Developments in Directional Brachytherapy

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Disclosure

• Research collaboration with Elekta Brachytherapy
Cervical Cancer

After long dormancy, there is a wonderful renaissance of clinical and technological innovations spurring in cervical cancer brachytherapy, motivated by use of 3D imaging, especially the MRI (and US, CT, PET)
DCE-MRI, DWI, FDG-PET for GTV$_B$

Fig. 2. Axial T2w MR and functional images of a patient with stage IIA cervical cancer at the time of brachytherapy. Both observers modified their T2w-derived GTV$_B$ based on clearer demarcation of the left lateral extent of the tumor via restricted diffusion and early DCE-MRI enhancement. Observer 1 also modified the HRCTV to incorporate the left lateral extent of GTV$_B$ that was not appreciated on T2w MR.

Han et al., Radiother Oncol 2016;120:519-525.
**Cervical Cancer**

<table>
<thead>
<tr>
<th>CTV</th>
<th>Conventional BT</th>
<th>IGBT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Imaging method</td>
<td>2D (X-ray)</td>
<td>3D (CT/MRI)</td>
</tr>
<tr>
<td>Size</td>
<td>Same</td>
<td>Different&lt;sup&gt;a,b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Invasion (shape)</td>
<td>Circle (cylinder)</td>
<td>Biased invasion&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Position</td>
<td>Same</td>
<td>Different&lt;sup&gt;d&lt;/sup&gt; (endophytic-/exophytic growth pattern)</td>
</tr>
<tr>
<td>OARs consideration</td>
<td>No</td>
<td>Yes&lt;sup&gt;a,b,c&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

- Pre-defined isodose shape (i.e., “pear”)
- Symmetric dose distribution, loading patterns w/ T&O, T&R, needles
- For delivering dose to an asymmetric cancers:
  - Extra needles are required, causes pain/trauma, **AND** additional physician training
- Patterns of RT for intact cervical cancer in USA; **Eifel et al., Red J 2014;89(2):249-**
  - >65% of patients get treatment in a facility that treats ≤3 eligible patients/yr
  - **Thus, difficult to maintain “needle-insertion” skills**
- Analysis of the SEER Report; **Han et al., Red J 2013;87(1):111-**
  - BT utilization rate has dropped to 58% in 2008, from 83% in 1988 (p<0.001)
  - BT use is independently associated with **significantly higher CSS and OS**
  - BT use is associated with significant resources & training!
  - Advances in technology, including ease-of-use †, could boost users?? (e.g., IMRT)
Problem & Opportunity

Potter et al., Radiother Oncol 2006;78:67-77.

Jastaniyah et al., Radiother Oncol 2016;120:404-411.
**Problem & Opportunity**

![Graph and diagrams](image)

**Fig. 2.** Local control as depending on CTV<sub>HR</sub> dose and volume according to the multivariate Cox regression model. The figure shows predicted 3-year actuarial local control as a function of CTV<sub>HR</sub> volume for three different dose levels: 75 Gy, 85 Gy and 95 Gy and for the median OTT of 49 days.

Tanderup et al., Radiother Oncol 2016;120:441-446.
The “Problem” = Geometry!
The “Opportunity”
The “Opportunity” - DMBT
What is DMBT?

• **Direction Modulated BrachyTherapy**
• **DMBT?**
  – Intensity modulation through inverse planning of *directional* $^{192}$Ir source dose profile achieved via intelligently-designed collimated shielding (*possibly* with **beam direction** & **energy dynamically controlled** by robotics) – *Sound familiar?*
  – Benefits in *cervical and rectal cancers* are demonstrated – *today*
DMBT Design

Han et al., Int J Radiat Oncol Biol Phys 2016;96(2):440-448.
DMBT Design
List of sintered heavy tungsten alloy samples in the market:

