The Future of SBRT

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Disclosures

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Accuray
BrainLab
Siemens Medical
Varian Medical
Viewray Inc.
VisionTree
“We’ve found a mass. The good news is we have weapons of mass destruction.”
SBRT Context: Advances in RT

- Diagnostics / Prognostics
- Planning:
  - Target identification / Imaging
  - Knowledge based planning / Automated planning
- Delivery:
  - Dose conformality / compactness: 3DRT, IMRT, Brachy, Protons
  - Guidance: Stereo / Surface / Imaging / Electromagnetic
  - Adaptation: Dose monitoring and adaptation
  - Combination with Drugs
- Safety:
  - Standardization / Automation / Redundance / Monitoring
  - Training, Retraining, and Testing
  - Quality QA / Accreditation
SBRT Context: Future practice of RT

- Efficacy
- Dose Equivalence;
- Biologic dose-escalation:
- Toxicity (late)
- Can we rely on BEDs?
- Economics: Cost versus Revenue
- Patient convenience / Provider convenience
- Fear
- Ignorance
- Blind faith
- Zeal
CONVENTIONAL FRACTIONATION  
versus  
HYPOFRACTIONATION  
versus  
STEREOTACTIC BODY RADIOSURGERY (SBRT) or SABR

<table>
<thead>
<tr>
<th>SBRT</th>
<th>Hypofractionation</th>
<th>Conventional</th>
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<tbody>
<tr>
<td></td>
<td>Number of fractions</td>
<td>~35 45</td>
</tr>
<tr>
<td>1</td>
<td>5</td>
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<tr>
<td></td>
<td>Fraction Size</td>
<td>1.8-2.0 Gy</td>
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<td>&gt;7 Gy</td>
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<td></td>
<td>Total Dose</td>
<td>~75-85 Gy</td>
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<td>~35-50 Gy</td>
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<td>~50-75 Gy</td>
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<tr>
<td></td>
<td>Biological Rationale</td>
<td>Normal tissue sparing</td>
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<tr>
<td>Ablative??</td>
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</table>
CONVENTIONAL FRACTIONATION
versus
HYPOFRACTIONATION
versus
STEREOTACTIC BODY RADIOSURGERY (SBRT) or SABR

What is considered SBRT?

6-7 fractions image-guided IMRT?

5 fractions, 5 Gy per fx, large field image-guided IMRT?
Future SBRT: New Knowledge

• Biology of (very) large fractions:  
  Understanding of underlying mechanisms  
  Vasculature, Immune response, DNA damage, etc…

• Technical delivery
  Perfection of the individual fraction compact delivery:  
  Imaging, Planning, On-line and off-line assessments, Adaptation  
  Safety considerations  
  Standardization / Automation / (Real Time) Monitoring

• Clinical impact of large fractions:  
  Clinical Trials  
  Registries  
  Case Reviews
Future SBRT

Technical delivery:
Perfection of the individual fraction delivery

- Compactness
- Localization
- Functional information
- Adaptation

Delivery machine

Imaging
Future SBRT

Evolution of Dose Conformality / Compactness:
• 3DRT
• IMRT
• Brachytherapy
• Protons / IMPT
• $\pi$ $4\pi$
Future SBRT: 4Pi Delivery

Simulation
Future SBRT: Dose Conformality / Compactness
4Pi Delivery

Fixed Field  VMAT  4 pi

Highly compact RT!
Future SBRT: Dose Conformality / Compactness
4Pi Delivery

Future SBRT

**Technical delivery:**  
Perfection of the individual fraction delivery

- Compactness
- Localization
- Functional information
- Adaptation

Imaging
Future SBRT

Technical delivery:
Perfection of the individual fraction delivery

- Compactness
- Localization
- Functional information
- Adaptation

MRI
MRI - 4D Imaging (Planar)

- 2-20 fps, low latency

ViewRay, Courtesy J. Michalski, Wash U. 2014
Pilot (Navigation) Scans
20 sec Pilot Scan
Track Tissues & Control Therapy
MR guided – RT

- 59 yo M with locally advanced pancreatic cancer, s/p FOLFIRINOX x 4 cycles → stable disease
- MR based localization on imaging study
Track Tissues & Control Therapy
MR guided – RT

ViewRay, Courtesy J. Michalski, Wash U. 2014
MR guided – RT

ViewRay, Courtesy J. Michalski, Wash U. 2014
MR guided – RT

ViewRay, Courtesy J. Michalski, Wash U. 2014
Automatically Identify & Locate Tissues
Predict Dose On Demand
Optimize On Demand
Physician’s Workstation: Overall review and supervision
RT Delivery: Safety / Monitoring

