EDUCATIONAL COURSE TU-A-BRB-1

Physics and Dosimetry of SBRT

Part III: Planning Case Studies
3 of the AAPM SBRT sessions

• **HOW** do we and some others do SBRT?
  – Tuesday 730 am, “Physics and Dosimetry of SBRT”, moderator M Miften, Educational Session

• **WHY** did we reach this place?
  – Tuesday 130 pm, “Establishing an SBRT Program”, moderator S Benedict, Practical Medical Physics

• **WHAT** have we accomplished so far?
Spectrum of applications of SBRT

• Intensified treatment to a primary cancer
  – Stage I lung cancer
  – Primary HCC
  – Pancreas cancer
  – Prostate cancer

• Palliation/control for challenging sites of recurrence
  – Spinal
  – Retroperitoneal
  – Previously irradiated volumes

• Adjuvant systemic cytoreductive therapy
  – “Radical” treatment for isolated liver, lung, spine, and other oligometastases
Top to Bottom: HOW do we and some others do SBRT?

- Recurrent head and neck cancer
- Early stage lung cancer
  - And lung metastases
- Pancreas cancer
- Hepatocellular cancer
  - And Liver metastases
- Spine/paraspinal lesions
- Prostate cancer
Top to Bottom: HOW do we and some others do SBRT?

- Recurrent head and neck cancer
- Early stage lung cancer
  - And lung metastases
- Pancreas cancer
- Hepatocellular cancer
  - And liver metastases
- Spine/paraspinal lesions
- Prostate cancer

Heron et al, IJROBP 2009
CPT code semantics

- SBRT term can be used for fractionated brain tumor
  SRS for the MD pro fee
    - But the delivery code is SRS
- SRS is the term used for primary OR BOOST treatment to base of skull region tumors
- SBRT describes an entire course of treatment, not a boost phase of treatment

Delivery code = SRS
MD pro fee = SRS if 1 fxn,
SBRT for 2-5 fractions
Can be boost

Delivery code = SBRT
MD pro fee = SBRT if 1-5 fxns
Complete course, not boost
Pittsburgh H&N SBRT
Rgiawe et al, AJCO 2010

• Previously established normal tissue dose limits in Phase I study
  • For Spinal cord:
    • 8 Gy in 1 fraction
    • 12 Gy in 2 fractions
  • 9 Gy for the brainstem
  • 20 Gy for the brain
  • 10 Gy for the retina, optic nerves, and chiasm
  • 6 Gy for the lens of the eye
  • 20 Gy for the carotid artery
  • 20 Gy for the esophagus and larynx.

• Immobilization via thermoplastic mask
• Treatment given every other day
Sample HN SBRT case, UCH

- 81 yo M with T3 N0 M0 SCC of the L true vocal cord. Pt with prior T1a SCC of L true vocal cord treated to 70 Gy/35 fractions in 11/2000.
- Plan: 25 Gy/5 fxns with cetuximab
- PTV (38.81cc): 94% volume gets 25 Gy
  - max=2941 cGy
  - min=1635 cGy
  - mean=2745 cGy
- GTV (12.11cc): 99.5% volume gets 25 Gy
  - max=2941 cGy
  - min=2345 cGy
  - mean=2813 cGy
- cord: 1% max=830 cGy @ approx C5-C6
  - max=1028 cGy
  - mean=413 cGy
- Esophagus: V15=0.59cc, max=2353 cGy, min=49 cGy, mean=551 cGy
- FOLLOWUP 7 mos:
  - NED on exam and PET
Top to Bottom:

**HOW** do we and some others do SBRT?

- Recurrent head and neck cancer
- **Early stage lung cancer**
  - And lung metastases
- Pancreas cancer
- Hepatocellular cancer
  - And Liver metastases
- Spine/paraspinal lesions
- Prostate cancer
The technical necessities for SBRT

• Immobilization
  – Needs to be comfortable since treatments sometimes lengthy

• Image guidance
  – Need to relocalize target prior to each treatment
  – Removes need for rigid body frame

