<td>12</td>
<td>4</td>
<td>-</td>
</tr>
<tr>
<td>Under analysis</td>
<td></td>
<td>12</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>or at institution</td>
<td></td>
<td>12</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>Unevaluable</td>
<td>12</td>
<td>6</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Year introduced</td>
<td>2001</td>
<td>2004</td>
<td>2004</td>
<td>2005</td>
</tr>
</tbody>
</table>

* 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

Two Examples:
1. IMRT
2. Protons
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

Exponential growth:
Factor 2 in 10 years

• “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
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
- ...
Heavier Ions
Bevelac @ LBL (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

Heavier Ions renewed interest
seed grants
• “If it was up to the NIH to cure cancer you’d have the best particle beam in the world but not a cancer cure.”

– Samuel Broder, former NCI director

Physical Sciences in Oncology Centers

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

<table>
<thead>
<tr>
<th>Thematic Areas</th>
<th>Project (PAR-15-021)</th>
<th>Center (PAR-14-169)</th>
</tr>
</thead>
<tbody>
<tr>
<td>The Physical Dynamics of Cancer</td>
<td>PS-OP</td>
<td>PS-OC</td>
</tr>
<tr>
<td>Spatial Organization and Cancer</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Mechanism</td>
<td>USA</td>
</tr>
<tr>
<td></td>
<td>Budget</td>
<td>$500K Direct / Yr</td>
</tr>
<tr>
<td></td>
<td>Letter of Intent Deadline</td>
<td>Oct 14 2015 and 4 additional dates</td>
</tr>
<tr>
<td></td>
<td>Application Deadline</td>
<td>Nov 25 2015 and 4 additional dates</td>
</tr>
<tr>
<td></td>
<td>Number of Projects</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Shared Resource Core</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Education &amp; Outreach Unit</td>
<td>0</td>
</tr>
</tbody>
</table>
Fractionation optimization for glioblastoma Stem cell model

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

Physical Sciences in Oncology Centers

And with that, says Davies, he was hooked. "If it had been just, 'Give us another beam,' I wouldn't have been interested," he says, referring to X-rays, particle beams, magnetic resonance imaging and the many other tools that physicists had provided to medicine. But an opportunity to contribute entirely new concepts and ways of thinking — "now that", says Davies, "was exciting."
Ask bigger questions!


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.