Stereotactic Body Radiation Therapy (SBRT)

- Fractional dose >5Gy
  - range: 5 - 34 Gy per fraction
- Number of fractions <5 range: 1 to 5
- Safe delivery is of utmost importance due to high fractional dose and small number of fractions.

CONVENTIONAL FRACTIONATION versus HYPOFRACTIONATION versus STEREOTACTIC BODY RADIOSURGERY (SBRT)

<table>
<thead>
<tr>
<th>SBRT</th>
<th>Hypofractionation</th>
<th>Conventional</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of fractions</td>
<td>~35 - 45</td>
<td>~35 - 45</td>
</tr>
<tr>
<td>Fraction Size</td>
<td>1.8-2.0 Gy</td>
<td>1.8-2.0 Gy</td>
</tr>
<tr>
<td>Total Dose</td>
<td>~50-75 Gy</td>
<td>~75-85 Gy</td>
</tr>
<tr>
<td>Ablative??</td>
<td>Biologically rationale</td>
<td>Normal tissue sparing</td>
</tr>
</tbody>
</table>

Stereotactic Body Radiation Therapy (SBRT)

- Fractional dose >5Gy
  - range: 5 - 34 Gy per fraction
- Number of fractions <5 range: 1 to 5
- Safe delivery is of utmost importance due to high fractional dose and small number of fractions.
Treatment Planning for SBRT

- The goal of SBRT treatment is to “ablate” tissues within the PTV, these tissues were not considered at risk for complications.
- Dose inhomogeneity inside the PTV was considered acceptable (potentially advantageous) and not considered a priority in plan design. Maximum point dose up to 160% of Prescription Dose is common for SBRT plans.
- The main objective of the plan is to minimize the volume of those normal tissues outside PTV receiving high dose per fraction.

SBRT planning principles are very similar to Cranial SRS planning principles

- Inhomogeneous Dose inside PTV
- Sharp Dose Fall Off outside PTV
- Multiple non-coplanar beams or arcs are needed to create conformal dose distributions.

Much more limited non-coplanar beam clearance compared with cranial SRS for LINAC based SBRT.

SBRT vs conventional IMRT/VMAT

**Spine**
- 1-3 lesions
  - Single Fraction: 16 Gy
  - Three Fraction: 24 Gy (8 Gy per fraction)

**Lung**
- Peripheral Lesions
  - Three fractions: 60 Gy (20 Gy per fraction)
  - Single fraction: 25 Gy
- Central Lesions
  - Five fractions: 50 Gy (10 Gy per fraction)
Spine SRS Dose

• Variable Dosing (16-24 Gy):
  – RTOG 0631 16 or 18 Gy
  – MSKCC 24 Gy
  – Stanford 20 Gy

Liver

Metastasis
• If lesions > 2 cm from Porta Hepatis/Bile Duct:
  Three Fractions 20Gy x 3
• If lesions ≤ 2 cm from Porta Hepatis/Bile Duct:
  Five Fractions 10Gy x 5

HCC
• Five fractions: 30-50 Gy
  (depends on Veff)

RTOG SBRT Protocols

• 0631 Spine
• 0236, 0813 and 0915 Lung
• 0438 Liver

These protocols specify detailed requirements for treatment planning:

  Dose Prescription
  Target Coverage
  Dose Constraints
PI: Robert Timmerman, MD

Eligibility
- Patients with T1, T2 (≤ 5 cm), T3 (≤ 5 cm), N0, M0 medically inoperable non-small cell lung cancer;
- Patients with T3 tumors chest wall primary tumors only
- No patients with tumors of any T-stage in the zone of the proximal bronchial tree.

