Proton Stereotactic Radiotherapy: Clinical Overview

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Acknowledgements

- Radiation Oncologists and Physicists at various institutions (MGH, MDACC, PSI, Clatterbridge, many more)

SRS History

- Gamma Knife original photon treatment (1950's)
- Ten years later (1960's): proton radiosurgery
- Linac based begun in 1980's and Cyberknife later
- Thousands of patients treated with Photon SRS—clinically proven technique

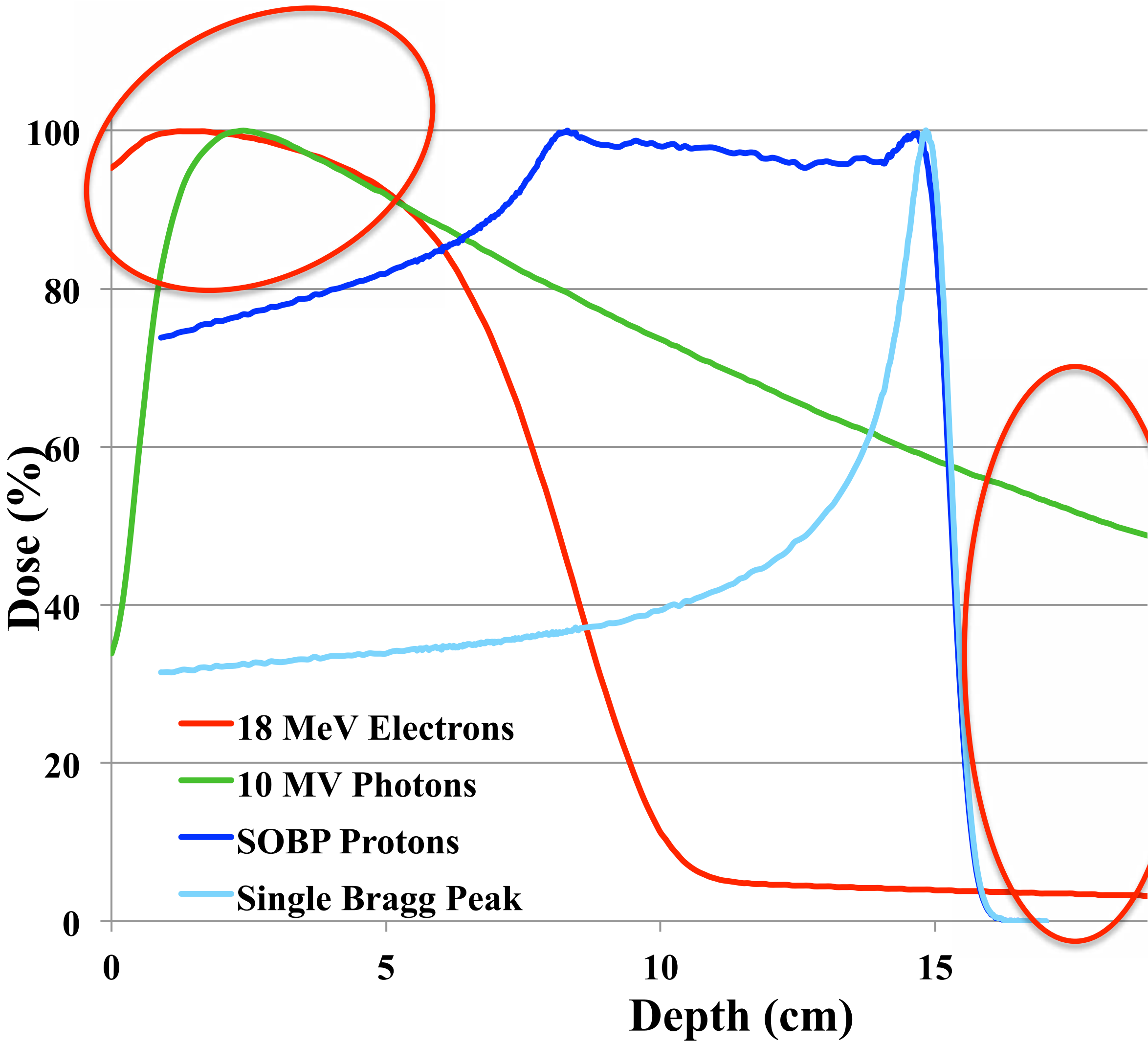
Stereotactic Proton Therapy

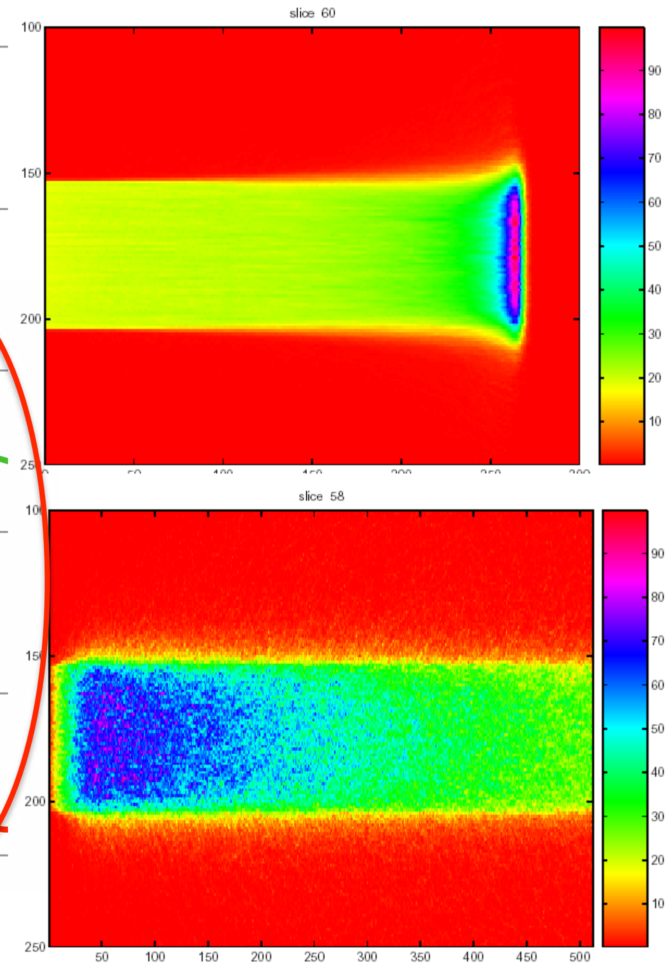
- Limited fractions (1-5)
- Higher doses/fraction
- Often smaller treatment volumes and smaller field sizes
- Magnified effects of random uncertainties

Why Proton SRT?

