20 Years of Robotic Radiosurgery:

History, Practical Applications, and Future Opportunities

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Disclosures

None
Key Challenges in Radiation treatment

Knowing what to treat
› target delineation

Knowing how to get the radiation to the target
› Accuracy
› Precision

Avoiding consequence of collateral damage
› Understanding normal tissue tolerance
› Normal tissue avoidance
Learning Objectives

1. TO REVIEW THE EVOLUTION OF IMAGE-GUIDED ROBOTIC RADIOSURGERY AND ITS IMPACT ON EXPANDING THE TECHNIQUES AND INDICATIONS OF RADIATION TREATMENTS

2. TO REVIEW THE APPLICATIONS OF IMAGE-GUIDED ROBOTIC RADIOSURGERY FOR INTRACRANIAL AND EXTRACRANIAL CONDITIONS

3. TO EXPLORE THE EMERGING APPLICATIONS OF ROBOTIC RADIOSURGERY AND FUTURE CHALLENGES

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Milestones in Radiosurgery

1950’s- Lars Leksell and Gammaknife; coins the term “radiosurgery”
1980’s- Gammaknife and LINAC radiosurgery introduced in US
Leksell’s Gammaknife

- Highly accurate stereotactic localization
- Large number of cross-fired beams provide for steep gradient
- Rigid immobilization
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Adler spends time in Stockholm

- Uncertain Accuracy
- Painful for patient especially children
- Limited ability to fractionate
- Can only treat tumors in & around skull
Concept Drawings of CyberKnife

1988

1989

1990

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CYBERKNIFE™ Image-Guided Stereotactic Radiosurgery System

- Diagnostic x-ray tube
- 6 MV linear accelerator
- Secondary Collimator
- Robot Gantry
- Silicon x-ray detectors
- Patient couch

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1994- FDA approves “Neurotron 1000” for clinical investigation first time patient was permitted to be present within a robot workspace
1994
First use of term “image-guided” Radiosurgery

Planning, Calibration and Collision-Avoidance for Image-Guided Radiosurgery *

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First use of term “image-guided” Radiosurgery

In radiosurgery a moving beam of radiation is used as an ablative surgical instrument to destroy brain tumors. Classical radiosurgical systems rely on rigid skeletal fixation of the anatomic region to be treated. This fixation procedure is very painful for the patient and limits radiosurgical procedures to brain lesions. Furthermore, due to the necessity of rigid fixation, radiosurgical treatment with classical systems cannot be fractionated. A new camera-guided system capable of tracking patient motion during treatment has been built to overcome these problems. The radiation source is moved by a 6 degree-of-freedom robotic arm. In addition to offering a more cost effective, less invasive, and less painful treatment, the robotic gantry allows for arbitrary spatial motion of the radiation source. Based on this feature we can treat non-spherical lesions with accuracies unachievable with classical radiosurgical systems. The system introduces a new class of radiosurgical procedures, called non-stereotactic, or image-guided radiosurgery. At the heart of these procedures are algorithms for planning both a treatment and the corresponding beam motion, given the geometric description of the tumor shape and relative locations in the particular case.
June 4, 1994

First patient treated by robotic radiosurgery worldwide at Stanford
First CyberKnife Treatment: June 4, 1994
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History of the STANFORD Extracranial Radiosurgery Programs

- 1994 – Cyberknife introduced
- 1995 -first spine treated
Early Cyberknife Treatment
Spinal Radiosurgery: Lessons Learned

- Small **dose-volume effects** exist for spinal cord
- Hypofractionated/Single high dose fractions can yield **durable pain relief and tumor control** for benign and malignant tumors
- Previously untreatable **spinal cord AVM’s can be obliterated** without spinal cord injury
- Spinal radiosurgery is a viable **alternative to surgery** for spinal hemangioblastoma, and other spinal tumors

