Present and Future of Radiation Therapy

ICTP School on Medical Physics
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Miramare, Trieste

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Overview

• Then
• Now
• Tomorrow
• Summary
Radiotherapy 1-D

KiloVoltage therapy for breast
Radiation therapy simulation... a note and a diagram in the chart
Radiotherapy 1-D and 2-D
Typical dosimetric calculation =

Computation of Beam-ON time for a Co-60 treatment

\[ \text{BOT}_i = \frac{\text{PD}_i}{100} \times T_{100,d,FS} \]
FIG. 11-37. A. Protection of vaginal disease onto the surface of the body. The cervical localizer, seen on the left side of the tray, consists of a plastic rod with a lead plug at its tip and a fluid level to assure its horizontal position. The plastic rod is introduced into the vagina, guided by the examining finger until contact is made with the lowest palpable vaginal disease. As the rod is then attached to the stand at exactly this level, the vertical pointer, which is in line with the tip of the rod, will project the location of the lowest palpable vaginal disease onto the surface of the body. The lower margin of the portal is drawn 2 cm below that projection. A verification film is taken immediately and adjustments are made until the field includes approximately 1 cm of tissue below the lead plug, which means that there will be at least 2 cm of normal vaginal tissues in the irradiated field.

Also seen on the tray are the compression cone for the 22-MeV electron with the lead blocks to shield respectively 2 and 4 cm of tissue at 30-cm depth. The end of compression cone for the 90Co unit is made of copper mesh to minimize secondary electron emission. The lead blocks can slide sideways to fit the isodose curves of the individual radium system.

FIG. 11-37. C. The same procedure used for the localization of the lowest palpable disease is also used to determine the center of the lateral portals. A Lucite bridge used for daily treatment duplication is also shown.
FIG. 3-124 (cont'd). C. Treatment for the ipsilateral neck. The anterior 60Co field extends from the lower border of the parotid field.

D. Isodose distribution of 60Co wedges. The tumor dose is taken at the 138% curve. The tissue volume included in the high dose range is not excessive.
The 90’s – the era of 3D

Perez and Brady - Principles and Practice of Radiation Oncology-1998, and others...
Cranio- spinal Irradiation
RFS vs. DOSE - RT alone

From: M.J. Zelefsky et. al.; IJROBP June 1998
Fig. 2. Kaplan-Meier prostate-specific antigen (PSA) disease-free survival curves of patients with intermediate-risk tumors (T1b, T1c, T2a, GS ≤6 and PSA >10 ng/mL but ≤20 ng/mL or T2b, GS ≤6 and PSA ≤20 ng/mL or GS 7 and PSA ≤20 ng/mL).

From: P. Kupelian et. al.; IJROBP Feb 2005
Fig. 2. Logistic response models for bNED for two pretreatment PSA groups.

From: G.E.Hanks et. al., IJROBP, June 1998
Morbidity vs. Dose

![Graph showing dose-response functions for actuarial five-year late morbidity.](image)

Fig. 5. Logistic response models for gastrointestinal and genitourinary radiation sequelae.

From: G.E. Hanks et. al., IJROBP, June 1998
Hypothesis ... for new technologies

More accurate dose delivery & better dose distributions yield better clinical outcomes!

Basic Strategy
• Reduce treatment volume
  - Irradiate a smaller volume of normal tissue

... allows dose escalation
  - higher doses to tumours

Tumour Control Probability (TCP)

Normal Tissue Toxicity (NTCP)

Courtesy: Dr Jacob (Jake) Van Dyk
Radiation Oncology Historical Trends

Clinical Benefit
(Survival)
(Conformality)

1895-1940s
- 100-400 kV x-rays
- Non-uniform dose
- High skin dose
- Brachytherapy
- Radium & radon
- Calculation systems


Discovery of x-rays & radioactivity

1950s
- Cobalt-60 MV x-rays
- Skin sparing
- Uniform dose
- Manual treatment
- Planning

1960s-70s
- Multi-energy linacs
- Computerized TPSs
- Simulators

1970s-80s
- CT, 3D-CRT
- Brachytherapy
- afterloading

1990s-2019
- IMRT, IGRT, ART, PET, MR-IGRT, Protons, Carbon ions

>2020s
- Next??

