Handout for Part I of the Refresher Course

Introduction to Extracranial Stereotactic Radiosurgery: (I) Physics and Technology, (II) Clinical Experience, (III) Radiobiological Considerations and Future Directions,

Stanley H. Benedict, Ph.D., Danny Song, MD, and Brian D. Kavanagh, MD, MPH

ESRT Part I: Physics and Technology

Presented by Stanley H. Benedict, PhD

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1. INTRODUCTION

This refresher course on Extracranial Stereotactic Radiosurgery (ESRT) will be presented in three parts, in order to cover the pertinent issues of physics and dosimetry, clinical experience, and radiobiological considerations and future directions.

Part 1: Physics and Technology,
Presented by Stanley H. Benedict, PhD
Virginia Commonwealth University, Medical College of Virginia Hospitals

Part 2: Overview of Clinical Experience,
Presented by Danny Song, MD
Virginia Commonwealth University, Medical College of Virginia Hospitals

- Patient selection considerations
- Review of reported clinical findings for treatments (lung, liver, etc)
- Prescription considerations: GTV, margins, adjacent critical regions, PITV,
- Why even consider ESR? ie, emphasis on clinical background
- Justification of ESR with general observations about gradual improvements in systemic treatment that justify aggressive treatment of solitary metastasis,
- Virtues of ESR as less invasive than surgery or other more invasive strategies
- Summary of reported outcomes form various series of liver and lung ESR

Part 3: Radiobiologicl Considerations and Future Directions
Presented by Brian Kavanagh, MD, MPH
Brian D. Kavanagh, MD, MPH
University of Colorado Health Sciences Center, Anschutz Cancer Pavilion

- Future Directions
- Biological evaluations: EUD, NTCP, etc
- Fractionation strategy (1 to 5 fractions, QOD, QD, etc)
- Chemotherapy
- Future approaches and goals
- Description of ongoing protocols—future goals

2. ABSTRACT OF INTRODUCTION TO EXTRACRANIAL STEREOTACTIC RADIOSURGERY: (I) PHYSICS AND TECHNOLOGY

This refresher course on Extracranial Stereotactic Radiosurgery (ESR) will be presented in three parts, including reviews of the current issues of (I) physics, dosimetry, and technology, (II) clinical history and experience, and (III) radiobiological considerations and future directions. The development of software and hardware components applied to radiosurgical treatments for specific extracranial tumors has been dramatic in recent years. In the physics and technology section the focus of the review will be on the high resolution beam delivery systems currently available and the precision patient specific immobilization and verification technologies that have been developed for ESR. A brief review of the novel developments and options in beam delivery systems will be presented, including intensity modulated radiotherapy with micro-multi-leaf collimator systems. Secondly, an overview will be presented of the successful practices of patient immobilization, simulation and relocalization/repositioning verification, and organ motion management, including infra-red technology to monitor patient positioning and the potential for optimized delivery with respiratory gating. These developments in beam delivery systems and patient immobilization and verification devices serve to provide the necessary technology for highly escalated doses to well defined gross tumor volumes and minimized damage to surrounding tissue and vital structures.

3. EXTRACRANIAL STEREOTACTIC RADIOSURGERY – What's in a name?

- ESRT is the use of external beams to treat lesions of the body with "surgical" doses and high precision tumor identification and relocalization employing "stereotactic" image guidance or implanted fiducials.
- Extracranial stereotactic radioablation/radiosurgery/radiotherapy
- Therapy vs. Surgery vs. Ablation
- According to the chief CPT code developer it will be called:

  Stereotactic Body Radiotherapy

4. ESRT REQUIRES:

- Higher confidence in targeting
- Reliable mechanisms for generating focused, sharply delineated dose distributions
- Specifically:
  a. Ability to describe the location of the target as a function of time
     - Reliable accurate patient positioning accounting for target motion related to time dependent organ movement
  b. Ability to shape the prescription isodose surface to the outline of the target volume surface itself
     - Generally requiring multiple beam directions with precise blocks, MLC, or cones
  c. Ability to construct radiation dose distributions with very rapid fall-off of dose from tumor to healthy tissues.
     - Requires a relatively large number of non-opposing beams/arcs to avoid entrance/exit beam interactions, preferably non-coplanar