<table>
<thead>
<tr>
<th>Sample</th>
<th>W</th>
<th>Fe</th>
<th>Ni</th>
<th>Cu</th>
<th>Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>$F_{3.0}N_{1.0}$</td>
<td>90.0</td>
<td>3.0</td>
<td>7.0</td>
<td>0.0</td>
<td>MT17F$^a$</td>
</tr>
<tr>
<td>$F_{1.5}N_{1.5}$</td>
<td>95.0</td>
<td>1.5</td>
<td>3.5</td>
<td>0.0</td>
<td>MT18F$^a$</td>
</tr>
<tr>
<td>$F_{1.0}N_{1.5}$</td>
<td>97.0</td>
<td>0.9</td>
<td>2.1</td>
<td>0.0</td>
<td>HE305$^b$</td>
</tr>
<tr>
<td>$F_{0.0}N_{1.0}$</td>
<td>90.0</td>
<td>0.0</td>
<td>6.0</td>
<td>4.0</td>
<td>MT18$^a$</td>
</tr>
<tr>
<td>$F_{0.0}N_{1.0}$</td>
<td>95.0</td>
<td>0.0</td>
<td>5.0</td>
<td>1.0</td>
<td>HA195$^b$</td>
</tr>
</tbody>
</table>

- Density = 18.0 g/cm³ (high)
- W is (weakly) paramagnetic
- Ni is (weakly) ferromagnetic
- Fe is (strongly) ferromagnetic

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**Table 1. Susceptibilities of water, tissue, and selected materials [25,44,49,68]**

<table>
<thead>
<tr>
<th>Material</th>
<th>Density (g/cm³)</th>
<th>Susceptibility (ppm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gold</td>
<td>19.3</td>
<td>−34</td>
</tr>
<tr>
<td>PEEK</td>
<td>1.3</td>
<td>−9.33</td>
</tr>
<tr>
<td>Water (37°)</td>
<td>0.933</td>
<td>−9.05</td>
</tr>
<tr>
<td>Human tissues</td>
<td>−0.92–1.05</td>
<td>−(11.0 to −7.0)</td>
</tr>
<tr>
<td>Air (NTP)</td>
<td>$1.29 \times 10^{-3}$</td>
<td>0.36</td>
</tr>
<tr>
<td>Aluminum</td>
<td>2.7</td>
<td>20.7–20.9</td>
</tr>
<tr>
<td><strong>Tungsten</strong></td>
<td>19.3</td>
<td>77.2–80</td>
</tr>
<tr>
<td>Titanium</td>
<td>4.54</td>
<td>182</td>
</tr>
<tr>
<td>Stainless steel</td>
<td>8.0</td>
<td>3520–6700</td>
</tr>
</tbody>
</table>

*PEEK – polyether ether ketone, NTP – normal temperature [20°C] and pressure [101.325 kPa]*


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**Shield Selection**

1.5T MRI

Soliman et al., Radiother Oncol 2016;120(3):500-506.
3T MRI

Elzibak et al., 2017 (in preparation).
Ultrasound-Guided Insertion

Elzibak et al., 2017 (in preparation).
T&O vs DMBT

On average, $D_{2cm^3}$ reductions for 75 plans from UCSD:
- **Bladder** $8.5\% \pm 28.7\%$
- **Rectum** $21.1\% \pm 27.2\%$

Best single-plan reductions:
- **Bladder** $40.8\%$
- **Rectum** $40.1\%$

Han et al., Int J Radiat Oncol Biol Phys 2014;89:666-673.
T&R+Needles vs DMBT

Han et al., Int J Radiat Oncol Biol Phys 2016;96(2):440-448.
Multi-Source Afterloader?

Multi-Source Afterloader?

TG43 → TG186 (MBDCA)

- TG43 – *Homogeneous water medium*
- TG 186 – *Came out in 2012*

**Model Based Dose Calculation Algorithms**

1. Monte Carlo
2. Collapsed Cone Convolution (ACE®)
3. Grid Based Boltzmann Solver (Acuros BV®)

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**Report of the Task Group 186 on model-based dose calculation methods in brachytherapy beyond the TG-43 formalism: Current status and recommendations for clinical implementation**

Luo Beaulieu

Département de Radio-Oncologie et Centre de Recherche en Cancérologie de l'Université Laval, Centre hospitalier universitaire de Québec, Québec, Québec, G1V 2J6, Canada and Département de Physique, de Génie Physique et d'Optique, Université Laval, Québec, Québec G1V 2J6, Canada.