Stanford University
History of the STANFORD Extracranial Radiosurgery Programs

- 1994 – Cyberknife introduced
- 1995 -first spine treated
- 1997 – Pancreas
Phase I Study Design: Locally Advanced Pancreatic Cancer

- Patients treated at 15 Gy, 20 Gy, and 25 Gy in a single fraction (SBRT)

- All patients treated with Cyberknife
  - Breath-hold technique
  - Respiratory tracking (Synchrony)
Robotic Radiosurgery
Pancreas Cancer

Pre-treatment

Post-treatment
Conclusions from Phase I/II Clinical Studies of Robotic Radiosurgery for Pancreatic Cancer

25 Gy given in a single fraction is feasible and results in no significant acute GI toxicity

1-yr local Control across 4 independent studies is 84% (vs. 50-70% using conventionally fractionated radiotherapy)

Stereotactic radiotherapy improves quality of life

- Decreases pain, prevents gastric outlet obstruction, 1 day treatment
History of the STANFORD Extracranial Radiosurgery Programs

- 1994 – Cyberknife introduced
- 1995 - first spine treated
- 1997 - Pancreas
- ~1999 – Lung
- 2001 - FDA approval
To provide treatment planning and image-guided radiosurgery and precision radiotherapy for lesions, tumors, and conditions anywhere in the body when radiation treatment is indicated.”
First Publication of Robotic Radiosurgery for Lung Tumors

- First dose level for Phase I escalation study
  - 15 Gy in 1 fraction
  - 23 patients (25 tumors)
- Technique
  - 9 breath hold
  - 14 respiratory tracking
- Outcome
  - No Grade 3-5 toxicity
  - 1 with worsened COPD
  - 2 CR, 15 PR, 4 SD, 2 PD
Robotic Radiosurgery for Lung Tumors: Improved LC/Survival

Figure 3: Peripherally located stage I NSCLC in a medically inoperable patient, treated with CyberKnife SABR to a dose of 50 Gy in four fractions. There was a complete response with only minimal fibrosis surrounding the implanted markers (arrow), and no evidence of disease 26 months after treatment.
Accuray/CyberKnife History

- **1987**: Initial NIH research @ Stanford
- **1990**: Initial investor funding
- **1992**: Founded by John Adler, 1st Beta system sold/installed at Stanford
- **1994**: 5 Beta systems sold in the US
- **1996**: Approval from Japan's Ministry of Health and Welfare
- **1998**: Filed 510(K) with FDA
- **1999**: 8 CKs delivered
- **2000**: FDA 510(k) for full body
- **1999**: FDA 510(k) approval CNS
- **2001**: 30 systems shipped
- **2002**: Marketing and sales launch in US
- **2003**: 2nd CK installed at Stanford
- **2004**: Multiple Japanese orders received
- **2007**: Multiple Japanese orders received
- **2006**: $40 M + Profits
- **2006**: First Patient treated at Stanford
- **2000**: 200 systems installed
- **2002**: 2nd CK installed at Stanford
- **2007**: IPO
- **2001**: Respiratory tracking 510(k) received
- **1995-7**: Bootstrap
- **1990**: 5 Beta systems sold in the US
- **1994**: $12.2M Raised
- **1996**: Approval from Japan's Ministry of Health and Welfare
- **1999**: Marketing and sales launch in US
- **2001**: 30 systems shipped
- **2002**: Multiple Japanese orders received
- **2007**: IPO
CyberKnife® Treatment with Synchrony
Respiratory Compensation
Increasing Use of Stereotactic body radiotherapy

In recent US survey of >550 respondents

- Lung is most common site for SABR/SBRT
- Spine is 2nd most common
- Liver is 3rd most common site for


Figure 4. Cumulative adoption of stereotactic body radiotherapy is shown for the 3 most common disease sites treated: lung, spine, and liver.
CyberKnife History: Past Decade

- **2007**: Accuray, Inc. IPO (ARAY)
- **2008**: IRIS Collimator Sequential Optimization
- **2009**: Monte Carlo Calculation
- **2010**: Multiple Japanese orders received
- **2011**: 30 systems shipped, respiratory tracking 510(k) received
Stanford Cyberknife
Intracranial vs. Extracranial