* Timmerman et al, *Technology in Cancer Research and Treatment* – 2003

5. OVERVIEW OF PHYSICS AND TECHNOLOGY FOR ESRT

- CT simulation
  - Determine if pt can tolerate immobilization
  - Assess tumor motion
- Immobilization
  - Custom fitting device to minimize motion
  - Minimize breathing effects (training, breathing restriction, gating)
- Planning
  - Small field dosimetry issues
  - Inhomogeneity corrections
  - Hot spots in GTV
  - Fixed fields, IMRT, Dynamic Arcs
- Repositioning
  - Set-up pt in simulated position
- Relocalization
  - Identify tumor in treatment field
- Treatment delivery techniques
  - Fixed Field Bouquets, Novalis, Cyberknife, Cones, μMLC

* Hadinger et al *Med Phys*. 2002.
* Hamilton et al, *Stereotactic Funct Neurosurg*, 1996
* Lohr, et al *Int J Radiat Oncol Biol Phys* 1999

6. An overview of the generalized systems utilized for ESRT include:

- High precision beam delivery systems (micro-MLC, cones)
- Custom fitting, high reproducibility, body immobilization devices
- Patient positioning and relocalization verifications systems using:
  IR, LED, US, Video (Active and Passive markers)
- Relocalization: CT prior to tx, ASi EPID, Dual KV Xray, and
  Implanted markers and/or set-up fiducials
- Motion tracking and gating systems, and automated breathing control systems
- Real-time tumor tracking systems and EPID Image guidance systems for on-line treatment verification

7. Treatment delivery technology and physics/technical problems

- Immobilization and repositioning techniques : external fiducial systems and patient/skin-marker systems.
- Patient positioning verification techniques, including EPID, IR markers, and video, LED systems.
- Beam delivery options: mini/micro-MLC, IMRT, d-arcs, robotic arm technology, etc.
- Problems associated with dosimetry of small/narrow field geometry
- Problems associated with small field inhomogeneity calculations in the lung
- Dose uniformity planning strategies (inclusion of intentional >50% hot spots)
- Patient prescription strategies (Radiobiological considerations, NTCP)
- Patient, organ and tumor motion (Margins, Gating, Patient monitoring, Breathing strategies)

8. Some commercial systems that market products for use in ESRT include:

- The following commercial systems will be reviewed briefly in terms of various characteristics that may be employed to increase confidence, precision, and verification for ESRT.
- No institution employs all or even the same measures … as far as I know
  1. Elekta Stereotactic Body Frame, Image Guidance Synergy Platform
  2. BrainLab ExacTrac IR patient positioning, Novalis Image Guidance
  3. Accuray Cyberknife – Robotic image guided radiosurgical system
  4. Precise Therapeutics patient immobilization and relocalization system
  5. Medical Intelligence BodyFix patient immobilization
  6. NOMOS, Bat Ultrasound Guidance system
  7. Helical Tomotherapy, Madison WI
  8. Zmed Linac Scalpel™ System

  .... And a wide array of customized institution specific devices (MSKCC, UCLA, VCU)

9. IMMOBILIZATION: Medical Intelligence - Features:

- Integrated indexed patient positioning
- Minimizes respiratory motion
- Accurate Non-Invasive Repeat Positioning
- Dual vacuum technology: Custom-Mold and Patient Immobilization
- Radio-translucent materials

10. ELEKTA STEREOTACTIC BODY FRAME

The frame has built-in reference indicators for CT or MR determination of target coordinates. A diaphragm control attached to the frame can be used to minimize respiratory movements. Horizontal positioning of the frame, in the scanner or on the treatment couch, is achieved using an adjustable base on the frame.