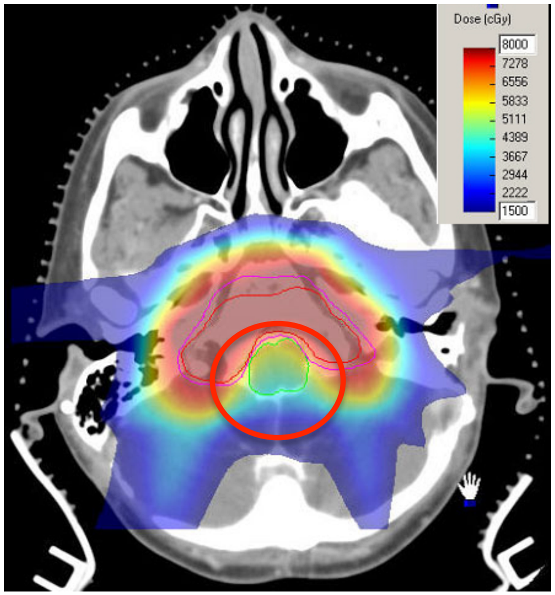
- Generally with respect to photon SRT
  - Distal Edge
  - Conformal for concave/complex geometries
  - Penumbra**
  - Integral Dose
  - **Higher TCP/Lower NTCP**

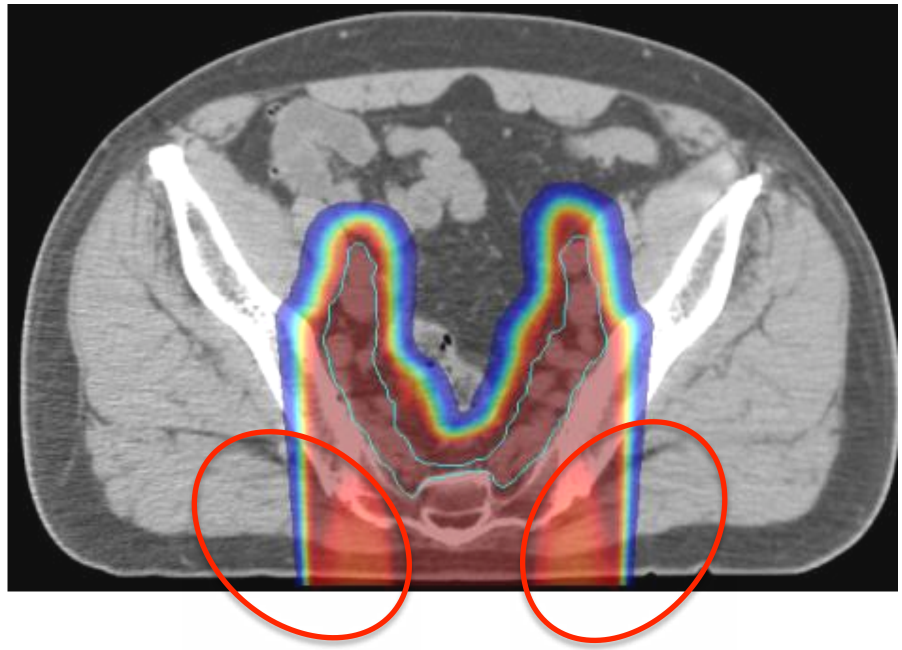
Dose Comparisons





Complex Geometries

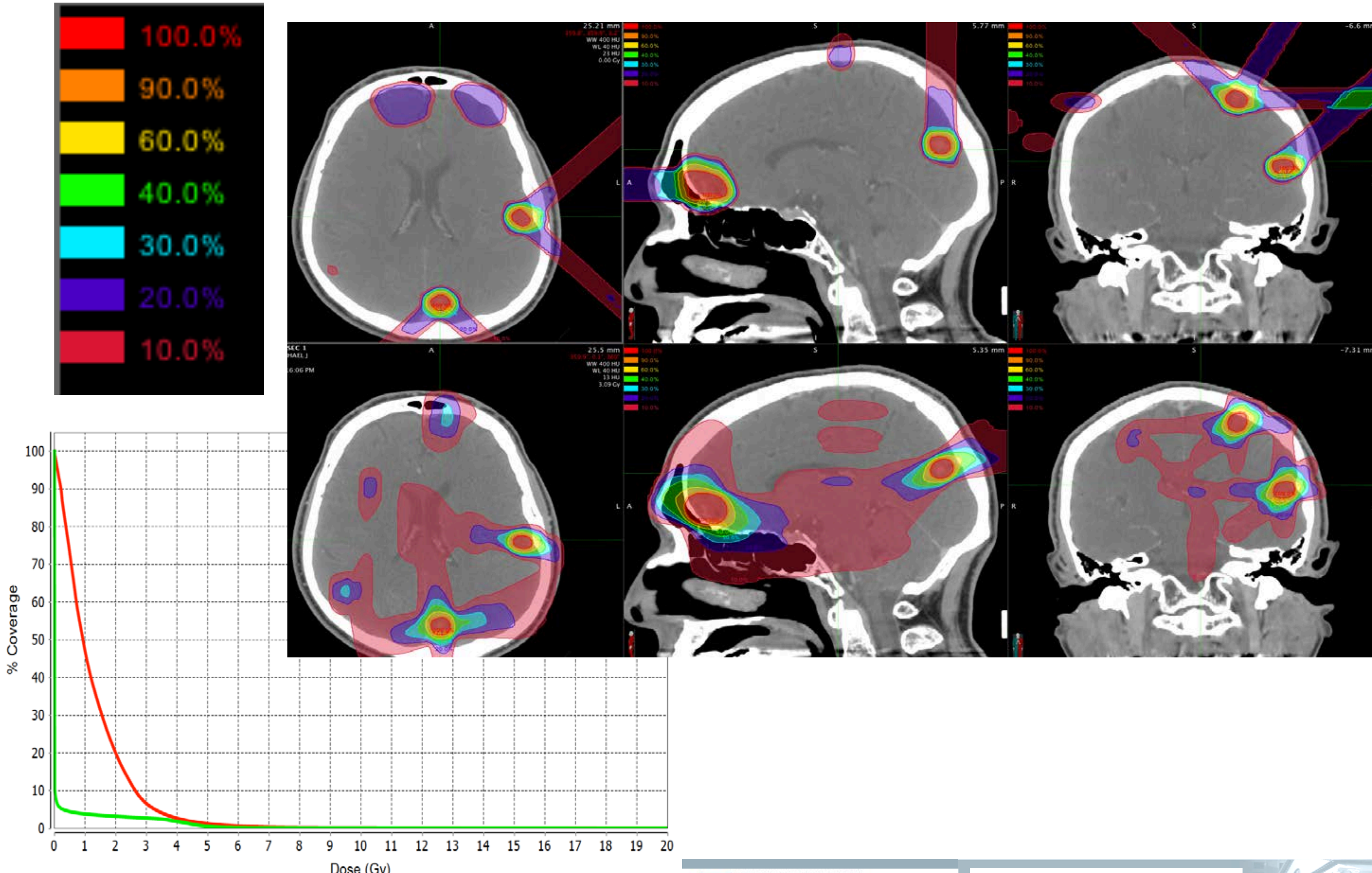




Penumbra

- Proton Penumbra can be sharper than photons but…
  - Air Gap
  - Range Compensator
  - Apertures
  - Spot Size
  - Beam Optics

Integral Dose

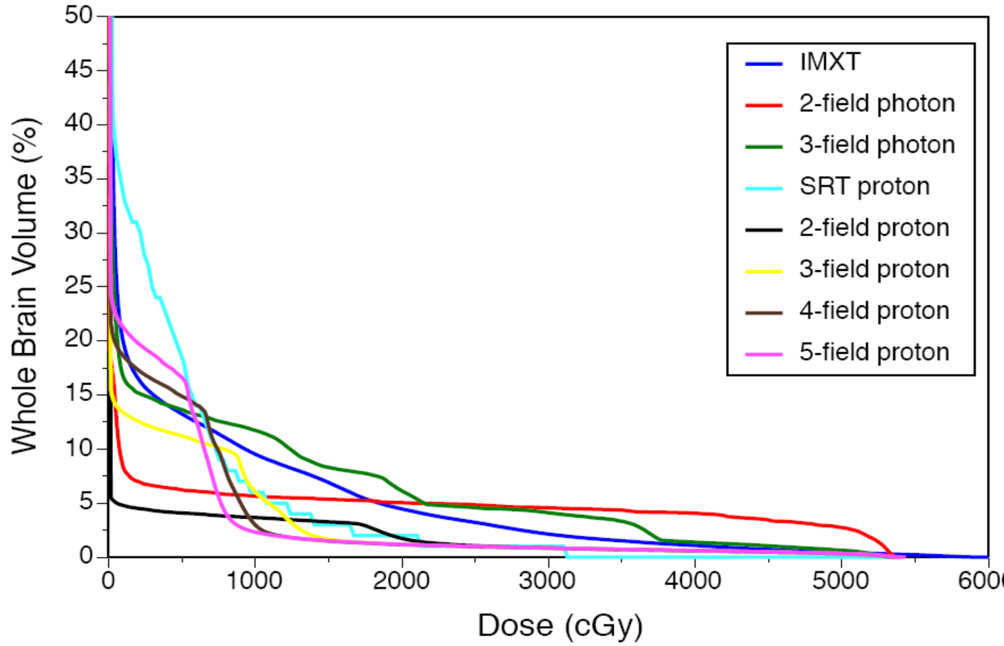


Integral Dose

- The V40% for protons is smaller than photons
- Due to the incorporation of uncertainties in planning, the conformality is tighter with photons for most SRT targets
- Abnormally shaped targets or targets close to an OAR can have tighter conformality
- Clinical Significance?