SBRT dose: 20 Gy x 3 fractions

Dosimetry specifications
- "Zone of the proximal bronchial tree" (figure)
- Target dose homogeneity limits
- Dose "isotropicity" limitation requiring falloff of approx 50% within 2 cm of PTV
- V20 < 10%
- Spinal cord, heart, esophagus, etc. limits

Requirements of SBRT Plan
- Maximum Dose: normalized to 100%, must be within PTV
- Prescription Isodose: must be ≥ 60% and < 90% of the maximum dose
- Prescription Isodose Surface Coverage: 95% of the target volume (PTV) is conformally covered by the prescription isodose surface (PTV V100%PD = 95%) and 99% of the target volume (PTV) receives a minimum of 90% of the prescription dose (PTV V90%PD > 99%)
- High Dose Spillage: The cumulative volume of all tissue outside the PTV receiving a dose > 105% of prescription dose should be no more than 15% of the PTV volume
- Intermediate Dose Spillage: The falloff gradient beyond the PTV extending into normal tissue structures must be rapid in all directions and meet the criteria in Table 1
- Meet the constraints of dose limiting organs at risk
Table 1: Conformity of Prescribed Dose for Calculations Based on Deposition of Photon Beam Energy in Heterogeneous Tissue

<table>
<thead>
<tr>
<th>PTV Volume (cc)</th>
<th>Ratio of Prescription Isodose Volume to the PTV Volume</th>
<th>Ratio of 50% Isodose Volume to the PTV Volume, ( R_{50%} )</th>
<th>Maximum Dose (in Gy) at 2 cm from PTV in Any Direction, ( D_{2\text{cm}} ) (Gy)</th>
<th>Percent of Lung Receiving 20 Gy Total or More, ( V_{20%} )</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Deviation</td>
<td>Deviation</td>
<td>Deviation</td>
<td>Deviation</td>
</tr>
<tr>
<td>1.8</td>
<td>&lt; 12</td>
<td>None</td>
<td>None</td>
<td>Minor</td>
</tr>
<tr>
<td>3.8</td>
<td>&lt; 12</td>
<td>Minor</td>
<td>None</td>
<td>Minor</td>
</tr>
<tr>
<td>7.4</td>
<td>&lt; 12</td>
<td>Minor</td>
<td>None</td>
<td>Minor</td>
</tr>
<tr>
<td>13.2</td>
<td>&lt; 12</td>
<td>None</td>
<td>None</td>
<td>Minor</td>
</tr>
<tr>
<td>22.0</td>
<td>&lt; 12</td>
<td>Minor</td>
<td>None</td>
<td>Minor</td>
</tr>
<tr>
<td>34.0</td>
<td>&lt; 12</td>
<td>None</td>
<td>None</td>
<td>Minor</td>
</tr>
<tr>
<td>50.0</td>
<td>&lt; 12</td>
<td>Minor</td>
<td>None</td>
<td>Minor</td>
</tr>
<tr>
<td>70.0</td>
<td>&lt; 12</td>
<td>None</td>
<td>None</td>
<td>Minor</td>
</tr>
<tr>
<td>95.0</td>
<td>&lt; 12</td>
<td>Minor</td>
<td>None</td>
<td>Minor</td>
</tr>
<tr>
<td>123.0</td>
<td>&lt; 12</td>
<td>None</td>
<td>None</td>
<td>Minor</td>
</tr>
<tr>
<td>163.0</td>
<td>&lt; 12</td>
<td>Minor</td>
<td>None</td>
<td>Minor</td>
</tr>
</tbody>
</table>

Note 1: For values of PTV dimension or volume not specified, linear interpolation between table entries is required.

Note 2: Protocol deviations greater than listed here as “minor” will be classified as “major” for protocol compliance (see Section 6.7).

Clinical Example #1:

Dual 6 MV arcs, lung tumour, surrounded by low density lung

Dose Differences: AAA - MC

Dose Differences: Acuros - MC

Overestimate observed up to 11%

Differences correspond with material cross-section assignments (air pockets)

** Isodose normalization to PTV containing lung significantly affected.

Courtesy of Karl Bush, Stanford
Montefiore-Einstein Cancer Center
SBRT Registry Study

Lung
Peripheral Lesions
- Three fractions: 60 Gy (20 Gy per fraction) (Based on RTOG 0618)
- Five fractions: 50 Gy (10 Gy per fraction) (Based on RTOG 0813)

For Lung cases, it is often necessary to have non-coplanar beams to achieve fast dose fall off.

We use three partial arc VMAT technique
Each arc at least 100 degree
Non-coplanar couch angle up to 20 degree
Non-coplanar multiple IMRT or 3DCRT is used.