- Treatment room workflows mirror operating rooms
  1. Slower rhythm; checklists, timeouts, etc…
  2. Increase automation
  3. Patient identification
  4. Treatment site recognition
  5. Treatment site monitoring
  6. Display of patient CT (internal anatomy)
  7. Collision monitoring
  8. Recording of treatment sessions
3D Virtualization of Treatment Room

• New generation of 3D cameras
  – Provide color images + 3D surface
  – Multiple cameras linked together (positioned at different locations in room) camera generate real-time digital model of treatment room
Positioning / Monitoring Example
Future SBRT: New Knowledge

- **Biology of (very) large fractions:**
  - Understanding of underlying mechanisms
  - Vasculature, Immune response, DNA damage, etc…

- **Technical delivery**
  - Perfection of the individual fraction compact delivery:
    - Imaging, Planning, On-line and off-line assessments, Adaptation
    - Safety considerations
    - Standardization / Automation / (Real Time) Monitoring

- **Clinical impact of large fractions:**
  - Clinical Trials
  - Registries
  - Case Reviews
Hypofractionated RT:

Current Clinical Use
Current Use of Hypofractionation

Hypofractionation = Small targets
- CNS sites (SRS, FSRT, SBRT)
- Lung cancers (Early stages)
- Partial breast RT
- Abdominal sites (Liver, Pancreas, Kidney)
- Localized prostate cancers
- Spine SBRT / Oligometastatic cites
- HDR: GYN

Where is hypofractionation not used?

Conventional fractionation = Large targets
- Large CNS targets: Gliomas, meningiomas, whole brain
- Head and Neck cancers
- Most breast cancers
- Most advanced lung cancers
- Large Pelvic targets (GI or GYN)
Future Use of Hypofractionation

Breaking down large targets?
Smaller targets within larger targets?
• Large CNS targets: e.g. GBM stem cell niches
• Head and Neck cancers:
  • Dose pain gross disease
  • Targeted nodal RT only
• Breast cancers: Partial breast / targeted nodal RT
• Advanced lung cancers:
  • SBRT to residual disease
  • Hypofractionation for gross dz

Novel Indications
• Oligometastatic disease / Drug resistant areas
• SBRT as immune response modulator / combination with other immune modulators: abscopal effects
• CNS benign conditions
• Bladder Ca / Rectal Ca
CNS

Hypofractionation / SRS
CNS - SRS

Current indications:
• Trigeminal Nerve RT
• Metastatic Disease: <6 lesions
• Spine SBRT

New indications (?):
• Recurrent GBMs
• Dose painting in primary GBM RT (mpMRI)
• Back pain: Dorsal nerve root zones
• Parkinson’s / Tremors
• OCD
• Excessive flushing
• Excessive sweating
Lung SBRT
Best example of SBRT success: Early Stage Lung Cancer

Elements:
1. Small target: No elective nodal irradiation
2. Ablative Doses
3. Image Guidance: Motion Management

Extensive experience in Japan
US experience (Timmerman et al)
Multiple institutional experiences
Current RTOG trials

Will probably become the standard of care in the era of Lung cancer CT screening.
Advanced Lung Cancer
Hypofractionation/SBRT
RADIATION THERAPY ONCOLOGY GROUP
American College of Radiology Imaging Network

RTOG 1106/ACRIN 6697

RANDOMIZED PHASE II TRIAL OF INDIVIDUALIZED ADAPTIVE RADIOTHERAPY USING DURING-TREATMENT FDG-PET/CT AND MODERN TECHNOLOGY IN LOCALLY ADVANCED NON-SMALL CELL LUNG CANCER (NSCLC)

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fengkong@umich.edu
N=138

**Stratify**

| MLD | 1. >14 Gy  
<table>
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<tr>
<th></th>
<th>2. ≤ 14 Gy</th>
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**PreGTV**

<table>
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<tr>
<th>≥200 cc</th>
<th>&lt;200 cc</th>
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**Histology**

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<th>Squamous</th>
<th>Non-Squamous</th>
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**Randomize**