2010s
- Survival=67%

1970s
- Survival=50%

“Real data”

1970s
"Real data"

Year
USA 5-yr Survival: ~1970s [●] to ~2010s [●]

- All cancers up
  - 50% → 67%
- Except cervix & uterus
- Prostate
  - 68% → 99%
- “early detection and improved treatment”

Our World in Data, University of Oxford
https://ourworldindata.org/uploads/2018/03/Five-year-cancer-survival-rates-USA-v2-01.png

Courtesy: Dr Jacob (Jake) Van Dyk
Prostate Cancer EBRT

Image guidance over the years

- Portal Imaging (film and digital)
- Fluoroscopic tracking (range of motion)
Gold coils implanted in the prostate are shown on a DRR (a) and on an MV portal image (b). Image matching structures obtained from the DRR are superimposed on the EPID to target the coils, rather than the bony anatomy.
Image guidance over the years

- On Board imagers (kV and MV)
Localization and 4D RF Tracking of Implanted Markers
Image guidance over the years

• U-Sound targeting (mainly distance or interface)
Image guidance over the years

• Optical surface matching (Visionrt)
Acoustic neuroma not clearly visible on CT image
Mass clearly seen on reformatted MRI image after fusion with CT
Current

Image-Guided Radiation Therapy (IGRT)

4-D Radiation Therapy

Reduction of systematic and random uncertainties

Adapted from Dr Jacob (Jake) Van Dyk
• **Do We Deliver the Correct Dose Distribution for every Treatment?**

For many anatomical sites we have limited control of the internal organ motion.
Conventional treatment
Effect of organ motion on **GTV** is accounted for by **PTV**, which is always inside the beam aperture.

IMRT treatment: summation of small beams
No organ motion delivered = planned
with organ motion delivered $\neq$ planned

**Effects of Intra-Fraction Organ Motion on the Delivery of IMRT with an MLC**

Courtesy of Dr C. S. Chui
Hybrid Technologies - Imaging and Therapy

- Linac/CBCT
In Room Radiographic guidance

BrainLAB ExacTrac 6D
X-ray tubes recessed in floor
Flat panels mounted to ceiling

Accuray CyberKnife
X-ray tubes mounted to ceiling
Flat panels recessed in floor
Hybrid Technologies-Imaging and Therapy

• Tomotherapy
• Halcyon
Hybrid Technologies-Imaging and Therapy
Cobalt/MR

- Rotating Gantry Assembly
- 3 Independent Co60 Headed Design
- Asynchronous Delivery
- Mounted with 120 degree separation
- 15,000 Ci per source
- ±240 degree Rotation for 2 or 3 Head Operation for Maximum Reliability.
- 3 Doubly Focused MLC Systems
- 180 MLC Leaves. 60 per Head
- Best-in-class MLC for Reduced Penumbra & Interleaf Leakage
Hybrid Technologies - Imaging and Therapy

- Linac/MR
Hybrid Technologies - Imaging and Therapy

- Linac/MR
Hybrid Technologies- Anatomy and Function

- PET/CT
- PET/MR
• Other advances

Autocontouring

Adaptive Radiation Therapy (ART)
Computing advances

Computer hardware (Moore’s “law”):
- Size ↓, Density ↑ (Doubling time < 2y)
- Processor Speed ↑

Software:
- Parallel processing
- Optimization
- Processing capability ↑↑↑
• Real-time adaptive RT
  • 4-D
  • Real-time replanning
  • Dose accumulation
Advanced algorithms

• Monte Carlo planning calculations, but much faster!
• Boltzmann transport
• Radiobiological models
• Accounting for Uncertainties (Robust Optimization)
Example of Robust Optimization

From:
Moe Siddiqui
April 08, 2017
RaySearch Labs
http://pubs.medicaldosimetry.org/pub/e5a
d0d52-782b-cb6e-2763-e6a918540f5c

Big difference
Little difference

End of PTV?
Adaptive technologies

• Image warping
• Daily-re-optimization
• Daily dose accumulation
• Real-time tracking of tumor markers
• Real-time tracking and correction of MLC apertures
More Adaptation ... example

- Tissue voxels move/change from day to day

Schaly et al, PMB 49: 791-805, 2004
Deformable Image Registration
Thin-Plate Spline Image Warping

Source
Target

Courtesy: Jeff Kempe
Deformable Image Registration
Thin-Plate Spline Image Warping

Result
Target

Courtesy: Jeff Kempe
Warping Example: 6-Field Prostate

Planned

Treatment fraction 1

Warped fraction 1

Difference: warped – planned

Note rectal distention … pushes prostate up

Schaly et al, PMB 49: 791-805, 2004
Will image guidance & dose warping improve treatment outcome?

Image-guided adaptive radiation therapy (IGART): dose escalation considerations for localized cancer.