MECC SBRT Registry: Lung

Constraints
Three Fraction (20Gy x 3) (Based on dose of RTOG 0619):
- Heart: Maximal point dose is 30 Gy (10 Gy per fraction)
- Ipsilateral brachial plexus: Maximal point dose is 24 Gy (8 Gy per fraction)
- Spinal Cord: Maximal point dose is 18 Gy (6 Gy per fraction)
- Esophagus: Maximal point dose is 27 Gy (9 Gy per fraction)
- Trachea/ipsilateral bronchus: Maximal point dose is 30 Gy (10 Gy per fraction)
- Whole lung minus GTV: V20 < 10%,
- Skin: Maximal point dose is 24 Gy (8 Gy per fraction)
- Ribs: Goal is 30cc of chest wall volume < 30 Gy without compromising PTV coverage

Courtesy of Linda Hong, Albert Einstein College of Medicine
Prescription Isodose Surface Coverage

PD = 100% = 20 Gy/fx x 3
PTV V100 = 95%

CAX

100% PD and Above

Cor

Sag

High Dose Spillage

PD = 100% = 20 Gy/fx x 3
Max PTV dose = 135.0%
100% covered volumes outside of PTV <= 15% of volume of PTV
Here PTV = 40.2 cc
V105-PTV = 0.1 cc (0.2 %)

CORSAG

Conformality : Prescription Dose Volume vs. PTV Volume

PD = 100% = 20 Gy/fx x 3
V100 / PTV volume <= 1.2
Here PTV = 40.2 cc
V100 = 41.0 cc
Ratio = 1.02

100% PD and Above
Intermediate Dose Spillage: R_{50\%} and D_{2\text{cm}}

For PTV = 40.2 cc
- R_{50\%} = 4.2, D_{2\text{cm}} = 52.6\%
- Here V_{50\%} = 169.5 cc

R_{50\%} = 4.2
D_{2\text{cm}} = 52.6\%

50\% PD and Above

25\% isodose restricted mainly in the ipsilateral lung

12.5\% isodose restricted mainly in the ipsilateral lung

Montefiore-Einstein Cancer Center
SBRT Registry: Lung

Constraints
Five Fraction (10 Gy x 5) Based on RTOG 0813:

- **Heart**: <15 cc receives ≥32 Gy (6.4 Gy/fx); maximum point dose ≤52.5 Gy
- **Trachea/ipsilateral bronchus (non-adjacent wall)**: <4 cc receives ≥18 Gy (3.6 Gy/fx); maximum point dose ≤52.5 Gy
- **Great vessels (non-adjacent wall)**: <10 cc receives >47 Gy (9.4 Gy per fraction); maximum point dose ≤52.5 Gy
- **Ipsilateral brachial plexus**: <3 cc receives ≥30 Gy (6 Gy/fx); maximum point dose ≤52.5 Gy (6.4 Gy per fraction)
- **Spinal Cord**:
  - <0.25 cc receives ≥22.5 Gy (4.5 Gy/fx)
  - <0.5 cc receives ≥13.5 Gy (2.7 Gy/fx)
  - Maximal point dose is 30 Gy (6 Gy per fraction)
- **Esophagus**: <5 cc receives ≥27.5 Gy (5.5 Gy per fraction); maximum point dose ≤52.5 Gy
- **Whole lung minus GTV**:< 1500 cc receives ≥12.5 Gy (2.5 Gy per fraction)
  - <1000 cc receives ≥13.5 Gy (2.7 Gy per fraction)
- **Skin**: <10 cc receives ≥30 Gy (6 Gy/fx). Maximal point dose is 32 Gy (6.4 Gy per fraction)

Same beam arrangements/techniques can be used as peripherally located tumor.
## Liver metastasis SBRT Reports

