SBRT: Treatment Planning and Immobilization

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KEY GOALS

- Definition of SBRT
- Radiobiological difference from conventional CRT
- IGRT’s role in simulation and treatment
- Immobilization techniques
- Treatment planning tips
- Future indications
What is SBRT?

- Stereotactic Radiosurgery (SRS) first described by Lars Leksell in 1951
  - Single Fraction
  - Intracranial
  - Replaces Surgery
- Stereotactic Body Radiation Therapy (SBRT)
  - Extracranial
  - Hypofractionated
What is SBRT?

- Noninvasive and powerful high-dose radiation to well delineated tumors
- Use of IGRT
- Dose escalation to tumor – very small margins
- Severity of potential toxicity is different than conventional 3D CRT
What is SBRT?

- Limited number of treatments @ very large dose per Fx
  - 1 – 5 Fx
- BED: at least 75-100 Gy or higher
- Expert dosimetry
  - highly conformal
  - sharp gradients from high to low dose areas
- High confidence in precision of dose delivery, even with moving targets
  - 95% probability of entire GTV within margin of 0.5cm – 1.0 cm
What is SBRT?

- Doses are very potent and biologically damaging
  - Dramatic tissue effects may occur in GTVs as well as normal tissues

- Tissue responses depend upon:
  - Dose delivered
  - Volume exposed
  - Natural tissue radiosensitivity
SBRT

- Hypofractionation: High Dose per Fx
  - Dose errors will be far more dramatic with geographical misses
    - High dose
    - Steep dose gradients
  - Treatment volumes must be small
  - Critical normal structures avoided
Radiobiology (Review)

LQ Model current means of predicting biological impact in Conventionally Fractionated Radiotherapy (CFRT)

\( \frac{\alpha}{\beta} \) ratio of most tumors ~ 10 (8-10)

\( \frac{\alpha}{\beta} \) ratio of most normal tissues ~ 3 (2-5)

If tx large volume of tissue, small doses per Fx will maximize the therapeutic ratio

- Commonly seen in CFRT
Radiobiology (Review)

a) Single Dose vs. Multiple Dose fractionation

b) Normal Tissues vs. Tumor Tissues during multiple-fraction exposure

Radiobiology in CFRT

Shoulder of the cell survival curve occurs for each conventional dose given (1.8 Gy – 2.0 Gy) over multiple fractions.

Shoulder due to the 4 Rs:

- Repair of sublethal damage
- Repopulation of cells
- Reassortment of cells through their cycle
- Reoxygenation, making all cells more sensitive
Radiobiology in CFRT

In CFRT, the 4 Rs seem beneficial:

- Normal tissues can REPAIR sublethal damage
- Normal tissues can REPOPULATE damaged cells
- Tumor cells will progress to sensitive mitotic phase during REASSORTMENT
- As tumor shrinks, the central necrotic core will REOXYGENIZE, making the tumor cells more sensitive
- However…
Radiobiology in CFRT

The 4 Rs also hurt us:

- Tumors can REPAIR sublethal damage
- Tumors can REPOPULATE in between fractions
- Normal tissues can become more sensitive during REASSORTMENT and REOXYGENATION
So Why do we Fractionate?

- Tradition

- Hypofractionation explored 100 years ago yielded prohibitive toxicity

- Strong belief that prolonged fractionation leads to better tumor control
However...

Total dose for total dose, hypofx is always more effective for any tumor cells that have a shoulder.

Hence, the real reason we use protracted Fx is to spare the normal tissues.

- Past technology not capable of limiting normal tissue within PTVs.

Therefore, CFRT during the last 80 years is a compromise, not an advantage.
CFRT and the $\alpha/\beta$ Model

$\alpha/\beta$ data has been collected with standard CFRT doses

Data is within range of shoulder

Due to prohibitive toxicity, Fx of very large doses could not historically be delivered

Therefore, $\alpha/\beta$ data does not exist past 6-10 Gy per fraction
Limitations of $\alpha/\beta$ Model

- $\alpha/\beta$ model over-predicts cell kill at large doses per fraction.
  - Tumor control translation will be overstated
  - Normal tissue translation will be understated

- Does not account for
  - Duration of treatment
  - Variation in architecture/function of tissue (lung vs. spinal cord)
  - Impact of nonchromosomal mechanisms of radiation damage (e.g., vascular injury)

- Therefore, using conventional $\alpha/\beta$ conversion without reservation for SBRT doses is very dangerous.
## Serial vs. Parallel Tissues

### Serial Tissues
- Spinal cord
- Esophagus
- Bowels
- Ducts
- Vessels
- Severe damage to any segment yields catastrophic dysfunction
- If tumor abuts serial organ, SBRT is only of limited benefit