• Breathing motion management
  – Passive
    • Margin-based
  – Active
    • Abdominal compression
    • Controlled breath-hold
    • Gated beam-on devices

cineMRI courtesy of Dr. Paul Read, Univ. of Virginia
Respiratory control for SBRT

- Abdominal compression
  - Forces shallow breathing
- Controlled breath-hold
  - Stabilizes tumor within the respiratory cycle
  - Can be device-assisted
- Tumor tracking
  - Implanted fiducials
- Gated beam-on devices
  - Treatment only given when tumor located within the beam
  - Respiratory tracing used
Quantitative analysis of abdominal pressure relative to breathing motion


Note: high compression force approx 90N, or approx 22 pounds, reduced diaphragm sup-inf motion from approx 15mm to 8 mm on average

Fig. 1. Stereotactic body radiation therapy frame showing load cell and panel mount signal conditioner.

Fig. 3. Motion of diaphragm at varying levels of abdominal compression.
4D CT simulation

*note: belt higher than for liver*
Comparison of the 2 lung SBRT chest/rib toxicity studies

Dunlap, IJROBP 2009
U Virginia & U Colorado

• 60 patients, minimum point dose 20 Gy in 3-5 fractions to chest wall
• Endpoint: severe pain (narcotics) or rib fracture
• DVHs analyzed:
  – Chest wall = all tissue (bone and soft tissue) peripheral to lung

Pettersson, Radiother Oncol 2009
Sahlgrenska U, Sweden

• 81 ribs in 26 patients, minimum point dose 21 Gy/3 fractions received
• Endpoint: rib fracture on CT
• DVHs analyzed
  – Ribs receiving >21 Gy contoured without margin for setup errors
Common finding: absolute volume predictive parameters

Dunlap et al:  
Keep absolute V30 < 30 cc

Petterssen et al:  
Keep $D_{2cc}$ as low as possible

Graphs showing:

- Risk vs. Volume above 30 Gy
- Probability of rib fracture vs. $D_{2cm^3}$ with $D_{50,2cm^3} = 49.8$ Gy and $\gamma_{50,2cm^3} = 2.05$
Solving irregular breathing: pranayama breathing
Free breathing

Pranayama breathing
Cautionary note:
Possible problems near the proximal airways

Freedom from grade 3-5 toxicity
2 responses to the IU proximal airway report
Chang et al, IJROBP 2008; 72(4) 967–971

• UT-SA experience (above)
  – n=9; dose = 3x12 Gy
  – No serious toxicity
    • Median f/u 11 mos (range, 3-42)

• MD Anderson experience
  – N = 27; dose = 4x10-12.5 Gy
  – No serious lung toxicity
    • Median f/u 17 mos (range, 6-40)
    • 1 brachial plexopathy (>40 Gy/4 fxns)
Another example case

- Aug, 2008:
  - 59yo F with h/o metastatic NSCLC s/p surgery/WBRT 1 year ago
  - only current site of disease = 5cm mass in rt mid lung.
  - plan: SBRT to rt lung mass
One year later: cough, dyspnea

Chest x-ray

Coronal reconstruction, CT scan
Bronchoscopy:
mucus plug cleared from RML bronchus

Lateral segment
RML bronchus:
Narrow but patent after clearing
This can also happen after hyper-fractionated RT
Miller et al, IJROBP 61: 64-69, 2005