<table>
<thead>
<tr>
<th>Patients</th>
<th>Lesions</th>
<th>SBRT (PTV dose)</th>
<th>PTV Timepoint</th>
<th>Local Control comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heidelberg</td>
<td>37</td>
<td>11-21 Gy x 1</td>
<td>GTV+6mm axial+10mm sup-inf</td>
<td>18 mos; Low dose (&lt;16); High dose (&gt;16); 81% 30 lesions CRC; MHD</td>
</tr>
<tr>
<td>Wuerzburg</td>
<td>39</td>
<td>7 Gy x 4</td>
<td>GTV+6mm axial+13mm sup-inf</td>
<td>2 yr; Low dose (28-30); 58% (2y); High dose (others); 82% (2y); P&lt;0.01 CRC same as others</td>
</tr>
<tr>
<td>Aarhus-Copenhagen</td>
<td>44</td>
<td>Not stated</td>
<td>GTV+5mm axial+10mm sup-inf</td>
<td>2 yr; 79% (2y) All pts CRC; 3 ulcers with intestinal dose &gt;30 Gy</td>
</tr>
<tr>
<td>Erasmus U. Rotterdam</td>
<td>17</td>
<td>10 Gy x 3</td>
<td>GTV+5mm axial+10mm sup-inf</td>
<td>2 yr; 86% (2y) 15 pts CRC; 1 late partial HTN in multiply treated patient</td>
</tr>
<tr>
<td>Colorado/multi-institutional</td>
<td>47</td>
<td>12-20 Gy x 3</td>
<td>GTV+5mm axial+10mm sup-inf</td>
<td>2 yr; ≤3cm: 100%; &gt;3cm: 75%</td>
</tr>
<tr>
<td>PMH</td>
<td>68</td>
<td>Variable, NTCP-based Median 7 Gy x 6</td>
<td>GTV+13mm or more</td>
<td>1 yr; 71% Better for higher dose, smaller volume</td>
</tr>
<tr>
<td>Stanford</td>
<td>19</td>
<td>18-30 Gy x 1</td>
<td>IV+3-5mm</td>
<td>1 yr; 77% Combined with 7 pts HCC or IHC MTD not reached</td>
</tr>
</tbody>
</table>

### Dose Constraints

**Non cirrhotic livers**
- Keep 700 cc normal liver <15 Gy (5 fractions)
- Keep 700 cc normal liver <12 Gy (3 fractions)

**Cirrhotic livers**
- Childs A – Keep 700 cc normal liver <12 Gy, 500 cc normal liver <7 Gy (3-5 fractions)
- Childs B – Keep 700 cc normal liver <12 Gy, 500 cc normal liver <7 Gy (5 fractions)
- Childs C – use SBRT with caution

*Courtesy of B. Kavanagh, University of Colorado – 3 fractions, Stanford – 1 fraction*
Stanford Experience – SBRT
Single fraction

<table>
<thead>
<tr>
<th></th>
<th>Regimen</th>
<th>MS</th>
<th>≥G2 Late GI tox</th>
</tr>
</thead>
<tbody>
<tr>
<td>Koong, et al IJROBP 2004</td>
<td>25 Gy CyK</td>
<td>8.0 mo @ 25 Gy</td>
<td>none reported</td>
</tr>
<tr>
<td>Koong, et al IJROBP 2005</td>
<td>45 Gy IMRT +5FU, 25Gy CyK</td>
<td>6.3 mo</td>
<td>6/16 (38%)</td>
</tr>
<tr>
<td>Schellenberg, IJROBP 2008</td>
<td>Gem + 25Gy CyK</td>
<td>11.4 mo</td>
<td>7/16 (44%)</td>
</tr>
<tr>
<td>Schellenberg, ASTRO 2008</td>
<td>Gem + IMRT / 25Gy Trilogy</td>
<td>NR</td>
<td>4/20 (20%)</td>
</tr>
</tbody>
</table>

Fractionated SBRT Pancreas Protocol

- 3-D CT, Multi-D evaluation, up to 3 doses Gem
- PET/CT: Treatment planning, no metastatic dz
- Gold fiducials placed, blood/tissue obtained
- Simulation: 4D CT if <5 mm motion treat FB
- If >5mm, re scan with ABC and IV/oral contrast
- Contour GTV/PTV and prox duod/stomach
- Conduct plan
- Central review plan/DVH

Phase II Multi-Institutional Study of Stereotactic Body Radiation Therapy for Unresectable Panceatic Cancer

Locally Advanced Pancreatic Cancer (Gemcitabine, up to 1 Cycle allowed)*

SBRT 6.6 Gy x 5 Mon-Fri 1 week break
Gemcitabine Chemotherapy (3 wks on, 1 wk off) Trel toxicity or progression

Primary endpoint: Late GI Toxicity > 4 months
Secondary: Tumor Progression Free Survival, pre-tx biopsy
QOL, tumor markers
N=60

Trial opened at Stanford, Johns Hopkins, Memorial Sloan Kettering.