11. ELEKTA STEREOTACTIC BODY FRAME

Reproducible positioning

Marker devices are used for reproducible positioning, after fixation of the patient in a vacuum pillow. A chest marker device, attached to the arc-ruler on the frame, is used for alignment of the patient. This is based on two skin marks over the patient's sternum. Longitudinal alignment is controlled by skin marks over the tibia using a frame-mounted laser. The co-ordinates used for patient positioning can be easily read on the arc-ruler and on the longitudinal ruler, along which the arc-ruler can be moved.

12. TREATMENT PLANNING – CAN WE DELIVER WHAT WE PLAN?

How are volumes defined?

13. HIGH PRECISION REPOSITIONING

- Fiducials on the set-up frame
- Skin marks/tattoos
- Infrared Patient Tracking
- Video Camera Tracking
- KV Xray technology

14. BRAINLAB – EXACTRAC REPOSITIONING VERIFICATION

15. BRAINLAB EXACTRAC REPOSITIONING VERIFICATION COMPONENTS

- **Reflective Body Markers**

Positions of your choice of Individual Marker Configuration

- **Infrared Camera Technology**

Detection of patient position
Permanent patient monitoring
Tracking accuracy 0.3mm

- **Video Camera**

Independent Verification and Documentation Images

- **X-ray sources**

150 kV imaging (Nominal focal spot: 0.6 mm) of bony structures or implanted markers and amorphous silicon detector. ASi high quality digital images: Resolution: 512 x 512 Pixels Receptor area: 204.8 x 204.8 mm^2 Accuracy: ± 0.2 mm

***** Soet, et al: Initial clinical experience with infrared-reflecting skin markers in the positioning of patients treated by conformal radiotherapy for prostate cancer, IJROBP 52:694-698, 2002.

* Wang LT, Solberg TD, Medin PM, Boone R. Infrared patient positioning for stereotactic radiosurgery of extracranial tumors.Comput Biol Med. 2001 Mar;31(2):101-11.

16. BRAINLAB EXACTRAC REPOSITIONING VERIFICATION - PHOTO INSERT

17. TREATMENT DELIVERY TECHNIQUES

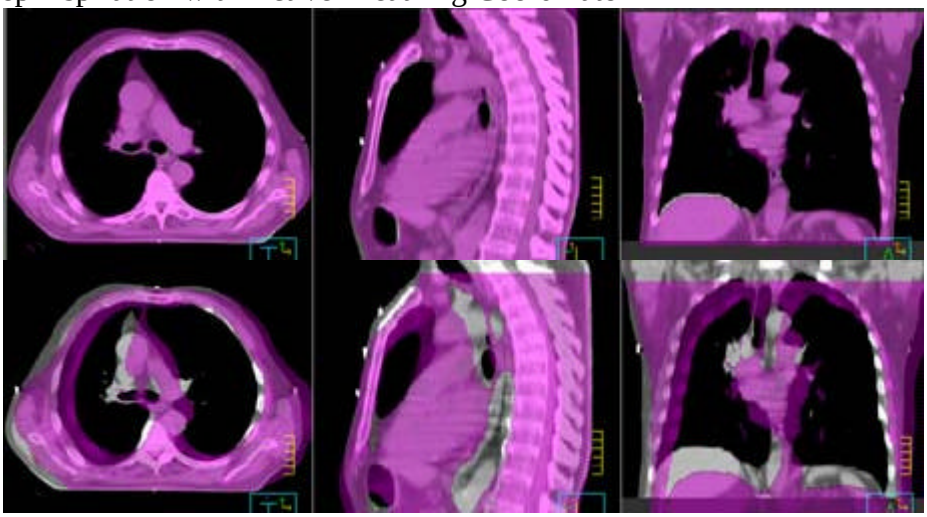
Impact of gating (respiratory/cardiac)
Beam delivery options: mini-MLC, IMRT, d-arcs (inhomogeneity vs uniformity)
Cyber-Knife