Proton SRT for Benign Cases: Secondary Cancer Risks

Acoustic → Sarcomatous Hanabusa, 2001
Acoustic → Glioblastoma Shamisa, 2001
AVM → Glioblastoma Kaido, 2001
Acoustic → Meningiosarcoma Thomsen, 2000
NF2 → Malig n. sheath (3 cases) Baser, 2000
NF2 → malignant meningioma Baser, 2000
NF2 → Malignant ependymoma Baser, 2000
Mening → Glioblastoma Yu, 2000
Acoustic → Malig Schwannoma Shih, 2000
Cav hem → Glioblastoma Salvati, 2003
Acromeg → Meningioma Loeffler, 2003
Acromeg → Vestibular Schwannoma Loeffler, 2003
AVM → Meningioma Sheehan 2006
Many more studies…



		Radiographic changes				
	Risk of 2nd cancer	Right temporal lobe		Left temporal lobe		Clinical symptoms
		EUD (Gy)	NTCP (%)	EUD (Gy)	NTCP (%)	NTCP (%)
SRT	32.1	23	<0.1	28	<0.1	<0.1
2-field photon	5.7	48	1.3	48	1.2	13
3-field photon	11.2	38	<0.1	40	0.1	2
IMRT	26.8	34	<0.1	37	<0.1	1
2-field proton	1.5	30	<0.1	35	<0.1	<0.1
3-field proton	4.3	29	<0.1	35	<0.1	<0.1
4-field proton	6.1	27	<0.1	34	<0.1	<0.1
5-field proton	6.8	26	<0.1	34	<0.1	<0.1

Winkfield, *et al*, 2011

Integral Dose and Risks: Mets

- Liver and lung toxicity
- Mediastinum
- Stomach and intestinal tract
- Spinal Cord
- Optics
- Brain dose and cognitive health

What is *not* a benefit of protons versus photon SRT?

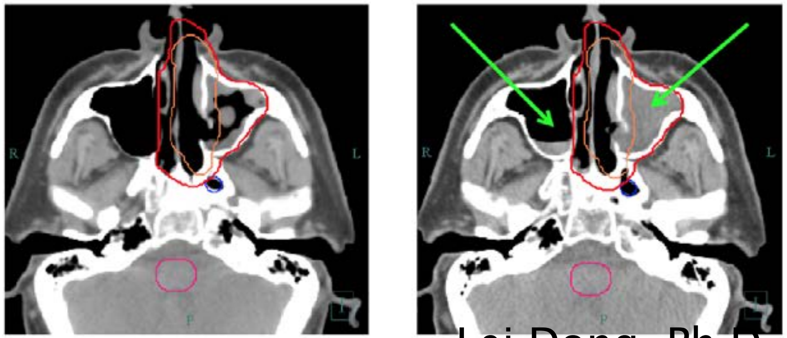
20%	1.	Distal dose reduction
20%	2.	Lower NTCP
20%	3.	Conformal for Complex Geometries
20%	4.	Less uncertainty in the dose delivery
20%	5.	Lower integral dose.

Uncertainties?

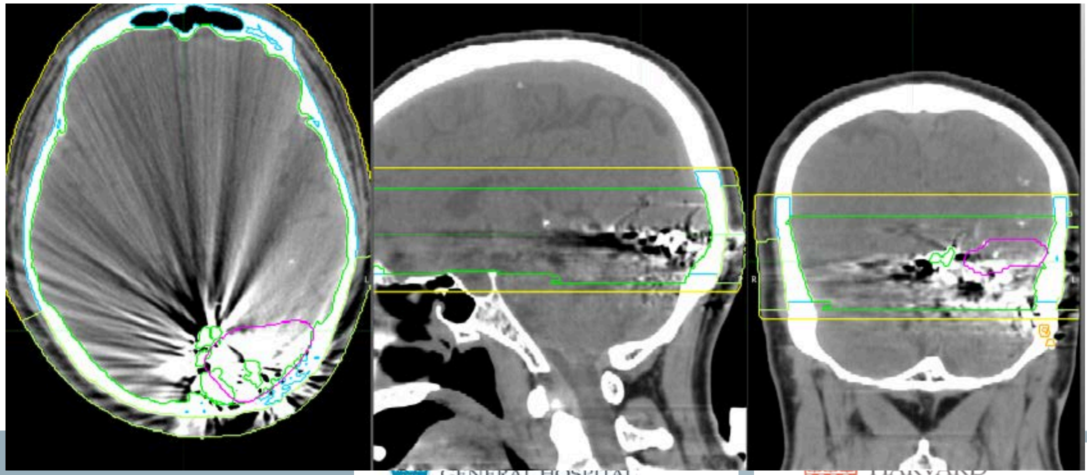
- Range uncertainties (CT, SPR, Motion, Setup, Geometric Patient Daily Variations)
- Motion-Miss Targets
- Field Size Effects
- Penumbra
- Online Imaging Limited
- ∴ Affect the conformality (Rx dose)

Proton range changes: Cranial SRT

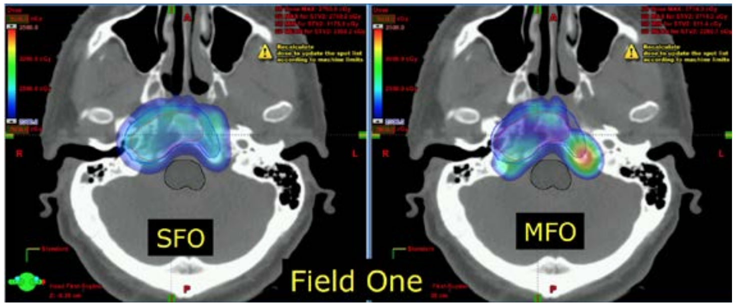
- Fluids in sinuses
- Scattering from heterogeneities
- Setup Uncertainties
- Air gap
- Onyx for AVM
  - Artifacts
  - WET

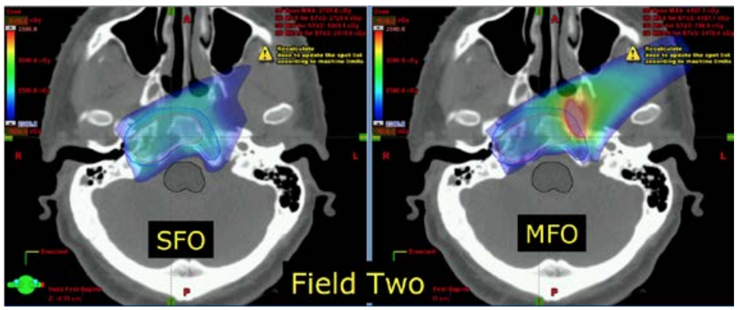


Lei Dong, Ph.D.



