



Evolving Role of Physics in Radiation Therapy --- Technology and Beyond

John Wong, Ph.D.

Johns Hopkins University

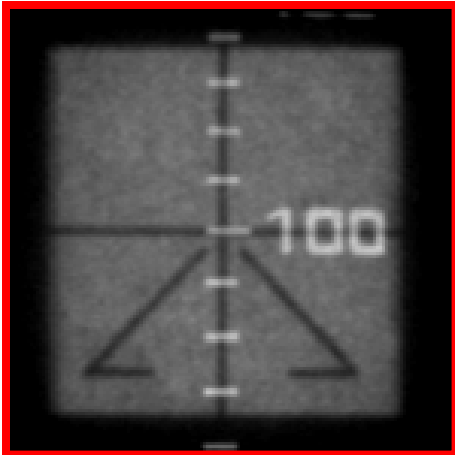
Acknowledgments

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- *Radiology, Neurosurgery, Neurology, ICMIC, Oncology*
- *JHU Physics & Astronomy*
 - Alex Szalay

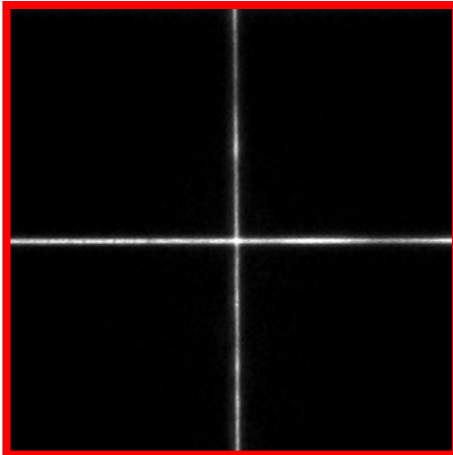
Disclosure

- *Small animal platform*
 - *NCI R01 CA158100*
 - *Gulmay Medical Inc. (Xstrahl) Research Agreement*
Tech transfer and Consultancy
- *Integrated x-ray CBCT and Ultrasound imaging*
 - *NCI R01 CA 161613*
 - *Elekta Research Agreement and Royalty*
- *Philips Research Agreement*
- *QA Box --- MD Biotech, MD TEDCO, JPLC Associates*