Best dose escalation strategy: Combine margin reduction (low NTCP) with daily IGRT technique (high TCP) to localize the daily moving/deforming target volume.

Song et al: Med Phys 32: 2193-203, 2005
IGRT Impact on Clinical Outcomes

Rectum: if distended @ planning ...
But not @ treatment ...
Prostate moves down out of high dose volume

Rectal distension not a predictor of urological toxicity ... due to IGRT

de Crevoisier, IJROBP, 62, 965, 2005
Kupelian, IJROBP (70), 1146, 2008

From Dr Jacob (Jake) Van Dyk
Technology advantages

- More efficient
  - VMAT, TomoTherapy, Halcyon

Example: Installation, commissioning, training
Technology advantages

• More efficient
  • IMAT, TomoTherapy, Halcyon

Example: Patient throughput

![Bar chart showing machine throughput](chart.png)

- **HALCYON**: 6 pts/hr
- **Line 3**: 45 Patients
- **Line 2**: 47 Patients
- **Line 1**: 46 Patients

3.5 pts/hr

Courtesy
T.F. Atwood, UCSF
Sept 2018
Trends Over the Next 10 Years

- More particles
  - Protons, carbon ions, ...
- Proton therapy
  - 92 operational (Feb 2019)
  - 45 under construction (Jan 2019)
    - Source Physics World, 25 Feb 2019
- Carbon ion therapy
  - ~11 carbon ion facilities (2017)
    - 6 in Japan

![Proton Therapy Facilities Trend](image)

Figure courtesy Thomas Bortfeld ... source: PTCOG
“Conservative Estimate”

- 10% of the patients who require radiation would benefit from proton therapy
  - From Thomas Bortfeld, MGH (2018)

- “… 10-20% of patients receiving radiotherapy might benefit from charged particle beams.”
  - From Jones & Burnet, BMJ 330: 979-980; 2005
More Compact ... Shrinking Proton Accelerators

Harvard (700 tons)

IBA/Sumitomo (220 tons)

US FDA Cleared Proton Therapy Systems

Varian/Accel (90 tons)

Mevion Medical Systems (<20 tons)

Courtesy: Mevion
Slide courtesy Thomas Bortfeld
Trends Over the Next 10 Years

- More hypofractionation (higher doses/fraction, SBRT)
- Breast cancer

Timeline of UK Breast RT Trials

<table>
<thead>
<tr>
<th>Trial</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
<th>Week 5</th>
<th>Total dose</th>
<th>Fractionation</th>
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<tbody>
<tr>
<td>Standard fractionation</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>50 Gy</td>
<td>2 Gy x 25</td>
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<tr>
<td>RMH/GOC</td>
<td>39 Gy</td>
<td>42.9 Gy</td>
<td>3 Gy x 13</td>
<td>3.3 Gy x 13</td>
<td></td>
<td></td>
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<tr>
<td>START A</td>
<td>39 Gy</td>
<td>41.6 Gy</td>
<td>3 Gy x 13</td>
<td>3.3 Gy x 13</td>
<td></td>
<td></td>
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<tr>
<td>START B</td>
<td>40 Gy</td>
<td></td>
<td>2.67 Gy x 15</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Canadian</td>
<td>42.5 Gy</td>
<td></td>
<td>2.66 Gy x 16</td>
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</tr>
<tr>
<td>UK FAST</td>
<td>28.5 Gy</td>
<td>30 Gy</td>
<td>5.7 Gy x 6</td>
<td>6 Gy x 5</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>FAST-Forward</td>
<td>26 Gy</td>
<td>27 Gy</td>
<td>5.2 Gy x 5</td>
<td>5.4 Gy x 5</td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

From Dr Jacob (Jake) Van Dyk

Yarnold BJR 92: 20170849; 2019

Fisher JCO 32:2894-2901; 2014
Brachytherapy

LDR

HDR

Figure 1h. Model 6711. [Reprinted from Haines, B. H., R. E. Wallace, and J. M. Haveri, “Comparison of I-125 sources used for permanent interstitial implants,” Med Phys 28:671–682. © 2001, with permission from AAPM.]


Palladium-103
e-Brachytherapy
Professional Communication

- Radiation Oncologists and Radiation Therapists
- Radiologists
- Interventional Radiologists (Cardiology, ENT, Gynecologists)
- Surgeons (Breast, Gynecology, H&N, s)
- Neurosurgeons
- Administration
- Engineers
- Computer Scientists
Thank you for listening!