Table 2. Dose-response data for incidence of bronchial stenosis

<table>
<thead>
<tr>
<th>Study</th>
<th>Treatment</th>
<th>Dose (Gy)</th>
<th>Rate of bronchial stenosis (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Current</td>
<td>b.i.d. EBRT</td>
<td>74</td>
<td>4 (3/67)</td>
</tr>
<tr>
<td>Current</td>
<td>b.i.d. EBRT</td>
<td>80</td>
<td>5 (1/20)</td>
</tr>
<tr>
<td>Current</td>
<td>b.i.d. EBRT</td>
<td>86</td>
<td>25 (4/16)</td>
</tr>
<tr>
<td>Hayakawa et al.</td>
<td>q.d. EBRT</td>
<td>80</td>
<td>80 (4/5)</td>
</tr>
<tr>
<td>Speiser and Spratling (13)</td>
<td>q.d. EBRT + endobronchial HDR 60 + 22.5–30 HDR</td>
<td>9 (6/68)</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: b.i.d. = twice daily; EBRT = external beam radiation therapy; q.d. = once daily; HDR = high-dose-rate brachytherapy.
* Patient numbers in parentheses.
Pre- and post-bronch to clear mucus plug
63 patients
  - 9/63 Grade 2+ RP
Correlated with MLD$_2$
  - No toxicity when MLD$_2$ $\leq$ 12 Gy
Median 4.8 months
Radiation Pneumonitis
Borst et al, Radiother Oncol 2009

- 128 patients treated with SBRT
- 10.9% pneumonitis
- Correlated to MLD₂
HOW do we and some others do SBRT?

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- Early stage lung cancer
  - And lung metastases
- Pancreas cancer
- Hepatocellular cancer
  - And Liver metastases
- Spine/paraspinal lesions
- Prostate cancer
A DOSIMETRIC MODEL OF DUODENAL TOXICITY AFTER STEREOTACTIC BODY RADIOTHERAPY FOR PANCREATIC CANCER
Murphy et al, IJROBP, in press

• 73 pts
  • No prior RT
  • Unresectable
  • Not recurrent after Whipple

• 25 Gy single fraction
  • PTV = GTV + 2 to 3mm
  • duodenum constraints:
    • 5% < 22.5 Gy
    • 50% < 12.5 Gy
    • the 50% isodose line should not reach the distal wall of the duodenal lumen on any CT image
A DOSIMETRIC MODEL OF DUODENAL TOXICITY AFTER STEREOTACTIC BODY RADIOTHERAPY FOR PANCREATIC CANCER
Murphy et al, IJROBP, in press

• Only 6/73 grade 3+ duodenal toxicity
• Numerous individual predictors significant on univariate
• NTCP also significant (not shown)
Murphy et al, continued

A. $p=0.015$

B. $p=0.002$

C. $p=0.002$

D. $p=0.010$

$V_{10} \geq 16\text{cm}^3$

$V_{10} < 16\text{cm}^3$

$V_{15} \geq 9.1\text{cm}^3$

$V_{15} < 9.1\text{cm}^3$

$V_{20} \geq 3.3\text{cm}^3$

$V_{20} < 3.3\text{cm}^3$

$V_{25} \geq 0.21\text{cm}^3$

$V_{25} < 0.21\text{cm}^3$
Pancreas SBRT vs conventional RT

Stanford, IJROBP 2010
• Primary unresectable
• 25 Gy/1 fxn
• 84% GEM-based chemo
• Toxicity:
  • 8% (6/73) G3-4 duodenal toxicity
  • Other toxicities not stated

RTOG, JAMA. 2008;299(9):1019-1026
• Adjuvant post-op, GTR
• 50.4 Gy/28 with 5FU
• GEM or 5FU neo and adj
• Toxicity:
  • 58% total non-hematologic toxicity G3-4
    • Diarrhea
    • Stomatitis
    • Other GI
    • etc
Other sources of guidance for SBRT normal tissue dose constraints

• Selected RTOG SBRT studies
• QUANTEC papers—very limited SBRT, mostly conventional
  • Liver
    • Pan et al, IJROBP 76(3) Suppl: S94–S100, 2010
  • Kidney
    • Dawson et al, IJROBP 76(3) Suppl: S94–S100, 2010
  • Stomach and small bowel
    • Kavanagh et al, IJROBP 76(3) Suppl: S94–S100, 2010
  • Mostly unvalidated but well considered estimates for 1, 3, and 5 fractions
### Three-Fraction Treatment