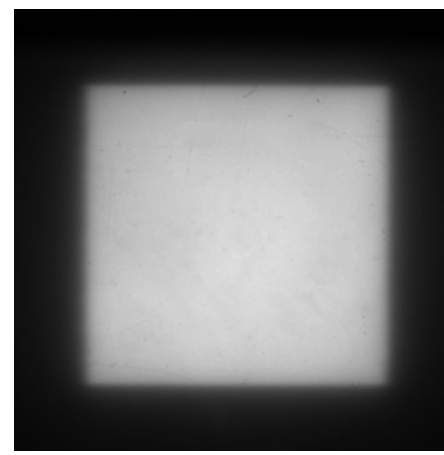
Technology Challenge: TG 142 QA



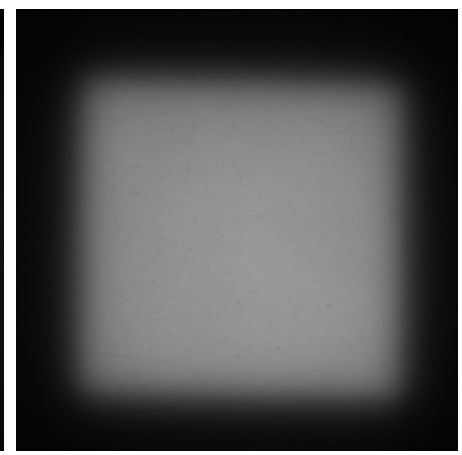
**Light field with
ODI**



**Room Lateral
Laser**



**6 MV x-ray at
dmax**

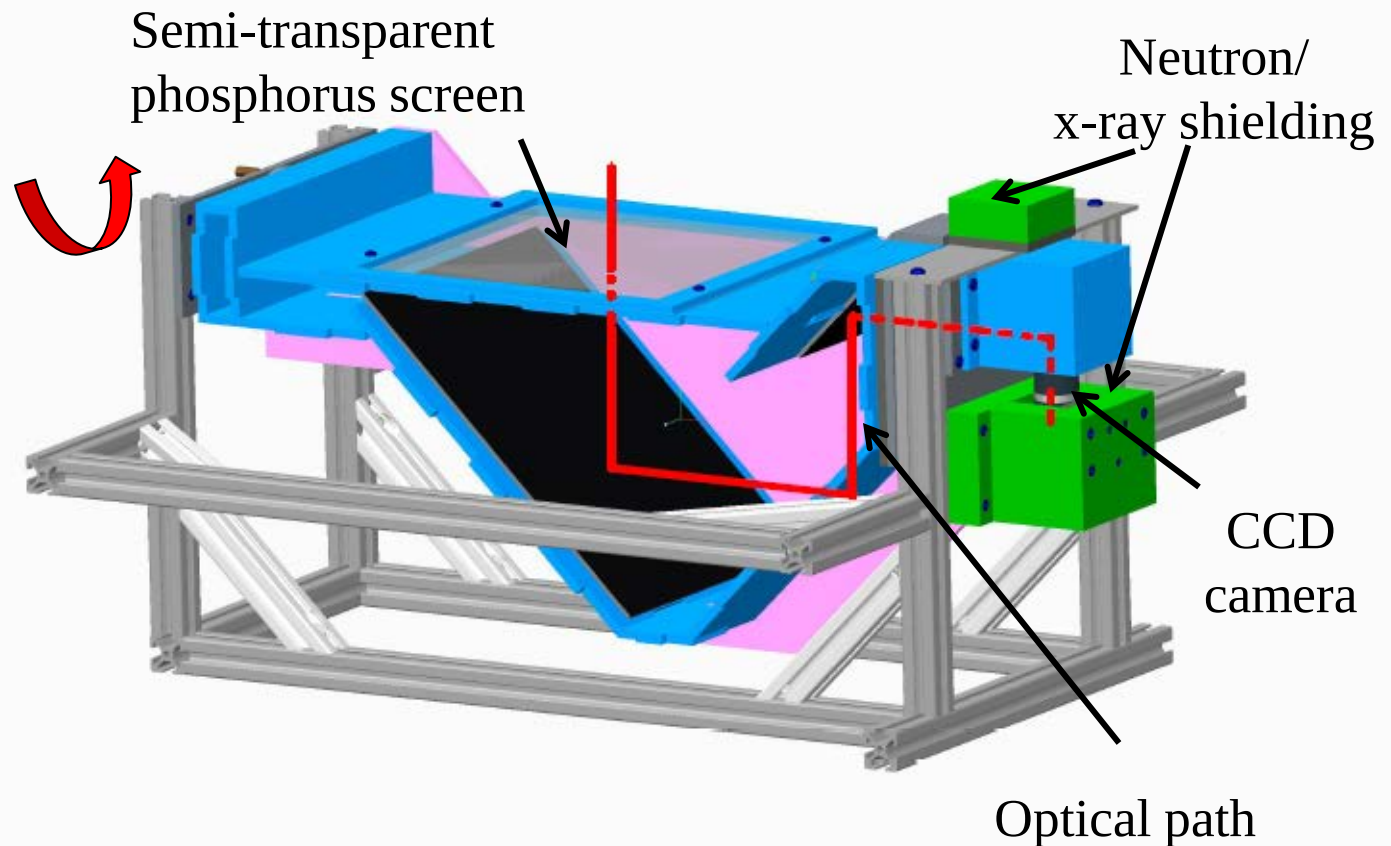


**12 MeV electron
at dmax**

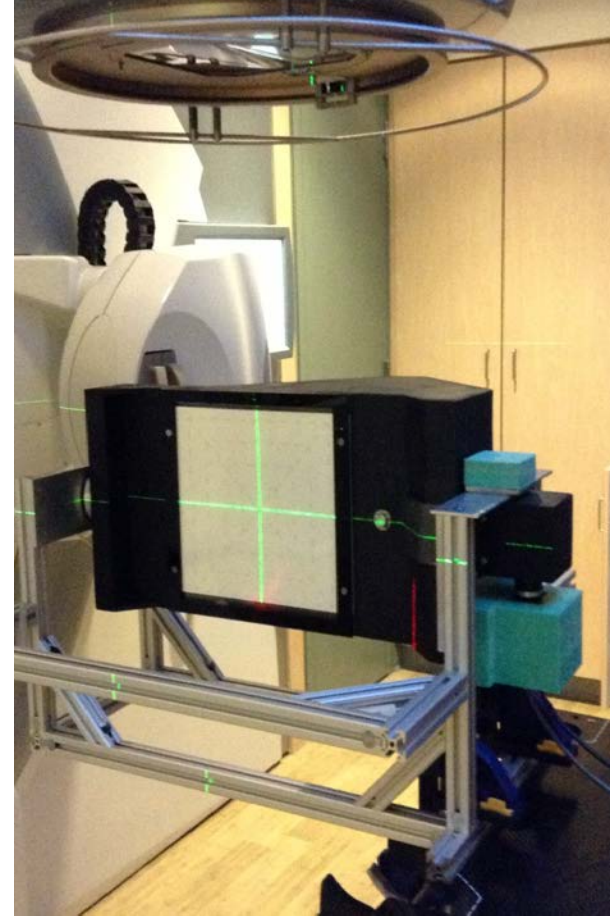
- 1.4 Mpixels, 16-bit, CCD camera to provide 0.2 mm x 0.2 mm per pixel resolution for a 20 cm x 20 cm image
- CCD operates at integration mode
- Optical / Laser imaging *without* buildup on phosphor
- Radiation imaging *with* buildup on phosphor

An Unified QA System for TG 142

- A mirror system that allows capturing images at the isocenter plane with a stationary camera



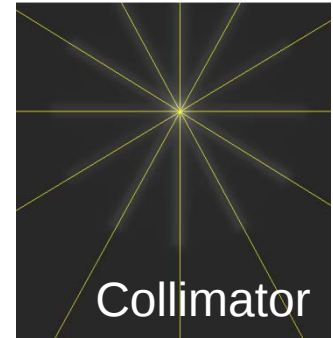
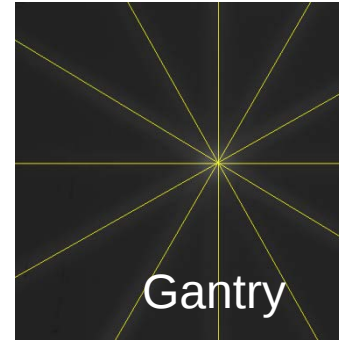
1st prototype



Suspended setup for gantry rotation measurements

Radiation Isocenter QA

- Results of isocentricity
 - Gantry Starshot diameter
 - Collimator Starshot diameter



- The use of **Center Of Mass (COM)** calculations of a small field (2x2 cm) for collimator, table and gantry rotation
- For collimator:

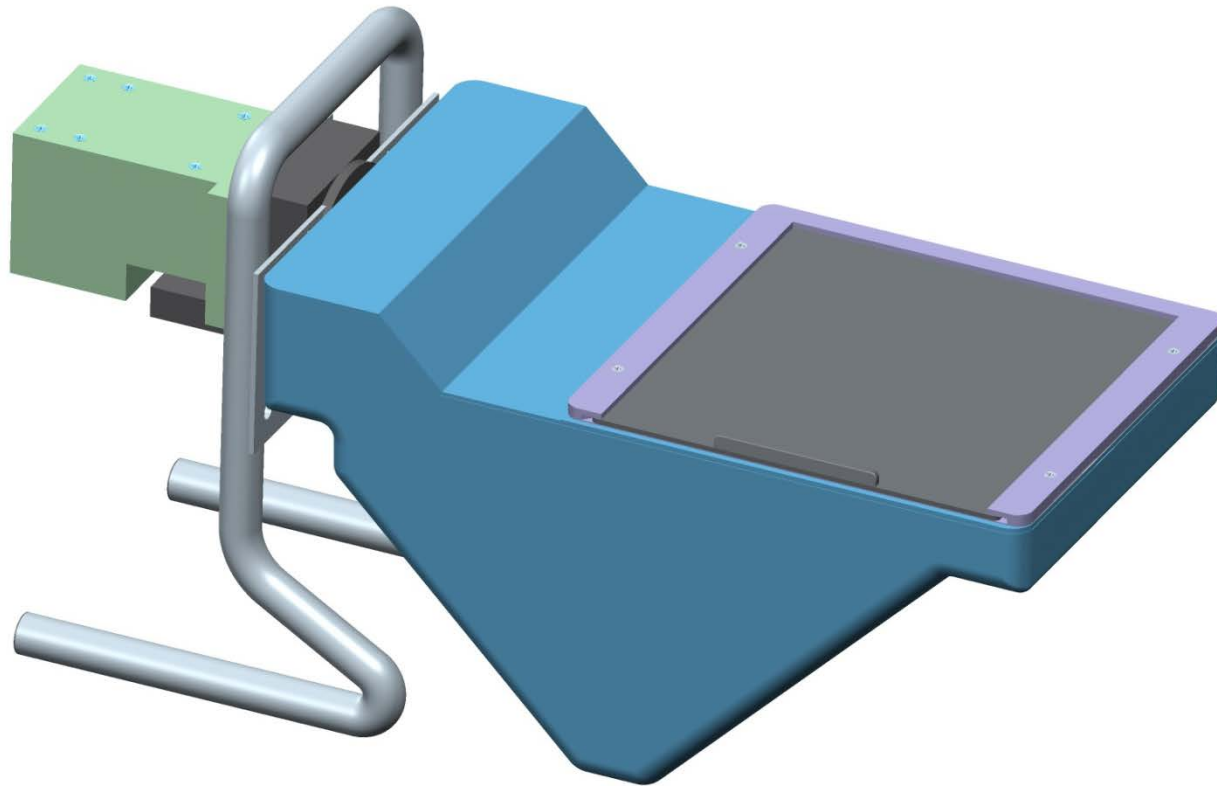


COM diameter = 0.3 mm

Film star-shot,
diameter = 0.7 mm

Method can be applied to gantry rotation instead of gantry star-shot

Raven QA: Product-Grade Prototype



Technology Challenges: IGRT of Soft Tissue Targets

Inter-fraction methods: Cone beam CT, MV CT

Pros

Adaptive Radiation Therapy

Cons

Ionizing radiation

Image Quality

Inter-fraction methods: Intra-modal ultrasound imaging

Pros

Soft tissue information

Non-ionizing

Cons

Snap Shot (at present)