**Arm 1: Concurrent Chemoradiotherapy**

RT to 50 Gy in 25 fractions in 5 weeks

4. Carboplatin and paclitaxel weekly

**Arm 2: Concurrent Chemoradiotherapy**

RT to 47.5-49.5 Gy in 17-22 fractions in 3-4 weeks

4. Carboplatin and paclitaxel weekly

**ALL PATIENTS: During-RT FDG-PET/CT Scan**

**Arm 1:** At fraction 20-23 (weeks 4-4.5)

**Arm 2:** At fraction ~14-21 (weeks 3-4)

**Arm 1:** Continuation of radiotherapy, not based on during-RT FDG-PET/CT scan with carboplatin and paclitaxel for a total of 6 weekly cycles

10 Gy in 5 fractions; overall total of 60 Gy in 30 daily fractions in 6 weeks

**Arm 2:** Adaptive radiotherapy, based on during-RT FDG-PET/CT scan with carboplatin and paclitaxel for a total of 6 weekly cycles

34-37.8 Gy in 8-13 fractions; overall total of up to 85.5 Gy in 30 daily fractions in 6 weeks

Individualized to MLD 20 Gy

**ALL PATIENTS: Consolidative Chemotherapy**

**Arms 1 and 2:** Carboplatin and paclitaxel q21 days X 3

IGRT is mandatory for this study (see Section 5.1).
## Personalized RT prescriptions

### Table 6.1.2a: Individualized Doses and Fraction Sizes for Arm 2 (Based on 74 Gy Screening Plan)

<table>
<thead>
<tr>
<th></th>
<th>(1) Mean Lung Dose for the screening plan (74 Gy PTV dose)</th>
<th>(2) Initial Dose per fx (Gy)</th>
<th>(3) # Fractions for ~50 Gy EQD2 Tumor Dose</th>
<th>(4) Physical Dose at this time point (Gy)</th>
<th>(5) Minimum # Fractions Before 2nd PET scan</th>
<th>(6) Adaptive Phase Largest allowed Boost Dose per fx (Gy)</th>
<th>(7) Adaptive Phase # of Fractions</th>
<th>(8) Adaptive Phase Largest allowed Physical Boost Dose (Gy)</th>
<th>(9) Largest allowed Total Physical Prescription Dose (Gy)</th>
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<tbody>
<tr>
<td>a)</td>
<td>&lt;13.5</td>
<td>2.85</td>
<td>17</td>
<td>48.45</td>
<td>14</td>
<td>2.85</td>
<td>13</td>
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<tr>
<td>b)</td>
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<td>2.85</td>
<td>17</td>
<td>48.45</td>
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<td>37.05</td>
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<td>c)</td>
<td>13.9</td>
<td>2.80</td>
<td>17</td>
<td>47.6</td>
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<td>2.9</td>
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<td>18</td>
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<td>18</td>
<td>3.85</td>
<td>9</td>
<td>34.65</td>
<td>84.0</td>
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Keep total 30 fractions:  
Fraction size range: 2.35 to 3.85 Gy
SBRT for residual disease after conventional RT

Clinical Investigation: Thoracic Cancer

Stereotactic Body Radiation Therapy Can Be Used Safely to Boost Residual Disease in Locally Advanced Non-Small Cell Lung Cancer: A Prospective Study

Jonathan Feddock, MD,* Susanne M. Arnold, MD,⁎† Brent J. Shelton, PhD,‡ Partha Sinha, MD,§ Gary Conrad, MD,§ Li Chen, PhD,‡ John Rinehart, MD,† and Ronald C. McGarry, MD, PhD*

Departments of *Radiation Medicine, †Medical Oncology, ‡Biostatistics, and §Radiology, University of Kentucky, Lexington, Kentucky

Received Sep 20, 2012, and in revised form Nov 6, 2012. Accepted for publication Nov 7, 2012
SBRT Boost to Residual Disease
Feddock J et al. IJROBP, 85, 1325-1331, 2013

PET-CT one month following conventional CRT (60 Gy)
An additional 20 Gy in 2 SBRT fractions in 1 week.
Central lesions: 6.5 Gy x 3 = 19.5 Gy
SBRT Boost to Residual Disease

Feddock J et al. IJROBP, 85, 1325-1331, 2013

62 patients screened. 35 eligible to boost.
Exclusion reasons:
- 31% persistent nodal disease
- 31% systemic progression
- 15% no residual local disease

Median follow-up: 13 mos

- Local control: 83%
- No Gr 4-5 Rad Pneumonitis.
- Acute grade 3 RP: 4 patients (12%)
- Late and persistent grade 3 RP: 1 patient (3%)