18. ACTIVE BREATHING CONTROL

Active Breathing Coordinator™ allows clinicians to pause a patient's breathing at a precisely indicated tidal volume and coordinate delivery with this pause. Using this technique for treatment of Hodgkin's Disease, clinicians have shown a median reduction of 12% lung mass irradiation1. It is also particularly useful for tangential fields in left breast treatments. By treating only when the heart is visibly out of the field, clinicians can reduce significantly or even eliminate irradiation of cardiac tissue.

19. ACTIVE BREATHING CONTROL

Moderate deep inspiration without Active Breathing Coordinator™
Moderate deep inspiration with Active Breathing Coordinator™



Overlaid scans of a patient at moderate deep inspiration. Two scans, six weeks apart and fused based on bony anatomy and external markers. Purple denotes regions of agreement, gray denotes disagreement

Jannifer S. Stromberg, M.D., Michael B. Sharpe, PH.D., Leonard H. Kim, M.M., Vijay R.Kini, M.D., David A. Jaffray, PH.D., Alvaro A. Martinez, M.D., FACR, and John W. Wong, PH.D.Department of Radiation Oncology, William Beaumont Hospital, Royal Oak, MI Active Breathing Control (ABC) for Hodgkins Disease: Reduction in Normal Tissue Irradiation with Deep Inspiration and Implications for Treatment Int J Radiat Oncol Biol Phys. Vol. 48, No. 3, pp.797-806, 2000.

Sixel K.E., Aznar M.C., Ung Y.C. Deep Inspiration Breath Hold to Reduce Irradiated Heart Volume in Breast Cancer Patients Int J Radiat Oncol Biol Phys. Vol. 49, No. 1, pp.199-204, 2001.