Excellent Local control

Courtesy of J. Herman

<table>
<thead>
<tr>
<th>Study</th>
<th>N</th>
<th>stages</th>
<th>Regimen</th>
<th>MS</th>
<th>≥G2 Late GI tox</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mahadevan, 2010</td>
<td>36</td>
<td>III</td>
<td>8-12Gy x 3</td>
<td>14.3 mo</td>
<td>5% crude G3</td>
</tr>
<tr>
<td>Polistina, Italy 2010</td>
<td>23</td>
<td>III</td>
<td>Gem, 10 x3</td>
<td>10.6 mo</td>
<td>0%</td>
</tr>
<tr>
<td>Didolkar, 2010</td>
<td>85</td>
<td>mixed</td>
<td>15-30 Gy /4 fx</td>
<td>8.7mo</td>
<td>22.3% crude G2/3</td>
</tr>
<tr>
<td>Rwigema, 2011</td>
<td>71</td>
<td>mixed</td>
<td>20-24Gy /1fx</td>
<td>10.3mo</td>
<td>2% G2</td>
</tr>
</tbody>
</table>
Spine and Prostate SBRT

The published protocols usually do not specify $R_{50\%}$ or $D_{2\text{cm}}$ requirements for spine and liver cases. Nevertheless, we find lung protocol criteria useful for spine and liver cases as well.

Montefiore-Einstein Cancer Center
SBRT Registry Study

Spine

1-3 lesions

- Single Fraction: 16 Gy (RTOG 0631)
  (for cases we have confidence in setup, for example: inferior T-spine and L-spine lesions)

- Three Fraction: 24 Gy (8 Gy per fraction)
  (for cases with setup uncertainty large, for example: C-spine and superior T-spine lesions)

RTOG 0631 (Spine)
Definition of Spine Metastasis Target Volume

Figure 2: Diagram of Spine Metastasis and Target Volume

An epidural lesion is included in the target volume provided that there is a ≥ 3 mm gap between the spinal cord and the edge of the epidural lesion.

International Spine Radiosurgery Consortium Consensus Guidelines for Target Volume Definition in Spinal Stereotactic Radiosurgery

Mark H. Ellis, MD; Daniel J. Spraitz, MD; Michael Lembersky, PhD; Mark H. Ellis, MD; Daniel J. Spraitz, MD; Michael Lembersky, PhD; Peter C. Gorelick, MD; Wei L. Shi; Wei Shi; Ari M. Dorenbos, MD; Scott J. Seltzer, MD; John H. Delp, MD; Melvyn Daube, PhD; David A. Miller, MD; and Yongtao Yan, MD.
For Spine Cases:
IMRT or VMAT is required to create concave dose distributions.

Two full RapidArcs, or two partial RapidArcs to avoid shoulders or arms, one arc with collimator at 0, the other with collimator at 90.

Multiple fixed IMRT fields can be used.
No need to do any non-coplanar beams (no clearance anyway).

We follow RTOG 0813 and RTOG 0915 lung protocols criteria for PTV coverage, high dose spillage and dose fall off

Maximum Dose: must be within PTV
Prescription Isodose: If PD = 100%, maximum dose must be at least 111.11% but not more than 166.67%

Prescription Isodose Surface Coverage:
95% of the target volume (PTV) is conformally covered by the prescription isodose surface (PTV V100% = 95%) and
99% of the target volume (PTV) receives a minimum of 90% of the prescription dose (PTV V90% = 99%)
**Prescription Isodose Surface Coverage**

- PD = 100% = 16 Gy
- PTV V100 = 95%
- 100% PD and Above

**High Dose Spillage**

- PD = 100% = 16 Gy
- Max PTV dose = 135.3%
- 100% covered volumes outside of PTV < 15% of volume of PTV
- Here PTV = 19.1cc
- V105-PTV = 1.4 cc (7.3%)

**Conformality: Prescription Dose Volume vs. PTV Volume**

- PD = 100% = 16 Gy
- V100 / PTV volume < 1.2
- Here PTV = 19.1cc
- V100 = 21.7 cc
- Ratio = 1.14