Expertise/operator dependence

Intra-fraction methods: Implanted Markers

Pros

Real-time monitoring

Non-ionizing option

Cons

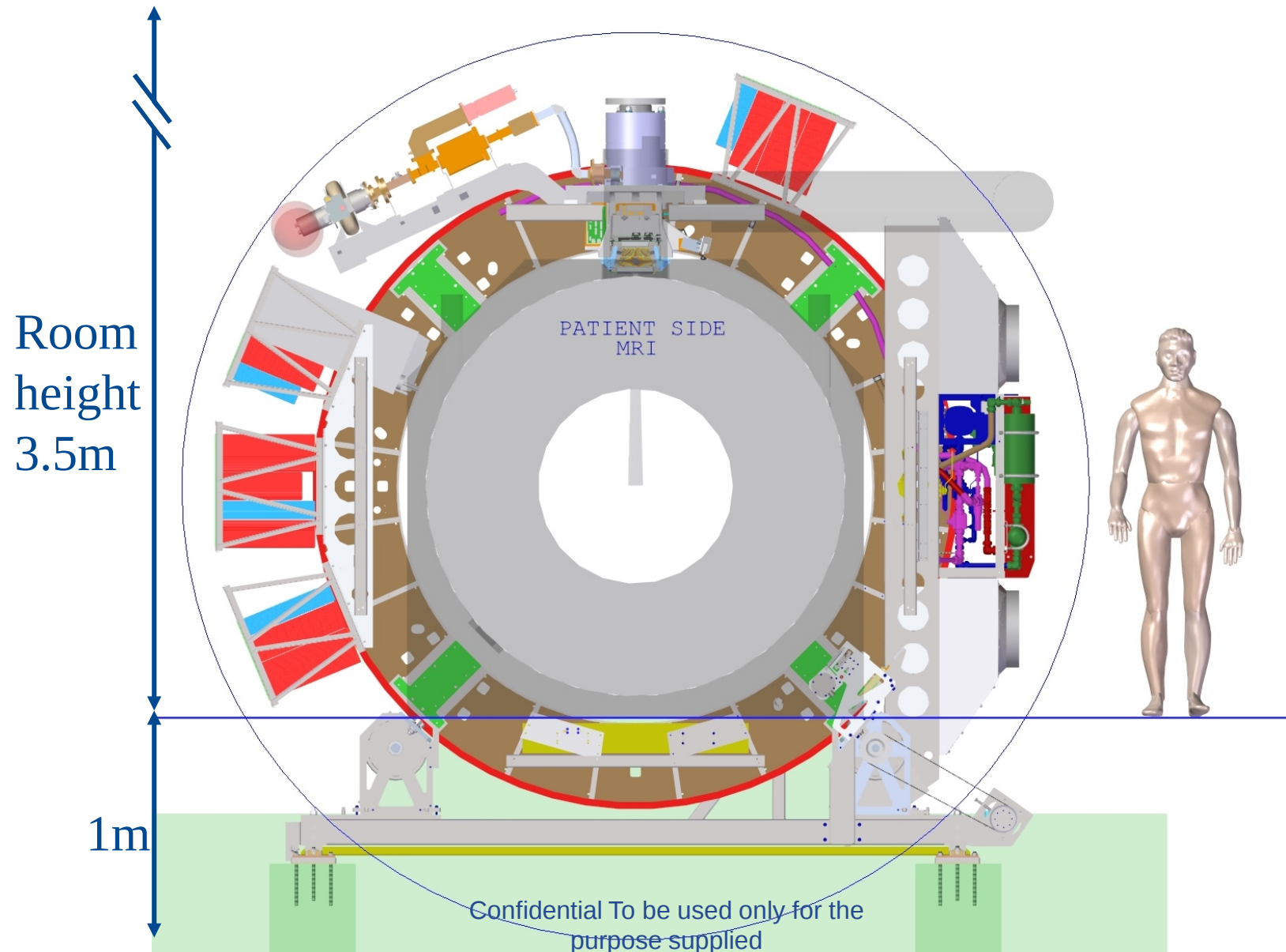
Invasive

Ionizing radiation

Soft tissue surrogate (truth?)

- Emergence of MRI-Radiation Machines

Phase 1 Prototype MRI-GRT



MRI-GRT project : Current Status

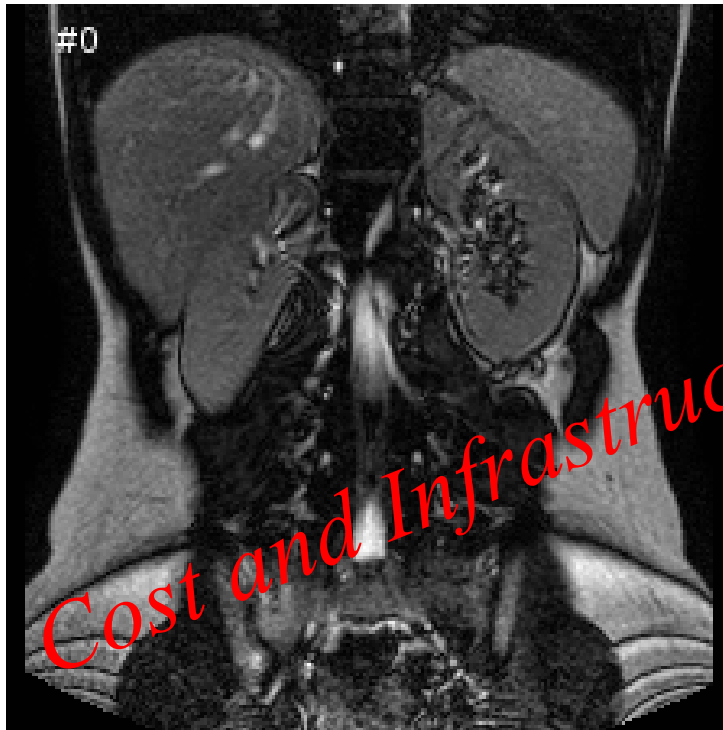
- MRI Magnet full on at 1.5T and able to image
- Linac able to radiate
- MLC able to move leaves
- Gantry able to rotate

At the same time !



