Real-time adaptation: Rationale, system overview and clinical experience

Prof Paul Keall
Director, ACRF Image X Institute
Disclosures

Publicly available at https://image-x.sydney.edu.au/home/disclosures/

- **Patents:** Several awarded patents and pending applications
- **Licenses:** Leo, Opus, Standard Imaging, Varian
- **Industry research grants:** Siemens (PI), Varian (CI)
- **New entities:** Cancer Research Innovations (Partner), Leo (Founder), Opus (Founder), SeeTreat (Founder)
Real-time adaptation: **Rationale** | system overview and clinical experience
5-year cancer survival is increasing with time

- **1930**: 23%
- **1980**: 48%
- **2020**: 69%

Cancer Australia
1 in 2 people with cancer need radiation therapy

Barton et al. Rad Onc 2014
Clinical benefit of improved IGRT

Symptomatic Pneumonitis vs. Mean Lung Dose

- MSKCC (10/78)
- Duke (39/201)
- Michigan-1 (17/109)
- MD Anderson (~49?/223)
- NKI (17/106)
- WU (52/219)
- Michigan-2 (9/42)
- Heidelberg (10/66)
- Milan (7/55)
- Gyeonggi (12/76)
- logistic fit
- 68% CI

Marks IJROBP 2010
Tumor motion varies from breath to breath and day to day.
Daily IGRT improves outcomes vs weekly IGRT

- 470 pts randomized between daily and weekly IGRT
- Biochemical progression-free interval significantly longer HR=0.45
- Late grade ≥1 rectal toxicity significantly lower HR=0.71
- Daily IGRT significantly improves local control and reduces rectal toxicity
Continuous Monitoring and Intrafraction Target Position Correction During Treatment Improves Target Coverage for Patients Undergoing SBRT Prostate Therapy

D. Michael Lovelock, PhD, * Alessandra P. Messineo, BS, * Brett W. Cox, MD, † Marisa A. Kollmeier, MD, * and Michael J. Zelefsky, MD *

Results: After the initial setup, 1.7 interventions per fraction were required, with a concomitant increase in time for dose delivery of approximately 65 seconds. Small systematic drifts in prostate position in the posterior and inferior directions were observed in the study patients. Without CMI, intrafractional motion would have resulted in approximately 10% of patients having a delivered dose that did not meet our clinical coverage requirement, that is, a PTV D95 of >90%. The posterior PTV margin required for 95% of the dose to be delivered with the target positioned within the PTV was computed as a function of time. The margin necessary was found to increase by 2 mm every 5 minutes, starting from the time of the imaging procedure.
Conclusion: This study shows that MLC tracking improves the consistency between the planned and delivered doses compared with the modeled doses without MLC tracking. The implications of this finding are potentially improved patient outcomes, as well as more reliable dose-volume data for radiobiological parameter determination. © 2015 Elsevier Inc. All rights reserved.
Real-time adaptive rationale

Planning

Delivery

Average 40% reduction in PTV

4D CT motion

Courtesy Jeremy Booth

Real-time

Standard
Real-time adaptation: Rationale, **system overview** and clinical experience
Real-time adaptive radiation therapy components

1. Detect motion
2. Correct for reaction time
3. Compute and actuate beam/target alignment

Treatment unit
Treatment beam
Moving Target (tumor)

Dieterich Med Phys 2008
Real-time tracking: The Pioneers in 1998

- Real-time fluoro imaging of gold markers with gating
- Markers inserted into/near the tumour in 10 patients
- No complications or local relapses within a 6 month follow-up
- “A real-time tumour-tracking system can improve the accuracy of radiotherapy and reduce the volume of normal tissue irradiated”
- 2014 applied technology to proton therapy
Real-time adaptive radiation therapy systems

**Robotic linac**
- CyberKnife
- Synchrony
- Clinical 2004

**Gimbaled linac**
- Vero/
- Mitsubishi
- Clinical 2011

**MLC**
- Clinical 2013
- Widely available
- Smallest, lightest
- 6 DoF
- Deformation

**Robotic couch**
- Clinical 20??
- Widely available
Real-time adaptive radiation therapy

Tipping point

Introduction of real-time 3D IGRT systems

Integration with standard linacs
What tools are available on standard linacs today?