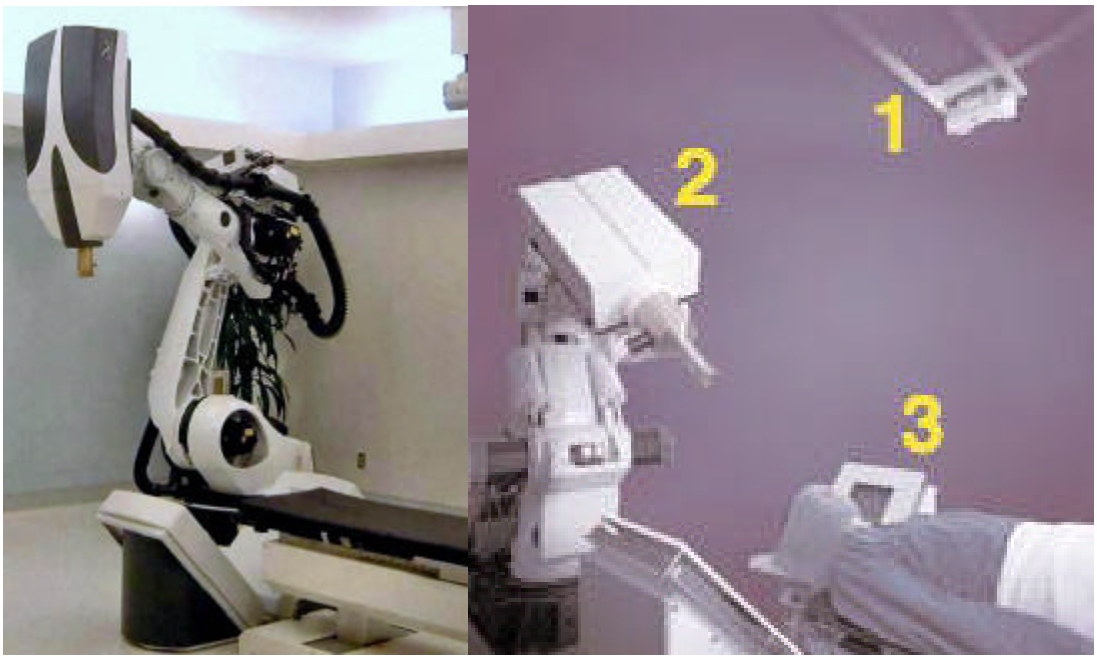
20. CYBER-KNIFE

(1) Real-time diagnostic imaging system with dual amorphous silicon detectors
(2) Robotically-mounted 6MV X-band LINAC with circular collimators from 5mm to 60mm (field diameter at 80 cm SAD)
(3) Control loop from imaging system to robot for automatic beam alignment & tracking

(4) Dedicated treatment planning system allowing both forward and inverse planning
(5) Cranial target localization based on bony anatomy
(6) Spine target localization based on implanted fiducials
(7) Soft tissue tumor localization based on implanted fiducials
(8) Synchronous tracking of breathing motion at a few selected Beta test sites

***** Chang et al , Neurosurgery. 2003

21. CYBER-KNIFE
Photo and Schematic of the technique to track breathing motion.



22. CYBER-KNIFE: *Compact linac moving in synchronization with a lung tumor*
VIDEO: Note there is a marker on the patient's chest that is continually tracked with an LED/camera system. The marker position is correlated with the tumor position observed in radiographs taken every few seconds. The correlation allows the tumor position to be inferred between radiograph acquisitions, and then sent to the robot to direct the beam.

* Murphy, et al, *Med Phys* 1997
* Murphy, et al, *Med Phys* 1996

23. CyberKnife stereotactic radiosurgery system uses image guidance technology.

- Utilizes the skeletal structure of the body as a reference frame — no invasive frame is needed.
- Continually monitors and tracks patient position during treatment.

1. Ceiling-mounted KV X-ray sources image patient's tumor treatment area
2. ASi image detectors capture X-ray images from ceiling-mounted X-ray sources
3. Operating system correlates patient location detected by image guidance system with reconstructed CT scan and directs robot to adjust position accordingly

4. Compact linear accelerator mounted on a computer-controlled robotic arm which adjusts position to maintain alignment with target, compensating for any small patient movement uses X-band technology for mobility

24. Med Tec pReference® frameless stereotaxy

Northwest Medical Physics Equipment's (NMPE)

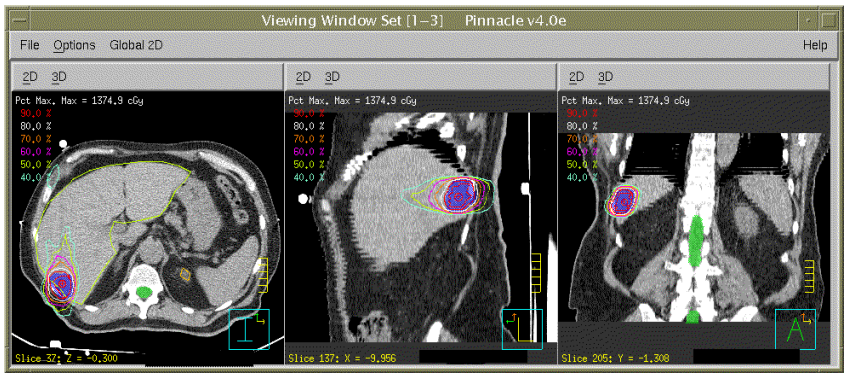
pReference is the original frameless system for fractionated stereotactic radiotherapy and single dose radiosurgery. pReference means "point reference" implanted fiducial technology for verified-accuracy, efficient, cost-effective stereotaxis. pReference is available in comprehensive and remote planning configurations.

Implanted Fiducial Technology –

Tiny gold markers establish a permanent, accurate, internal patient reference system. Image-guided software verifies submillimeter localization accuracy for all setups.