**PTV**

- 2cm-3cm ring

**Construction**

- PTV V90% > 99%
- 90% PD and Above

- Max PTV dose = 135.3%
- 105% covered volumes outside of PTV ≤ 15% of volume of PTV
- Here PTV = 19.1cc
- V105-PTV = 1.4 cc (7.3%)

**Conformality**

- PD = 100% = 16 Gy
- V100 / PTV volume < 1.2
- Here PTV = 19.1cc
- V100 = 21.7 cc
- Ratio = 1.14
Intermediate Dose Spillage: $R_{50\%}$ and $D_{2\text{cm}}$

For PTV = 19.1 cc

$R_{50\%} < 4.6; D_{2\text{cm}} < 52.7\%$

Here $V_{50\%} = 77.0\%$

$R_{50\%} = 4.0$

$D_{2\text{cm}} = 43.6\%$

$D_{2\text{cm}}$: Maximum dose in $\%$ of PD at 2 cm beyond PTV in any direction

$R_{50\%}$: Ratio of 50\% PD volume/PTV volume

No need to do any non-coplanar beams (no clearance anyway).

12.5\% PD and Above

$16\text{Gy} \times 12.5\% = 2\text{Gy}$

Single Arc Collimator 45

Two Arcs: Collimator 0 and 90

100\% PD and Above
Single Arc Collimator 45

Two Arcs: Collimator 0 and 90

Additional 15 cc volume of normal tissue receiving 5% PD

Single Arc Collimator 45

Two Arcs: Collimator 0 and 90

Fixed IMRT Fields

Jaw opening area twice as much when compared to collimator at 0 or 90.

More leakage dose in superior and inferior beyond PTV.

Leaves parked inside jaws when unused for RapidArc.

Can meet similar R_{50%} and D_{2cm} constraints.
Fixed IMRT Fields: 7-9 posterior beams

Sometimes difficult to meet $R_{50\%}$ and $D_{2\text{cm}}$ constraints if you use those constraints.

Cord:
Sometimes difficult to meet 10Gy constraints, even though max point dose 14Gy can be met.

CyberKnife Treatment Planning

<table>
<thead>
<tr>
<th>Dose Statistic Table</th>
</tr>
</thead>
<tbody>
<tr>
<td>VOI</td>
</tr>
<tr>
<td>------</td>
</tr>
<tr>
<td>Tumor Site (C)</td>
</tr>
<tr>
<td>Cord</td>
</tr>
</tbody>
</table>

AVM Obliteration

16Gy x 1
volume = 0.3cc

Courtesy of Iris Gibbs, Stanford
Intra-fraction Movement of Spine

Spinal Movement During Treatment:

- Cine MRIs
- Absolute Motion <0.5 mm
- Recommend ITV of 0.5 mm
- Less for L Spine

Spinal Cord Motion

Dose - Stanford

One Year Local Failure:
- SSEDose:
  - $\leq 15\, \text{Gy}$: 38%
  - 15-18 Gy: 11%
  - $\geq 18\, \text{Gy}$: 8%

RTOG: $D_{\text{max}}$ 14 Gy ($v_{14} < 0.03\, \text{cc}$), $V_{10} < 0.35\, \text{cc}$
HFH: $V_{10}$ of 10%
Stanford: $D_{\text{max}}$ 14 Gy
MSKCC: $D_{\text{max}}$ 14 Gy
PMH: $D_{\text{max}}$ 12 Gy
MDACC: $D_{\text{max}}$ 12 Gy
UPMC: $D_{\text{max}}$ 12 Gy

Soltys ASTRO 2012
HYPOFRACTIONATION PROTOCOLS: Phase III trials

Australian Hypofractionation Study: Low / Intermediate Risk Cases
Yeoh et al, IJROBP 81, 1271-8, 2011

- N=217 patients
  - Hypofractionated: 55 Gy in 20 fractions
    - n = 108
  - Conventional: 64 Gy in 32 fractions
    - n = 109

- July 1996 to August 2003
- Median follow-up = 90 months (range, 3–138)
- At 90 months: bRFS
  - Hypofrac 53%
  - Conventional 34%

- Conventional schedule worse on multivariate analysis.