Find the target
kV and MV X-ray imaging systems
Respiratory monitoring
Hit the target
Multileaf collimator
MLC tracking real-time adaptive therapy options

Conformal

IMRT
MLC tracking real-time adaptive therapy future options

Rotation + Translation

Deformation
MLC tracking real-time adaptive therapy future options

Single Deformation

System Deformation

Conformal RT

IMRT
Real-time adaptation: Rationale, system overview and clinical experience
Long-term Outcomes of Stereotactic Body Radiotherapy for Low-Risk and Intermediate-Risk Prostate Cancer

Amar U. Kishan, MD; Audrey Dang, MD; Alan J. Katz, MD, JD; Constantine A. Mantz, MD; Sean P. Collins, MD, PhD; Nima Aghdam, MD; Fang-I Chu, PhD; Irving D. Kaplan, MD; Limor Appelbaum, MD; Donald B. Fuller, MD; Robert M. Meier, MD; D. Andrew Loblaw, MD; Patrick Cheung, MD; Huong T. Pham, MD; Narek Shaverdian, MD; Naomi Jiang, MD; Ye Yuan, MD, PhD; Hilary Bagshaw, MD; Nicolas Pronas, MD, PhD; Mark K. Buyyounouski, MD, MS; Daniel E. Spratt, MD; Patrick W. Linson, MD; Robert L. Hong, MD; Nicholas G. Nickols, MD, PhD; Michael L. Steinberg, MD; Patrick A. Kupelian, MD; Christopher R. King, MD, PhD

A

Biochemical recurrence

Cumulative Incidence

\( P < .001 \)

No. at risk

<table>
<thead>
<tr>
<th></th>
<th>Low</th>
<th>Fav-Int</th>
<th>Unfav-Int</th>
</tr>
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<tbody>
<tr>
<td>00</td>
<td>1185</td>
<td>1116</td>
<td>1010</td>
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JAMA Network Open. 2019;2(2):e188006
# Long-term Outcomes of Stereotactic Body Radiotherapy for Low-Risk and Intermediate-Risk Prostate Cancer

<table>
<thead>
<tr>
<th>Toxic Event</th>
<th>Crude Incidence, No. (%)</th>
<th>Cumulative Incidence Estimate (95% CI)</th>
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<tbody>
<tr>
<td></td>
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<td>5 y</td>
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<tr>
<td><strong>Grade 2</strong></td>
<td></td>
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</tr>
<tr>
<td>Acute GU</td>
<td>153 (9.0)</td>
<td>NA</td>
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<tr>
<td>Acute GI</td>
<td>56 (3.3)</td>
<td>NA</td>
</tr>
<tr>
<td>Late GU</td>
<td>163 (9.6)</td>
<td>11.2 (9.7-12.8)</td>
</tr>
<tr>
<td>Late GI</td>
<td>67 (3.9)</td>
<td>4.5 (3.6-5.6)</td>
</tr>
<tr>
<td><strong>Grade ≥3</strong></td>
<td></td>
<td></td>
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<tr>
<td>Acute GU</td>
<td>13 (0.6)</td>
<td>NA</td>
</tr>
<tr>
<td>Acute GI</td>
<td>2 (0.09)</td>
<td>NA</td>
</tr>
<tr>
<td>Late GU</td>
<td>46 (2.1)</td>
<td>1.8 (1.3-2.5)</td>
</tr>
<tr>
<td>Late GI</td>
<td>7 (0.3)</td>
<td>0.4 (0.2-0.8)</td>
</tr>
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</table>
Dose with and without MLC tracking
The TROG 15.01 Stereotactic Prostate Ablative Radiotherapy With KIM (SPARK) Trial

Prostate SABR + KIM
### SPARK: Primary outcome – dosimetric improvement

<table>
<thead>
<tr>
<th></th>
<th>Plan</th>
<th>Treated with KIM</th>
<th>Treated without KIM</th>
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</thead>
<tbody>
<tr>
<td><strong>Largest prostate</strong></td>
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<tr>
<td>benefit with KIM</td>
<td></td>
<td><strong>Patient dose = plan</strong></td>
<td><strong>Bladder hit</strong></td>
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<tr>
<td></td>
<td></td>
<td><strong>Prostate missed</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>Rectum</strong></td>
<td><strong>Patient dose = plan</strong></td>
<td><strong>Rectum hit</strong></td>
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<tr>
<td></td>
<td><strong>Bladder</strong></td>
<td><strong>Prostate missed</strong></td>
<td></td>
</tr>
</tbody>
</table>

Keall IJROBP 2020
SPARK: Primary outcome – dosimetric improvement

Prostate PTV D95%

- With KIM real-time tracking
- Without real-time tracking

Difference from plan (%)
SPARK: Primary outcome – dosimetric improvement

Rectum V30Gy

With KIM real-time tracking
Without real-time tracking

Keall IJROBP 2020
Real-time adaptation: Rationale, system overview and clinical experience

Summary
Summary: Real-time adaptive radiation therapy …

… has fast-growing clinical uptake

… has compelling clinical drivers and clinical results

… has demonstrated the combined benefit of increased accuracy and increased efficiency