“No dosimetric parameters evaluated for SBRT protocol treatment, including MLD, V2.5, V5, V10, and V20, correlated with RP development”
Image-Guided Hypofractionated Radiotherapy with Stereotactic Boost and Chemotherapy for Inoperable Stage II-III Non-Small Cell Lung Cancer Phase I/II Protocol (UCLA) - PI: Percy Lee

**PET-CT, 4D CT Simulation**

4 Gy x 10 fractions Involved Field RT

**PET-CT, 4D CT Re-Simulation / Adaptation**

(at the 8th or 9th fraction)

Dose-escalation cohorts: SBRT Boosts

- 5 Gy x 5
  - N=15
- 6 Gy x 5
  - N=15
- 7 Gy x 5
  - N=15

**3 WEEK COURSE**
Image-Guided Hypofractionated Radiotherapy with Stereotactic Boost and Chemotherapy for Inoperable Stage II-III Non-Small Cell Lung Cancer

Prior to RT

After 40 Gy in 10 Fractions
Prostate SBRT
Prostate SBRT Doses

Dose ranges:
- $6.70 \times 5 = 33.5 \text{ Gy}$
- $7.25 \times 5 = 36.25 \text{ Gy}$
- $7.5 \times 5 = 37.5 \text{ Gy}$
- $9.0 \times 4 = 36.0 \text{ Gy}$
- $8.0 \times 5 = 40.0 \text{ Gy}$
- $9.0 \times 5 = 45.0 \text{ Gy}$
- $9.5 \times 5 = 47.5 \text{ Gy}$
- $10.0 \times 5 = 50.0 \text{ Gy}$
- $24 \times 1 = 24 \text{ Gy}$

BED
- 146 Madsen IJROBP 2007
- 168 Fuller IJROBP 2008
- 198 King RO 2013
- 248 Boike JCO 2011 / Kim ASTRO 2013
- 273
- 300
- 312 Greco, Lisbon

King IJROBP 2009
Friedland TCRT 2009
Katz BMC Urol 2010
Wiegner IJROBP 2010
Bolzicco TCRT 2010
Aluwini J Endourol 2010
Freeman RO 2010
Townsend AJCO 2011
Kang Tumori 2011
Jabbari IJROBP 2011
Mantz IJROBP 2011
Greco, Lisbon
UCLA High-Risk Prostate Ca SBRT Trial

SBRT: Not delivery platform specific.

CT/MRI planning

8 Gy x 5 (40 Gy*) to prostate PTV

5 Gy x 5 (25 Gy) to pelvic LN (optional)

SV: Full dose or 5 Gy x 5 (respecting ROI constraints)

*Minimum dose, 30-50% heterogeneous ‘Hot Shell’
Head and Neck?
UCLA Head & Neck Postop “SBRT” Trial

Postoperative Head and Neck cancers

No change in volumes

3 Dose levels:
7 Gy x 5 (35 Gy)
6 Gy x 5 (30 Gy)
5 Gy x 5 (25 Gy)
Conclusions

Fewer and larger size fractions, seem associated with better (or at least) equivalent outcomes in most cancers.

SBRT treatments are associated with increased workloads, scrutiny and safety.

The higher therapeutic ratio of currently used hypofractionated regimens is expanding indications.

Dose / fractionation schemes are still unclear and need proper outcomes documentation with appropriate clinical trials or case registries.
areas if desired. Volume adjustments would be routine as would be individualization of dose, which makes sense given the large variation of tumor size and burden in patients with head and neck cancers, and the biologic differences of individual tumors, as obvious currently in HPV+ vs HPV cases. Adjustments would allow better normal tissue sparing, particularly salivary gland sparing. DW MRI could also allow for assessment of changes within the salivary glands predicting for late effects. However, further improvement will come from identifying nodal areas that are microscopically involved. Although unimaginable today, as with lung cancer currently, elective nodal irradiation could be abandoned for head and neck cancers, replaced with more targeted nodal irradiation, thus decreasing treatment volumes and making head and neck RT a much more tolerable treatment than what it is today.

Ablation of Pancreatic Cancers or Liver Cancers

Upper abdominal targets have presented a challenge owing to relatively aggressive biology, sensitive OARs such as the small bowel, and significant motion and deformation issues. Pancreatic cancer is a particularly difficult disease to approach with RT. In localized pancreatic cancers, the efficacy of radiation therapy could be improved with larger than conventional fraction sizes. Definition of peripancreatic (eg, vascular involvement) and intrapancreatic (cancer tissue) targets would allow dose painting, with in-room MRI being used to track those targets.