### Parallel Tissues
- Peripheral lung
- Peripheral liver
- Peripheral kidney
- Catastrophic dysfunction depends on amount of tissue damaged.
- If volume can be limited with smaller margins, SBRT will be advantageous
Serial vs. Parallel Tissues

Serial vs. Parallel Tissues

Serially Functioning Tissue: Macroscopic Architecture

**Linear Tubular Structures**
- severe damage to any segment results in total and catastrophic dysfunction
- e.g.: esophagus, GI tract

**Branching Tubular Structures**
- severity of dysfunction depends on the position of the damage within the branches
- e.g.: hepatic ducts, bronchus of lungs

In either case, damage to both types tends to manifest as late toxicity ~ 4-6 months post Tx
SBRT and Ablation

- Typical dose schedules in SBRT are cell ablative
- Surrounding normal tissue just outside target will also be ablated
  - Similar to a surgeon’s knife
  - Leaves the tissues totally disabled both at point of contact and downstream
- In surgery, if remove portion of serial organ (e.g. esophagus), would reconnect the ends
- In SBRT cannot reconnect ends
- Ablative doses cannot be used near such organs
SBRT and Ablation

- Nerves and blood vessels very prone to ablation at high doses
- Ablative dose ranges = at least 10 Gy per Fx for 3 – 5 fractions
- Tumor control probabilities near 90% with ablative doses
Deviation between physical and biological doses is more pronounced for late-responding tissues than for early-responding tissues.

- Due to different curvatures of their single-dose cell survival curves
- e.g.: SBRT better than SBRS for tumor surrounding spinal cord.

*Slotman, BJ; Solberg, TD; Verellen, D (eds): Extracranial Stereotactic Radiotherapy and Radiosurgery; Taylor and Francis Group, 2006, p. 139.*
SBRT Radiobiology in Summary

- Dose constraints for CFRT do not apply to SBRT
- Biggest obstacle to SBRT is in treatment of tumors near serially functioning tissues
- Good results in parallel tissues; may change future patterns of care for many diseases
- LQ model and BED convenient to use for starting points, but applications of LQ model and BED in SBRT still require more study and research
Resultant SBRT Strategy

4 Requirements:

- Prophylactic radiotherapy not required
- Account for tumor motion
- Rapid dose falloff to normal tissues
- Excellent targeting accuracy
2 Important Issues

Accurate and reproducible patient immobilization
  - During simulation and treatment

Internal mobility of tumors and normal tissues
  - During simulation and treatment
Account for Tumor Motion

Account for Tumor Motion

- Motion maps show target position during all phases of respiratory cycle
  - Modern 4-D scanners helpful

Better to let patient breathe normally (coached), rather than in artificial fashion with deep breath-holds, etc.

- Maximum inspiration/expiration CTs may dramatically increase target volume during free-breathing treatment (more toxicity).
Respiratory Inhibition

2 Techniques:

- Forced breath hold
  - Effectively restricts tumor to a stable position where beam is turned on
  - Increases overall treatment time considerably

- Abdominal compression
  - Limits diaphragmatic breathing and thus target margins due to target motion
Abdominal Compression
Retrospective Gating

Slotman, BJ; Solberg, TD; Verellen, D (eds): Extracranial Stereotactic Radiotherapy and Radiosurgery; Taylor and Francis Group, 2006, p. 118.
Respiratory Gating

Varian RPM™ Respiratory Gating Software
IGRT

Retrospective gating used for CT-Simulation

- ITV created
- PTV added to ITV

Same accuracy required for treatment

- CBCT before each fraction
- kV-kV match selected fields
- Good immobilization crucial
Orthogonal kV images filmed and compared to planning DRRs

Perform CBCT pre with MD and Medical Physicist present

- Necessary couch shifts are made to match planning CT with CBCT
SBRT Treatment

- Per MD’s preference, port films of each field may also be taken
- All fields treated at 600 MU/min
- Cine view may be used by MD (esp. lung)
- Additional CBCT may be taken mid-treatment or post-treatment
SBRT Immobilization and Treatment Systems
Body Pro Lock™ System by CIVCO
Body Fix®
Body Fix®
Varian Trilogy
Anatomic Sites

- Liver
- Spine
  - RPCI examples
- Lung
  - RTOG protocols
  - RPCI examples
Diaphragm motion an issue

- Safety margins in cranio-caudal direction range from 1 cm to as much as 3 or 4 cm.