Stanford Cyberknife 1994-2007

Year

# lesions

Extracranial
Intracranial

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History of the STANFORD Extracranial Radiosurgery Programs

- 1994 – Cyberknife introduced
- 1995 - first spine treated
- 1997 - Pancreas
- ~1999 – Lung
- 2001 - FDA approval
- 2003 – Prostate
- 2004 – Liver
- 2006 – 2nd Cyberknife installed
CyberKnife: A Disruptive Technology
CyberKnife History: Past Decade

- **2007**: Accuray, Inc. IPO (ARAY)
- **2008**: IRIS Collimator Sequential Optimization
- **2009**: Monte Carlo Calculation
- **2010**: Stanford treats 5000th patient
- **2011**: M6 Introduced
- **2012**: Multiple Japanese orders received
- **2013**: 30 systems shipped, respiratory tracking 510(k) received
- **2014**: 291 CK’s worldwide

Stanford treats 5000th patient
History of the STANFORD Extracranial Radiosurgery Programs

- 1994 – Cyberknife introduced
- 1995 - first spine treated
- 1997 - Pancreas
- ~1999 – Lung
- 2001 - FDA approval
- 2003 – Prostate
- 2004 – Liver
- 2006 – 2nd Cyberknife installed
- 2009 – 1st treatment of psychiatric d/o
- 2010 – 5000th patient treated
1348 Publications: Robotic Radiosurgery or Cyberknife Radiosurgery
Where do we go from here?
Milestones in Transport Innovation
Automobile
More Efficient than prior land travel

Trains
More Efficient and faster
Limited to land and bridges

Planes
Faster
Able to travel over bodies of water

Space Ships
Travel beyond earth
Milestones in Robotic Radiosurgery

- Early “Image-guided” Radiation
  Conventional RT with Fluoro

- Cyberknife- “Robotic Radiosurgery”
  image-guided precision brain SRS
  Early extracranial applications

- Cyberknife with Synchrony
  More Efficient and faster
  Respiratory tracking for moving targets

- Cyberknife G4
  Flexible platform with higher dose rate
  IRIS Collimator
Milestones in Robotic Radiosurgery

- Faster cars
  Automated and Driverless

- Better Trains
  More Efficient

- Better Planes
  More Efficient

- ??Future??
Where do we go from here?
Future of Robotic Radiosurgery

Noninvasive stereotactic radiosurgery (CyberHeart) for creation of ablation lesions in the atrium

Arjun Sharma, MD,* Douglas Wong, MD, PhD,† Georg Weidlich, PhD, ‡ Thomas Fogarty, MD, ‡ Alice Jack, † Thilaka Sumanaweera, PhD, † Patrick Maguire, MD, PhD †

Abscopal Effects after Conventional and Stereotactic Lung Irradiation of Non–Small-Cell Lung Cancer

Shankar Siva, MBBS, FRANZCR,* † Jason Callahan, BAppSci, MedRad, † Michael P. MacManus, MD, MRCP, FRCR, FRANZCR, † Olga Martin, PhD, MSc, † † Rodney J. Hicks, MBBS, MD, FRACP † and David L. Ball, MD, MBBS, FRANZCR †

FIGURE 2. Serial PET scans in the patient, focusing on changes in the left humerus metastasis (inset above) and the right adrenal metastasis (inset below). PET, positron emission tomography; SABR, stereotactic ablative radiation therapy.
Future Opportunities/Challenges

• Back pain
• Psychiatric disorders
• Cardiac
• Optimal use with Immunologic and biologic agents
• Novel radiation sources
Summary

- Advances in imaging and technology have paved the way for expanded applications in robotic radiosurgery.

- We must continue to work in an interdisciplinary way in order to define the indications and optimal populations suitable for innovative radiation techniques.
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