Intrafractional Motion





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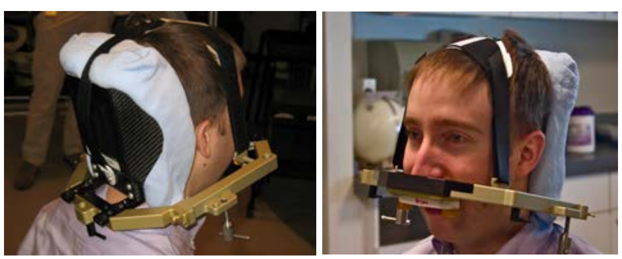
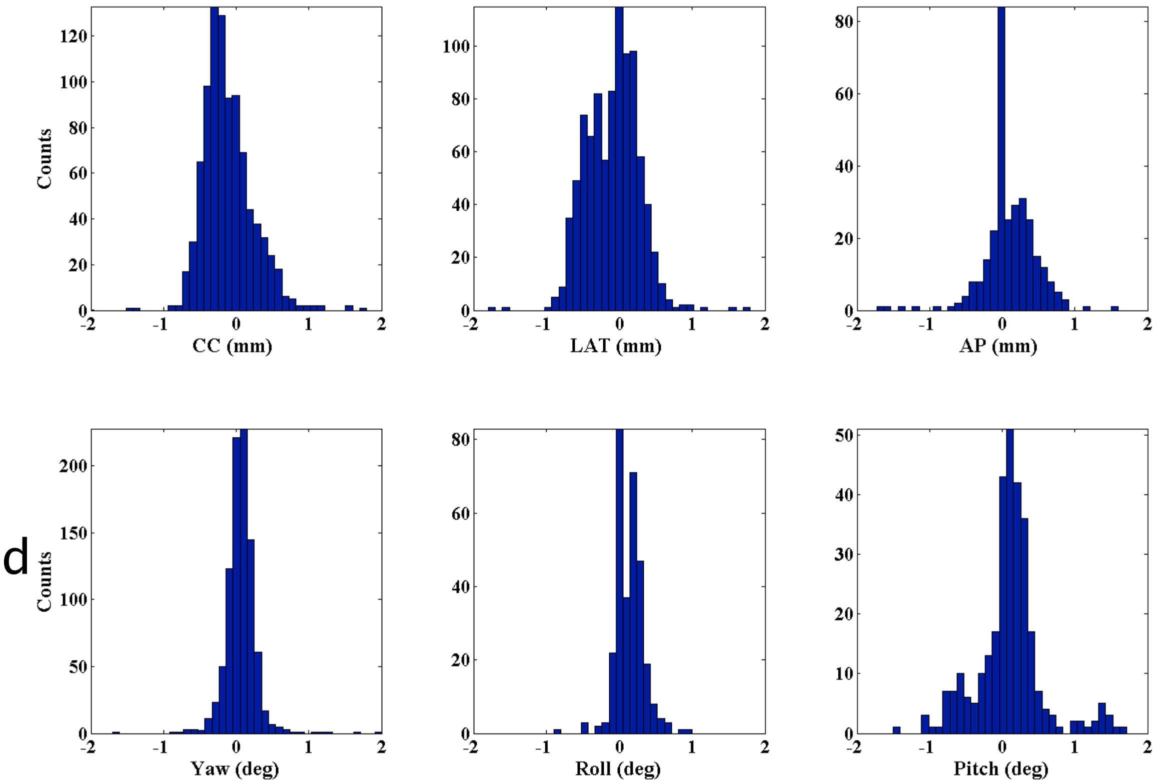
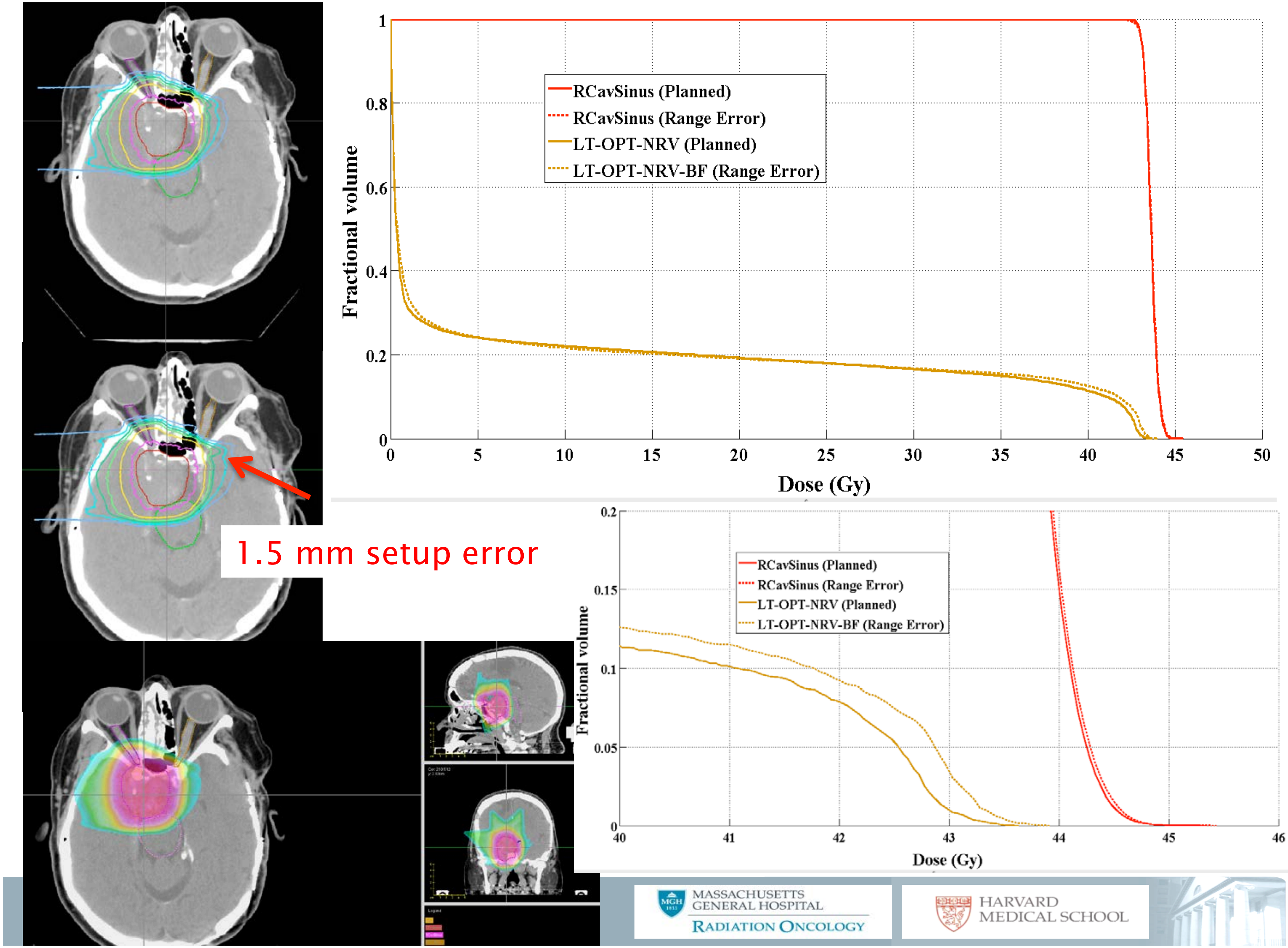
Impact on MFO Planning
Less impact on Passive Scattered