Consortium of Australian Radiation Oncology Groups (CAROG) 2009: "Australian Hypofractionated Radiation Therapy in Low and Intermediate Risk Prostate Cancer: Updated Analysis of the Australian Hypofractionation Study (AHS) and the Australian Prostate Cancer Early Detection Trial (APC-EDT)." J Clin Oncol, 28(28), 4248-55.

HYPOFRACTIONATION PROTOCOLS: Phase III trials

Australian Hypofractionation Study: Low / Intermediate Risk Cases
Yeoh et al, IJROBP 81, 1271-8, 2011

- Need time to see difference: Impact of long term follow-up

- Hypofractionated: 55 Gy in 20 fractions
- Conventional: 64 Gy in 32 fractions

- At 90 months: bRFS
  - Hypofrac 53%
  - Conventional 34%

- Conventional schedule worse on multivariate analysis.

Consortium of Australian Radiation Oncology Groups (CAROG) 2009: "Australian Hypofractionated Radiation Therapy in Low and Intermediate Risk Prostate Cancer: Updated Analysis of the Australian Hypofractionation Study (AHS) and the Australian Prostate Cancer Early Detection Trial (APC-EDT)." J Clin Oncol, 28(28), 4248-55.
Phase II trial. Started 2003
N=67 early stage patients, 57 evaluable
T1-T2a, PSA ≤10, GS 3+3 or low volume 3+4
No TURP or other treatment
Low IPSS score (<20)
DOSE: 725 cGy x 5 = 36.25 Gy

Treatment delivered either daily or every other day
Delivery with the Cyberknife
Prescription line: 89%
PTV margin: 3 mm post., 5 mm elsewhere
3 fiducials
No intrarectal balloon
FOLLOW-UP: Median 2.7 yrs, Maximum 5.9 yrs

Grade 3 urinary toxicity: 2 cases / Urethral strictures
Persistent dysuria and frequency / Slowly resolving
Multiple cystoscopies and dilatations

Literature: Urethral strictures: Surgery: ~8%
Brachytherapy: ~5%
EBRT: ~3%

<table>
<thead>
<tr>
<th>RTOG Grade</th>
<th>GU</th>
<th>GI</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>68% (39/57 pts)</td>
<td>84% (48/57 pts)</td>
</tr>
<tr>
<td>I</td>
<td>23% (13/57 pts)</td>
<td>14% (8/57 pts)</td>
</tr>
<tr>
<td>II</td>
<td>5% (3/57 pts)</td>
<td>2% (1/57 pts)</td>
</tr>
<tr>
<td>III</td>
<td>3.5% (2/57 pts)</td>
<td>0</td>
</tr>
<tr>
<td>IV</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>
SBRT DOSE

How high can we go?

UT SOUTHWESTERN SBRT PROSTATE PROTOCOL

Phase I/II trial. Multi-institutional. Started 2006

Phase I  45 patients
  5 fractions: 9 Gy, 9.5 Gy, 10 Gy

Phase II  50 patients
  T1-T2b
  PSA ≤10
  GS 6 and PSA <20
  GS 7 and PSA <15
  Gland <60 cc
  No TURP or other treatment
  Low IPSS score (<15)

Boke et al, JCO, 2011

Courtesy of P. Kupelian, UCLA

STEREOTACTIC BODY RADIOTHERAPY

UT Southwestern Protocol (R. Timmerman)
10 Gy x 5 = 50 Gy

Stereotactic, Image guidance

RT QOD

RTOG 09-35

Randomized Phase II trial

N=174 low risk patients

Stratification: Linac vs Cyberknife vs Protons

Arm 1
36.25 Gy in 5 fx of 7.25 Gy over 2 ½ weeks (15-17 days)

Arm 2
51.6 Gy in 12 daily fx of 4.3 Gy over 2 ½ weeks (16-18 days)

Primary Objective: To demonstrate that 1-year health-related quality of life for at least one hypofractionated arm is not significantly lower than baseline.

Courtesy of P. Kupelian, UCLA
SUMMARY

• Treatment protocols for lung, liver, pancreas, spine, prostate.
• Basic philosophy of SBRT planning.
• Dose calculation issue.
• Energy selection
• Coplanar vs planar beams.