Extracranial stereotaxy Indications: hepatomas and hepatic metastases, pancreatic malignancy, pulmonary lesions, and spinal lesions

25. Liver and Lung Mets Planned with multiple Beams – SAMPLE CASES

26. 

27. INHOMOGENEITY CONCERNS

- **INHOMOGENEITY TISSUE/CALCULATIONS**

  - Inhomogeneity corrections were rarely an issue with cranial procedures but in lung/pelvis the situation is different.

- Calculations with small/narrow fields require verification because of the complicated/minimized lateral scatter, and loss of electronic equilibrium in inhomogenous tissue (lung).

* Solberg et al, TD.*Radiother Oncol*. 1998 Oct;49(1):73-84.
***** Jones et al *Med Phys.* 2003
***** Rustgi SN, *Phys Med Biol.* 1998
***** Wang et al, *Int J Radiat Oncol Biol Phys*. 2001

- **DOSE: HOT SPOT VS UNIFORMITY**

Dose gradient within the target are acceptable for ESRT since appropriate targets should contain no normal tissue. In fact, as long as an acceptable minimum dose is delivered to all parts of the target, higher target doses (hot spots) may be desirable if they facilitate steeper normal tissue dose fall-ff outside of the target within normal tissue. Moreover, these hot spots may be useful in treatinf hypoxic radioresitant cells in the tumor core.

* Lax et al, *Acta Oncol*, 1994

28. WITH ESRT THERE IS A DRAMATICALLY INCREASED NEED FOR TREATMENT DOSE AND POSITIONING VERIFICATION – AND DOCUMENTATION

29. SUMMARY: Potential solutions and approaches

- Gating (respiratory/cardiac), and breathing control systems
- On-line patient monitoring of repositioning and relocalization accuracy
- Requirements for and limitations of patient immobilization and repositioning
- Dose verification and in-vivo dosimetry strategies
- Dose specification and criteria for appropriate CTV/PTV margins
- High precision mMLC
- Radiobiological solutions

30. SUMMARY: Establish terminology and reporting conventions

- Prescription considerations: GTV, margins, adjacent critical regions, PITV, inhomogeneity and dose uniformity considerations
- Biological evaluations: EUD, NTCP, etc
- Fractionation strategy (1 to 5 fractions, QOD, QD, etc)

31. SUMMARY: Technical elements of QA

The physicist should be responsible for all technical QA procedures:

• Imaging equipment
• Localization and simulation equipment
• Treatment planning and evaluation system
• Treatment delivery equipment
• Treatment verification equipment

32. SUMMARY: Clinical elements of QA

A physician should carry out all clinical QA procedures:

• Consistent target volume and organs–at–risk delineation

- Quantitative assessment of target and organ motion during imaging and treatment
- Quantitative assessment of setup variation during imaging and treatment
- Patient–specific QA

33. Summary of Clinical Implementation of ERS – Problems and Approaches

- Recommended commissioning and acceptance-testing procedures
  - LINAC and beam delivery systems
  - Image guidance and immobilization/repositioning systems
  - Treatment planning systems
- Continuing QA procedures
  - Periodic QA protocol for system devices
  - QA/Verification/Recording procedures for clinical procedure
- New industry solutions and novel applications of existing technology
- Ideally patients should be enrolled in an IRB and/or departmental approval process considerations to address the clinical pros and cons of different options and treatment selection guidance.
- Estimate of the resources needed for establishing an ESRT program, including technique procedure, equipment, personnel, time for initial set-up and on-going processes.
- **As sophisticated as all of the equipment employed for ESRT can be "These ESRT techniques are unusual in the high technology realm of radiation treatment in that they require more specialized <u>training</u> of physicians and physicists rather than specialized <u>equipment</u>." (Timmerman et al).**

34. Acknowledgements

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Martin Murphy, PhD – Accuray
BrainLab, MedTec, CyberKnife, Medical Intelligence, Lebienger, Z-med

35. Bibliography of Body SRS & Frameless Stereotaxy

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