Cranial Intrafractional Motion



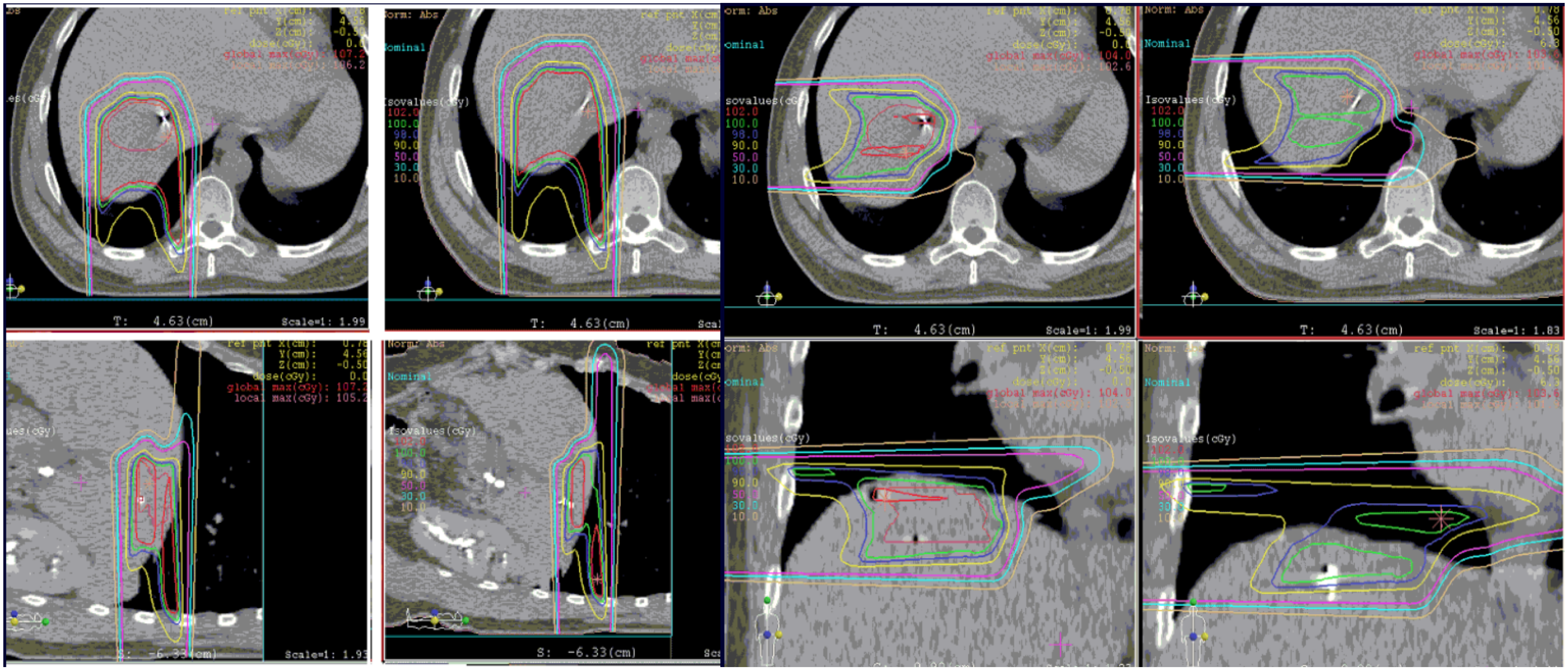


RCavSinus (Planned)
RCavSinus (Range Error)
LT-OPT-NRV (Planned)
LT-OPT-NRV-BF (Range Error)
Fractional volume
Dose (Gy)
1.5 mm setup error
RCavSinus (Planned)
RCavSinus (Range Error)
LT-OPT-NRV (Planned)
LT-OPT-NRV-BF (Range Error)
Fractional volume
Dose (Gy)
MASSACHUSETTS GENERAL HOSPITAL
RADIATION ONCOLOGY
HARVARD MEDICAL SCHOOL

Perils Due to MCS

- Multiple Coulomb Scattering (MCS)
- Range Uncertainties, especially along a heterogeneous boundary
- Motion Uncertainties in Heterogeneous Materials
- Differences in Output, PDD, and Penumbra compared to Photons