- Use abdominal compression to reduce respiratory motion.
  - Can reduce safety margins to 1 cm or less (in cranio-caudal direction)

- Gate, if possible
  - Tx delivery time increased by factor of 2 or more
LIVER

- Surgery is treatment of choice
  - SBRT option for non-surgical candidates

- RILD (Radiation Induced Liver Disease): limiting factor for dose to liver

- Radiation dose depends on volume of spared normal liver volume
  - More limited for patients with cirrhosis
  - Currently recommend tumor size limit of 5-6 cm
LIVER

- Mean dose to normal liver is predictor for radiation hepatitis
- Escalation to 66 Gy achieved complete response in 80% of patients.
- Hypodensity observed post SBRT tx is a normal response, not usu. progression of disease.
- At least 700 cm³ uninvolved liver under cumulative dose of 15 Gy
- With above constraint, 60 Gy in 3 Fx was given without reaching maximum liver tolerance
LIVER

This difference must be >700 cm³

SPINAL + PARASPINAL LESIONS

Diseases:
- Mets (very common)
- AVMs
- Meningiomas
- Other lesions, NOS
- Nerve sheath tumors
- Hemangioblastomas
- Chordomas

Challenging – close to spinal cord (serial tissue)

Least affected by breathing (supine)
- Late-responding tissue, usu. 5 Fx

Goals
- Relief of pain
- Improvement in neurologic function
- Limit tumor progression
Gibbs @ Stanford University reported 2 – 5 day Fx schemes to avoid a single Fx dose of ≥ 10 Gy to the spinal cord.

102 metastatic lesions treated w/ mean f/u of 9 months.

16 – 25 Gy were given in 1 - 5 Fx.

84% of patients who presented with pain reported resolution.
SPINAL + PARASPINAL LESIONS: The Stanford Experience

No complications occurred when volume of spinal cord receiving a BED of 12 Gy in single Fx (i.e. $\text{BED}_3$ of 58 Gy) was less than 0.15 cm$^3$.

- New goal for future treatment is to limit volume of cord receiving a dose of 10 Gy to $\sim 0.3$ cm$^3$.

4 patients developed spinal cord myelopathy

- 2 had prior irradiation
- 2 were exposed to agents that alter local vasculature
SPINAL + PARASPINAL LESIONS:
Stanford’s Clinical Guidelines

- Symptomatic cord compression should not be treated by SBRT.

- SBRT can be used to treat previously irradiated patients
  - Avoid reirradiation within 6 months of prior radiation, unless SBRT is being used as a boost
    - Lower prescription dose.

- Avoid spinal SBRT when targeted antiangiogenic therapy is planned within 2 months of the procedure.
SPINAL + PARASPINAL LESIONS:
Stanford’s Clinical Guidelines

- Limit volume of spinal cord at BED of 10 Gy in a single fraction to less than 0.3 cm³.

- Though no complications occurred among intramedullary tumors or AVMs up to 5 cm³, intramedullary lesions > 1.5 cm³ in volume should be routinely avoided.
LUNG

- Toxicity is related to dose outside the target
- Omit irradiation of radiographically uninvolved tissues
- Reasonable to omit CTV expansions
  - Pulmonary CT windows needed to distinguish tentacles extending from GTV.
  - Use PET-CT or MRI to better define tumor
  - GTV = CTV
  - With high dose given to GTV margin, fall-off dose will be sufficient to eradicate these extensions.
- Must respect PBT + 2cm, proven by results
LUNG SBRT

2.0 cm Margin
SBRT Lung: RPCI

Pre-Tx CT 7-18-07  Post-Tx CT 7-22-08
SBRT Lung: Watch Out

- Indiana U. experienced pleural effusions in tumors located near pleural surface.
- When tumor near ribs, rib fractures were seen 9 – 16 months post tx.
- Tracheal necrosis observed 15 months post tx.
- Skin toxicity seen when less than 10 beams were used (most common was 7 beams in these cases).
DOSIMETRY

- Must be of very high quality
- Potent dose must only hit target
- Very sharp fall-off dose gradients outside region of tumor
- Proper dosimetry creates a cloud of radiation dose that allows the tumor to discreetly move within the volume.
Unlike CFRT, no effort to construct uniform dose distribution within target
- Entire target is contained within prescription dose.
- Toxicity is limited by optimizing dose fall-off outside target

10 or more beams (6 Mv) usually used (usu. 10-15)
- Multiple degrees of gantry and couch rotations (be aggressive)
- ALL non-opposing beams
- Noncoplanar fields encouraged
- Must check all beams @Linac prior to plan approval. 95% of time, collision.
- Ensure no overlap of beams at skin surface or just beneath if less than 10 beams.
- Effectively mimics radiosurgery of brain, Nothing like CFRT
A Phase II Trial of Stereotactic Body Radiation Therapy (SBRT) in the Treatment of Patients with Medically Inoperable Stage I/II Non-Small Cell Lung Cancer