<table>
<thead>
<tr>
<th>Serial Tissue</th>
<th>Volume (mL)</th>
<th>Volume Max (Gy)</th>
<th>Max Point Dose (Gy)</th>
<th>Endpoint (≥ Grade 3)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Optic pathway</td>
<td>&lt;0.2</td>
<td>15 (5 Gy/fx)</td>
<td>19.5 (6.5 Gy/fx)</td>
<td>Neuritis</td>
</tr>
<tr>
<td>Cochlea</td>
<td>&lt;1</td>
<td>18 (6 Gy/fx)</td>
<td>20 (6.67 Gy/fx)</td>
<td>Hearing loss</td>
</tr>
<tr>
<td>Brainstem</td>
<td>&lt;0.25</td>
<td>18 (6 Gy/fx)</td>
<td>23 (7.67 Gy/fx)</td>
<td>Cranial neuropathy</td>
</tr>
<tr>
<td>Spinal cord</td>
<td>&lt;1.2</td>
<td>11.1 (3.7 Gy/fx)</td>
<td>22 (7.33 Gy/fx)</td>
<td>Myelitis</td>
</tr>
<tr>
<td>Cauda equina</td>
<td>&lt;5</td>
<td>21.9 (7.3 Gy/fx)</td>
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<td>Sacral plexus</td>
<td>&lt;3</td>
<td>22.5 (7.5 Gy/fx)</td>
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</tr>
<tr>
<td>Esophagus*</td>
<td>&lt;5</td>
<td>21 (7 Gy/fx)</td>
<td>27 (9 Gy/fx)</td>
<td>Stenosis/fistula</td>
</tr>
<tr>
<td>Ipsilateral brachial plexus</td>
<td>&lt;3</td>
<td>22.5 (7.5 Gy/fx)</td>
<td>24 (8 Gy/fx)</td>
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<td>Heart/pericardium</td>
<td>&lt;15</td>
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<td>30 (10 Gy/fx)</td>
<td>Pericarditis</td>
</tr>
<tr>
<td>Great vessels</td>
<td>&lt;10</td>
<td>39 (13 Gy/fx)</td>
<td>45 (15 Gy/fx)</td>
<td>Aneurysm</td>
</tr>
<tr>
<td>Trachea and ipsilateral bronchus*</td>
<td>&lt;4</td>
<td>15 (5 Gy/fx)</td>
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<td>Jejunum/ileum*</td>
<td>&lt;5</td>
<td>16.2 (5.4 Gy/fx)</td>
<td>27 (9 Gy/fx)</td>
<td>Enteritis obstruction</td>
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<td>Colon*</td>
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### Parallel Tissue

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Methods

– Standard 3+3 Phase I design
– Starting dose, 12 Gy x 3 = 36 Gy total
– Safe escalation to pre-selected maximum dose
  • 20 Gy x 3 = 60 Gy

• Critical volume model
  – At least 700 cc normal liver received < 15 Gy cumulative

Schefter et al, IJROBP 62:1371-78, 2005
## Mostly Unvalidated Normal Tissue Dose Constraints for SBRT

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*Timmerman RD. Sem Rad Onc. 18(4) :215-222, 2008*
Liver Case: 3DCRT vs. IMRT

Prescription Dose: 54 Gy to PTV in 3 Fxs

GTV in RED, PTV in CYAN

Both plans use 10 coplanar fields
UC Liver SBRT Phase II Results, Toxicity
No RILD, no Gr 4-5 toxicity of any kind
1 case of grade III soft tissue toxicity

What not to do:
Insufficient number of fields

Photo taken 8 mos after SBRT
At last followup 17 post-SBRT, lesion controlled.
Necrosis is slowly healing.
Chest wall contouring

Note:
In this case we accepted a slightly high chest wall V30 of 44 cc. The pain syndrome reported had typical onset 7 mos post-SBRT and lasted approx 4 mos. Most pt recovered to zero pain level. Thus, an important consideration but should be judged relative to overall clinical goal.
MINIP vs MIP: a few comments

Notice one obvious difference between MINIP and MIP is the volume of liver projected, since the lower density adjacent tissues that move with respiration provide the minimum HU voxels.
We generally use ITV+5mm margin for lung and liver.
MIP usually helpful for lung ITV
MINIP often helpful for liver ITV, but be careful with lesion near the dome.