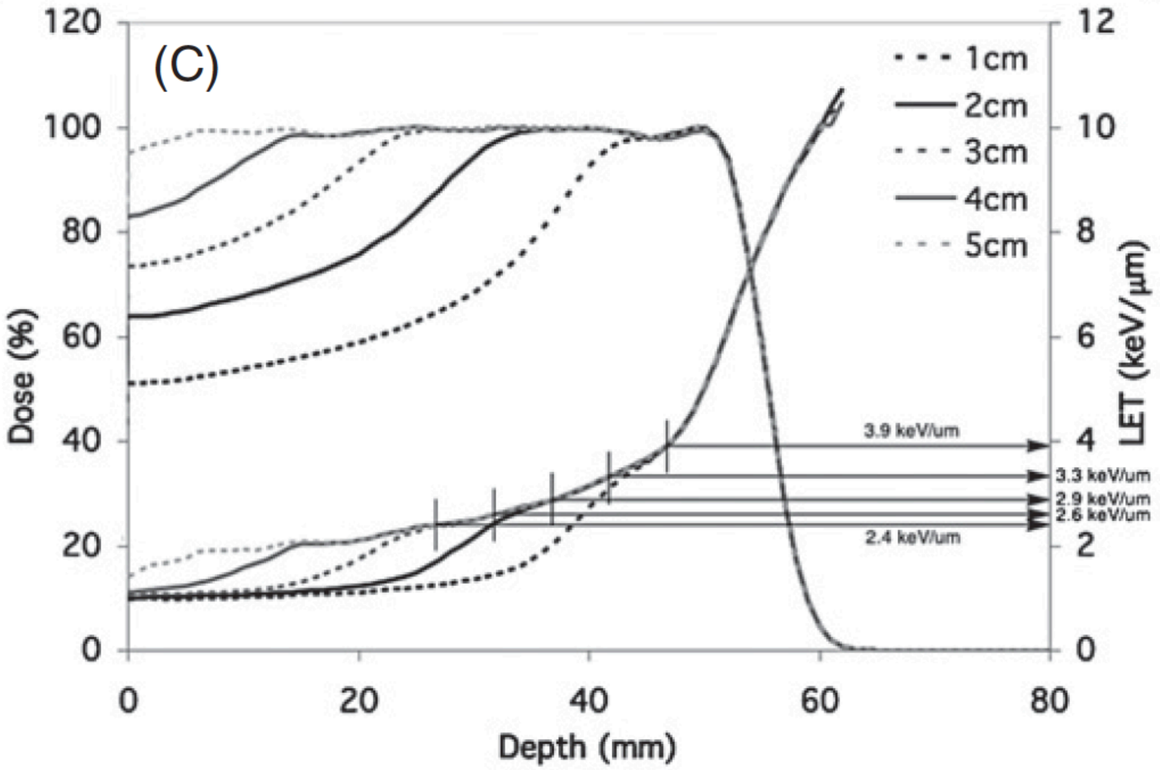
Liver Motion



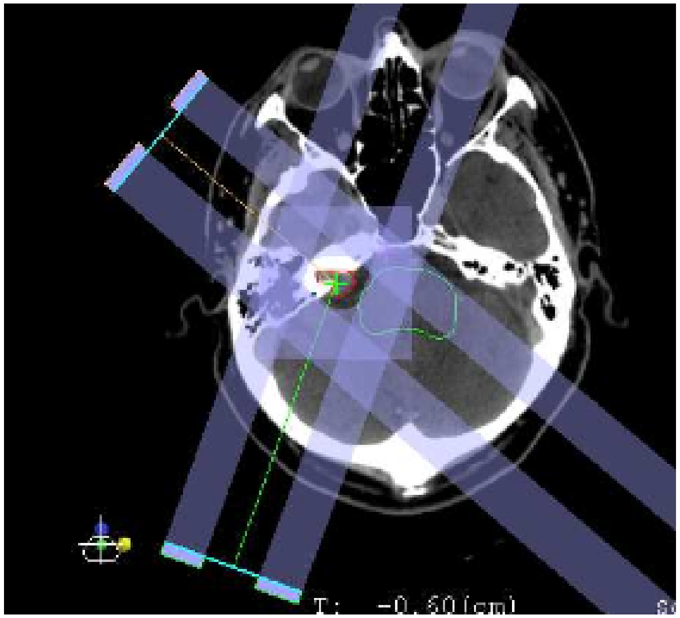
H-M Lu, Ph.D

LET/RBE

- Danger of the distal edge



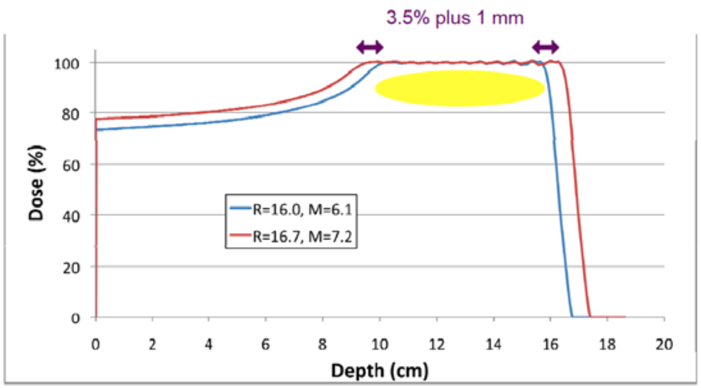
Bednarz, et al 2013

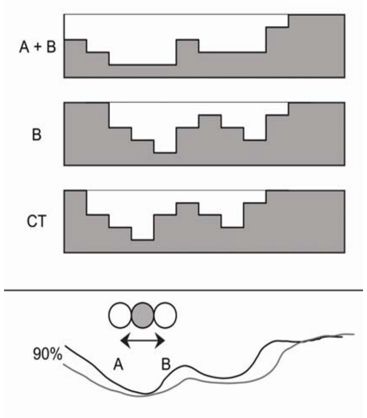


RBE for a single fraction??

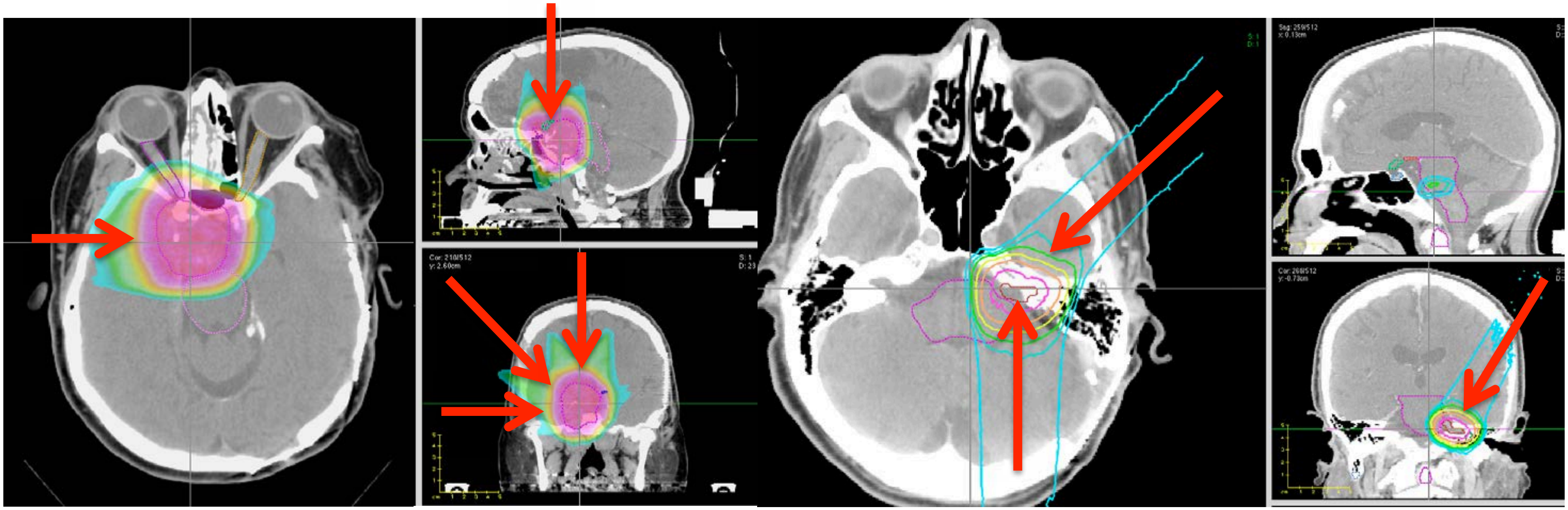
Uncertainty Mitigation

- What do we do with all of this information:
  - Margins: Distal/Proximal
  - Beam angle selection
  - Smearing
  - Feathering
  - Gating
  - OARs