3D Virtual Model

DMBT Tandem – Oncentra Brachy® 3D Model
3D Virtual Model

DMBT Tandem – Oncentra Brachy® 3D Model

Han et al., Int J Radiat Oncol Biol Phys 2016;96(2):440-448.
Dosimetric Verification w/ Film
Dosimetric Verification w/ Film

Open Conventional Tandem – Single Dwell

DMBT Tandem – Single Dwell
State-of-the-Art Applicators

What is consistently **not** changing?

Venezia™ (Elekta Brachytherapy)

Rectal Cancer

• Recurrences after surgery occurs mostly **within the tumor bed**; therefore, eradicating local disease is critical [Mendenhall et al., IJROBP 1983;9:97-]
  – HDR can be given as an **additional boost** to standard CRT for subpopulation of resistant tumors

• McGill phase II trial [Vuong et al., *Semin Colon Rectal Surg* 2010;21:115-119]
  – Neoadjuvant HDR **only** (no CRT); 650x4, 285 patients treated (mostly T3, Nx)
  – 27% pCR compared with RT/CT regimens...
  – Grade 3 acute proctitis occurred in only 1% vs 25-30% in CRT
A highly significant dose-response relationship is found (p<0.002). For complete response, $D_{50}=92$ Gy EQD2.
## Treatment Options

<table>
<thead>
<tr>
<th>Treatment Techniques</th>
<th>Dose Conformality?</th>
<th>Non-Invasive?</th>
</tr>
</thead>
<tbody>
<tr>
<td>External Beam Radiation Therapy (EBRT)</td>
<td>✓</td>
<td>✓</td>
</tr>
<tr>
<td>Single-Channel Intracavitary HDR</td>
<td>✓✓</td>
<td>✓✓</td>
</tr>
<tr>
<td>Interstitial LDR/HDR</td>
<td>✓✓✓✓</td>
<td>✓</td>
</tr>
<tr>
<td>Segmented Shielding HDR</td>
<td>✓✓✓✓</td>
<td>✓✓</td>
</tr>
<tr>
<td>Intra-Operative Brachytherapy</td>
<td>✓✓✓✓✓</td>
<td>✓</td>
</tr>
<tr>
<td>Superficial X-ray (Papillon Technique)</td>
<td>✓✓✓✓</td>
<td>✓✓</td>
</tr>
<tr>
<td>CAPRI Applicator (13 Channels) HDR</td>
<td>✓✓✓✓</td>
<td>✓✓</td>
</tr>
<tr>
<td>Intracavitary Mold Applicator (8 Channels) HDR</td>
<td>✓✓✓✓</td>
<td>✓✓</td>
</tr>
<tr>
<td>Direction Modulated Brachytherapy (DMBT) HDR</td>
<td>✓✓✓✓✓</td>
<td>✓✓</td>
</tr>
</tbody>
</table>
Intracavitary Mold Applicator (ICMA)

Devic et al., JACMP 2005;6(2):44-49.
Why DMBT?

Lambrecht et al., Radiother Oncol 2010;96:339-346.
DMBT Design

- Tungsten=18.5g/cc; 1.9-cm diameter & 4.5-cm length
- This results in ~2.5% transmission in the shielded-end

- Use voxel sizes of 2.5mm² within 5cm, and 5mm² outside
- 80 million particle histories are used to insure variance of ≤ 5% everywhere
  - This takes about, using 8 CPUs, ~2.5 days
- Geometric symmetry is exploited for speeding up calculations
- Measure [MeV/g], per voxel, per history
My Vision
In-Room MR Compatible Design
The Future of Brachytherapy Suites

Utrecht Medical Centre, The Netherlands

Sunnybrook Hospital, Toronto, Canada (Sept 23, 2016)
36 Clinical Plans from JGH, Montreal

(ICMA) VS (DMBT)
36 Clinical Plans from JGH, Montreal

- Non-surgery cases
- Rx = 10Gy
- Total dwell times:
  - ICMA = 5.21±0.95 min.
  - DMBT = 15.94±3.97 min.

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Appelt et al., 2013

Emerging Technologies in Brachytherapy

- William Y Song, Kari Tanderup, Bradley Pieters - Editors
- 31 Chapters
- 100+ leading experts contributed from academia & industry
- Release Date: May 2017
Questions?