MINIP (above) helpful to show ITV for 2 of the three lesions, but 4D CT cine view (right) shows actual motion of dome lesion outside of MINIP-based ITV.
Non-protocol patient:

\[ \text{max pt to stomach} \geq 10 \text{ Gy/txn} \]

Pale, denuded mucosa; progressed to ulceration but eventually healed in approx 3 mos.
Sometimes you just can’t do 3 fractions and keep max GI point dose to <10 Gy/fractions

Yes, that is a liver metastasis—unusual anatomy! Stomach, not small bowel, adjacent

Stomach V40 = 2.25 cc
“4/40 rule” = keep total GI tract volume >40 Gy to <4cc
Top to Bottom:

**HOW** do we and some others do SBRT?

- Recurrent head and neck cancer
- Early stage lung cancer
  - And lung metastases
- Pancreas cancer
- Hepatocellular cancer
  - And Liver metastases
- Spine/paraspinal lesions
- Prostate cancer
# Range of applied cord constraints

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<tr>
<th>Institution</th>
<th>Dose Constraint</th>
</tr>
</thead>
<tbody>
<tr>
<td>MSKCC</td>
<td>14 Gy Dmax</td>
</tr>
<tr>
<td>UPMC</td>
<td>10 Gy Dmax</td>
</tr>
<tr>
<td>HENRY FORD</td>
<td>V10Gy ≤ 10%</td>
</tr>
<tr>
<td>MDACC</td>
<td>12 Gy Dmax TO 0.1 CC</td>
</tr>
<tr>
<td>PMH</td>
<td>12 Gy Dmax TO THECAL SAC OR CORD + 2mm</td>
</tr>
<tr>
<td>CLEVELAND CLINIC</td>
<td>14Gy Dmax AND V10Gy ≤10%</td>
</tr>
<tr>
<td>STANFORD</td>
<td>14 Gy Dmax, V12Gy ≤ 0.3 CC, V10Gy ≤ 0.5 CC V8Gy ≤ 1 CC</td>
</tr>
<tr>
<td>DALLAS</td>
<td>14 Gy Dmax, V10Gy ≤ 0.35CC, V8Gy ≤ 1.2CC</td>
</tr>
</tbody>
</table>

Yosh Yamada, MSKCC, from ASTRO IGRT mtg, 2009
The easy part for spinal targets: motion is not a major problem

cineMRI courtesy Dr Paul Read, U of Virginia
Spinal Target volumes, from “Partial Volume Tolerance of the Spinal Cord and Complications of Single-Dose Radiosurgery”
Ryu et al, Cancer, 2007

- Cord drawn 6mm above and below target
- Major constraint: no more than 10% of cord receives dose above 10 Gy
- Only 1 observed cord complication among 177 pts
Sample case: 60 y/o F

- 5/04 T1N2M0 NSCLC
  - Adjuvant chemo (gem/carbo)
- 5/05 bone mets
  - Erlotinib started 9/05
- Mid-2006
  - spine SRS T7, sacrum
  - Brain SRS 3 lesion
- Early 2007
  - SRS to another brain met
- Late 2007
  - SRS to 2 other brain mets
- Early 2008
  - Progressing spine lesions at T10, L3
Target volume and plan
Top to Bottom:

**HOW** do we and some others do SBRT?

- Recurrent head and neck cancer
- Early stage lung cancer
  - And lung metastases
- Pancreas cancer
- Hepatocellular cancer
  - And Liver metastases
- Spine/paraspinal lesions
- Prostate cancer
From Katz et al, BMC Urology 2010
7.25 Gy x 5 F
Note: caution with testis dose using CK system

Multi-institutional trial
First UC patients
10 Gy x 5F
Note: balloon placed to displace rectum and take advantage of reduced backscatter dose
Thanks for your attention!