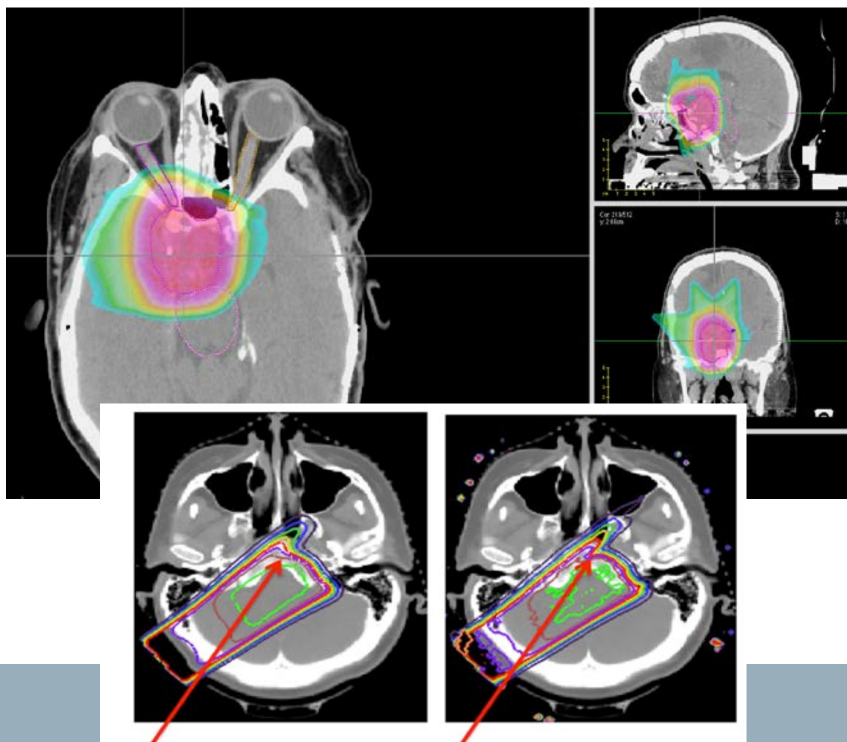
Beam Angle Selection

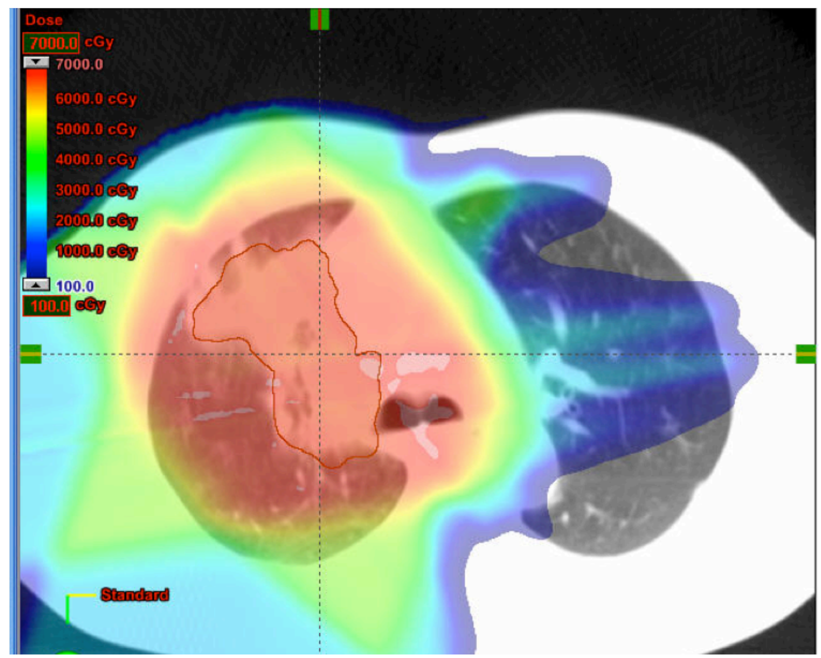


1. Avoid beam entrance angles along and through heterogeneous boundaries
2. Avoid distal edge sparing.
3. <u>Use multiple beams to reduce uncertainty of a single beam!</u>

OARs

- AVOID distal edge sparing!
- If unavoidable, use multiple fields to spread the risk and reduce the dose to the OAR if there is an error.

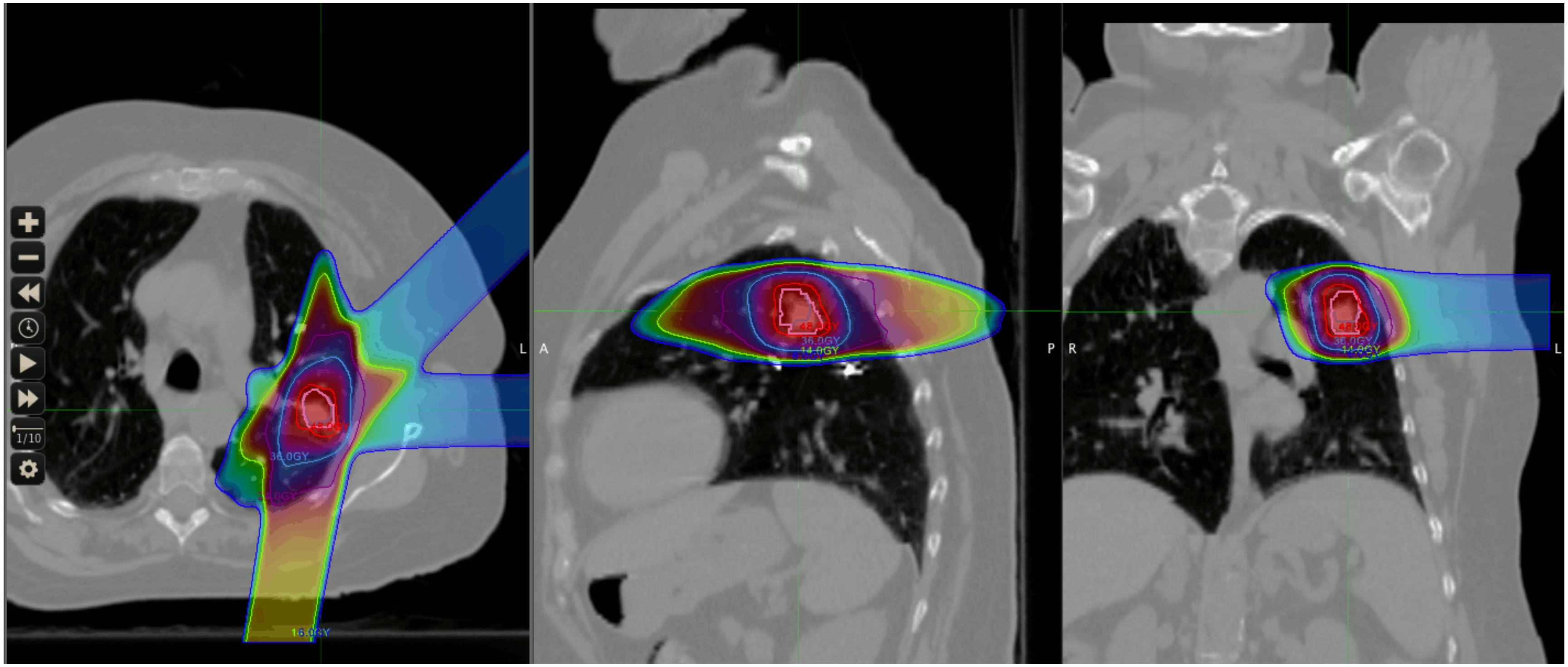




Gating

- Gating can greatly reduce the range uncertainties of targets close to the diaphragm where motion is typically the greatest

Large Margins: Range, Motion, Smearing



What is the best method to minimize the effects of dose delivery uncertainties in proton SRT?

20%	1.	Increased image guidance
20%	2.	Use multiple beams
20%	3.	Use a single beam
20%	4.	Increase the margins
20%	5.	If it moves, don't treat it.

Using Multiple Beams

- Spreads uncertainty due to range, patient setup, LET, and patient motion
- Difference in lateral and distal uncertainties
- Increases conformality for both scanned and scattered delivery
- Increased Robustness

Patient Setup

- Immobilizations similar to photons
  - Vac Lock bags
  - Masks and Frames
- Need to be aware of proton WET
- Image guidance:
  - Most 2D currently available
  - CT and CBCT coming soon
  - Patient motion, target motion, gantry wobble, Apertures, etc.

Routine QA

- Some QA common to Photons:
  - Output, flatness, symmetry, mechanical, isocentricity, etc.
- Differences:
  - Energy/Range dependent variables and device sensitivities
  - Machine specific factors (timing, feedback, scattering devices, etc)
  - Scanning versus Scattering

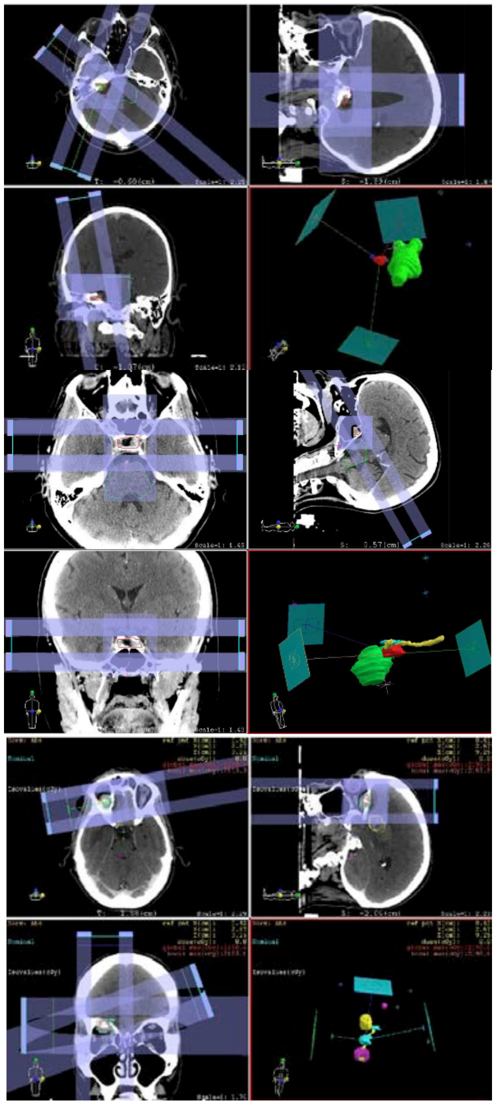
Treatment Sites

- Cranial and ocular targets are the most documented and historically most common
- Spines treated later (attached to rigid body surrogate)
- Recently: Body sites of lung, liver and pancreas