Stereotactic Body Radiation Therapy (SBRT), 20 Gy per fraction for 3 fractions over 1½-2 weeks, for a total of 60 Gy

Patient Population: (See Section 3.0 for 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*. Patients with T3 tumors based on mediastinal invasion or < 2 cm toward carina invasion are not eligible.
RADIATION THERAPY ONCOLOGY GROUP

RTOG 0618

A Phase II Trial of Stereotactic Body Radiation Therapy (SBRT) in the Treatment of Patients with Operable Stage I/II Non-Small Cell Lung Cancer

**Patient Population:** (See Section 3.0 for Eligibility)
Patients with T1, T2 (≤ 5 cm), T3 (≤ 5 cm), N0, M0 operable non-small cell lung cancer; patients with T3 tumors must have chest wall primary tumors only; no patients with tumors of any T-stage in the *zone of the proximal bronchial tree*. Patients with T3 tumors based on mediastinal invasion or < 2 cm toward carina invasion are *not* eligible.
RTOG 0813

RADIATION THERAPY ONCOLOGY GROUP

RTOG 0813

Seamless Phase I/II Study of Stereotactic Lung Radiotherapy (SBRT) for Early Stage, Centrally Located, Non-Small Cell Lung Cancer (NSCLC) in Medically Inoperable Patients

SCHEMA

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<th>Dose Level</th>
<th>Level 1</th>
<th>Level 2</th>
<th>Level 3</th>
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<td>52.5 Gy</td>
<td>55 Gy</td>
<td>57.5 Gy</td>
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*Protocol treatment begins at Level 5. Levels 1-4 will be employed if dose-limiting toxicity is seen with the Level 5 (10 Gy) starting dose.*

Patient Population: (See Section 3.0 for Eligibility)

Patients with stage T1-2, N0, M0, non-small cell lung cancer, tumor size ≤ 5 cm, who are not candidates for a complete surgical resection in the opinion of a thoracic surgeon, only patients with tumors within or touching the zone of the proximal bronchial tree or adjacent to mediastinal or pericardial pleura (see Section 3.1.5 for details).
RTOG 0915

RADIATION THERAPY ONCOLOGY GROUP

RTOG 0915
(NCCTG N0927)

A RANDOMIZED PHASE II STUDY COMPARING 2 STEREOTACTIC BODY RADIATION THERAPY (SBRT) SCHEDULES FOR MEDICALLY INOPERABLE PATIENTS WITH STAGE I PERIPHERAL NON-SMALL CELL LUNG CANCER

Patient Population: (See Section 3.0 for Eligibility)
Medically inoperable, biopsy proven early stage T1, T2 (< 5 cm) NSCLC patients; clinically node negative by PET, with peripherally located tumors (> 2 cm in all directions around the proximal bronchial tree; see figure below)

ARM 1: 34 Gy in 1 Fx

ARM 2: 48 Gy in Once-Daily Consecutive Fx
RTOG 0631

RADIATION THERAPY ONCOLOGY GROUP

RTOG 0631

PHASE II/III STUDY OF IMAGE-GUIDED RADIOSURGERY/SBRT FOR LOCALIZED SPINE METASTASIS

- Phase II: 16 Gy in OneFx

- Phase III:
  - Arm 1: 16 Gy in One Fx
  - Arm 2: 8 Gy in One Fx
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<th>B</th>
<th>C</th>
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Additional Anatomic Sites

- Head and Neck
- Prostate
- Pancreas
- Kidney
- Retroperitoneal Tumors
CONCLUSIONS

- Large doses per fraction associated with increased late effects.
  - Normal tissue tolerances to SBRT doses remain unclear.

- Toxic late effects may not become manifest for years after tx

- More research is to be done with LQ Model and BED at such high doses.

- If starting an SBRT program, site visit is highly recommended.
  - Include MD, Medical Physicist, CMD and an RTT on the visit
  - Many more details to cover not covered today.
References

Megavoltage Cone-Beam CT: System Description and Clinical Applications; Olivier Morin, Amy Gillis, Josephine Chen, Michèle Aubin, M. Kara Bucci, Mack Roach, Jean Pouliot; Medical Dosimetry; Spring 2006 (Vol. 31, Issue 1, Pages 51-61).


Extracranial Stereotactic Radiotherapy and Radiosurgery; Ben J. Slotman, Timothy D. Solberg, Dirk Verellen; Taylor and Francis Group, 2006.