Cranial Patients Treated

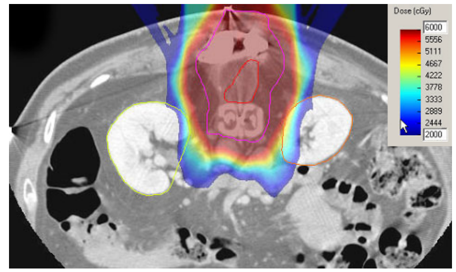
- Benign Neoplasms:
  - Acoustic Neuromas
  - Meningiomas
  - Pituitary Adenomas
- Arteriovenous Malformations
- Metastatic Lesions
  - Multiple Lesions
  - Close proximity to surface or critical structures (optics, brainstem)

Eyes: very high LC

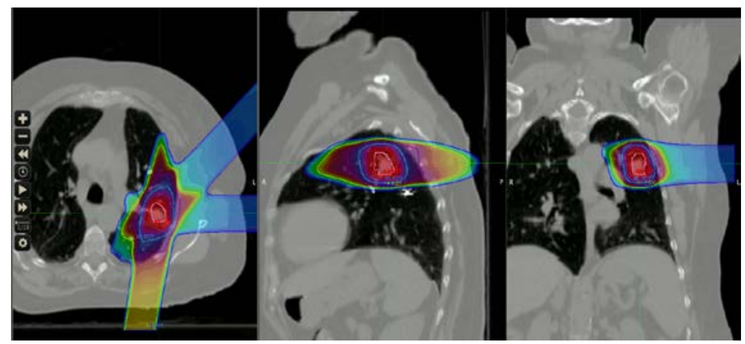


Extra-cranial Patients Treated

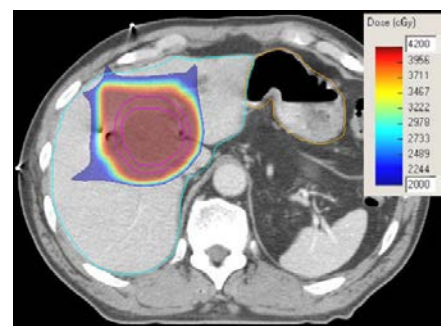
- Spine
  - Mets
  - Small primary lesions



- Lung
  - Multiple trials
  - Reduced V5 and V20
  - Reduces dose to contralateral lung



- Liver: Reduced liver toxicity
- Pancreas: Reduced digestive tract dose

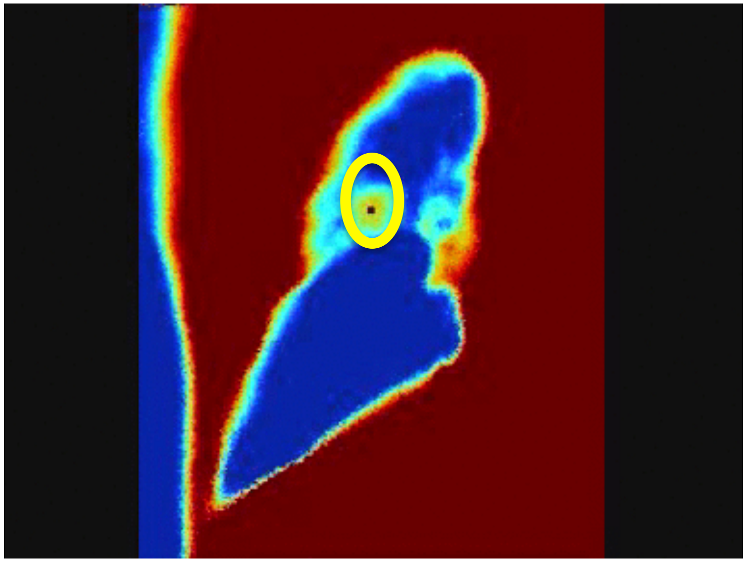


Which Proton SRT site is the most technically challenging?

20%	1.	Eyes
20%	2.	AVM
20%	3.	Spine
20%	4.	Lung
20%	5.	Pituitary

Lung Challenges

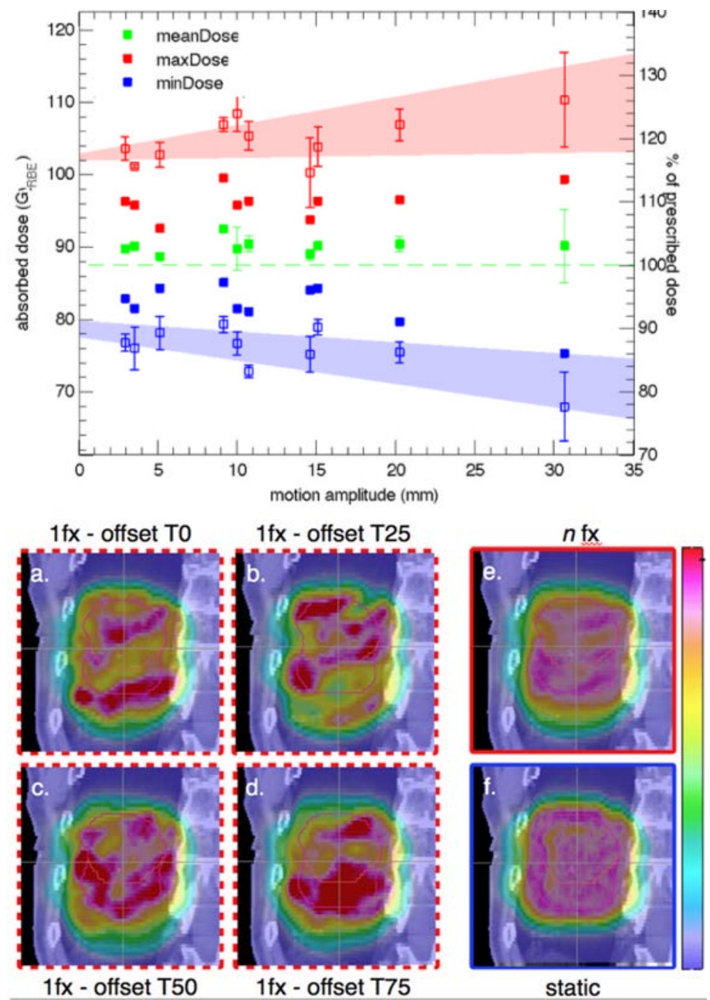
- Motion
- Density variations
- Range uncertainties
- Treatment planning
- Image Guidance
- OARs



G. Chen

Lung Challenges

- Motion
- Density variations
- Range uncertainties
- Treatment planning
- Image Guidance
- OARs
- Robustness
- Interplay



Grassberger, et. al.

Robustness

- Include probability estimates in the treatment planning optimization
- Reduce high gradients in close proximity to OARs
- Include Range Uncertainties, Setup Uncertainties, and Motion

Summary

- Proton SRT is a viable option SRT
- Benign cases probably have the most benefits with protons → Integral Dose, late effects
- Malignant
  - Close proximity to OARs/Quality of life or necrosis concerns
  - Multiple brain metastases: is quality of life affected?
  - Volume toxicities in the body
- Currently, less conformal due to uncertainties:
  - Online range verification
  - Robust planning
  - Patient Imaging

Thank You!

http://gray.mgh.harvard.edu