Cine MRI on MRI-GRT concept platform

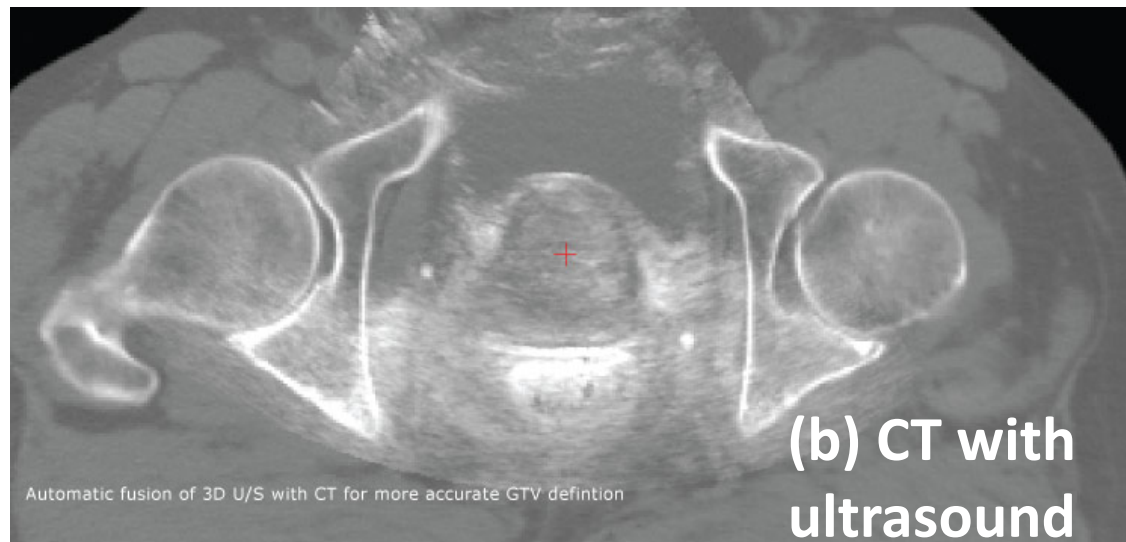
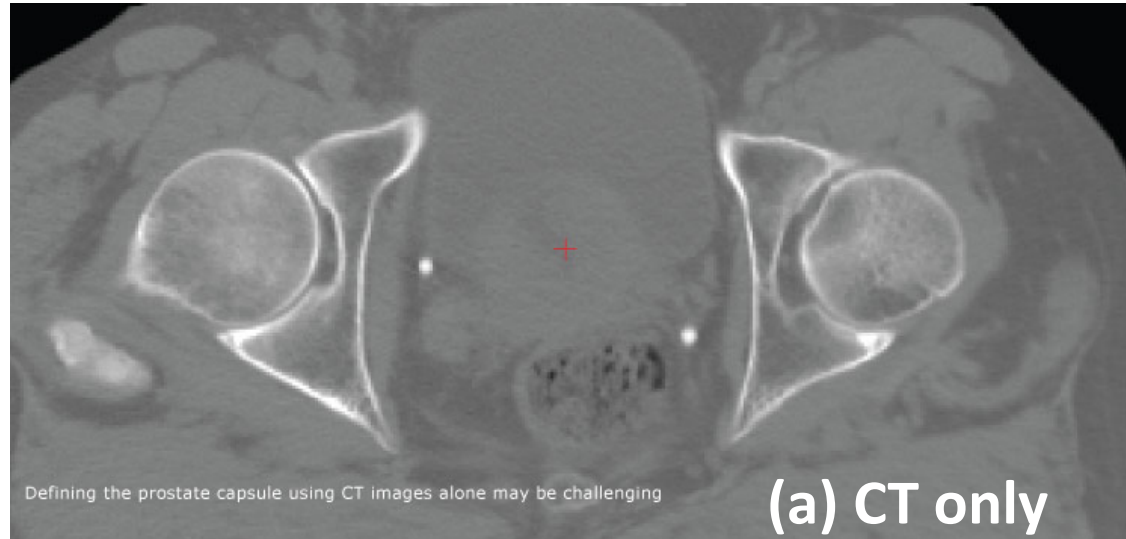
- 2 frames per second
- Kidneys, liver and spleen can be followed in real time



Integrated 3D ultrasound/CBCT imaging for soft tissue IGRT

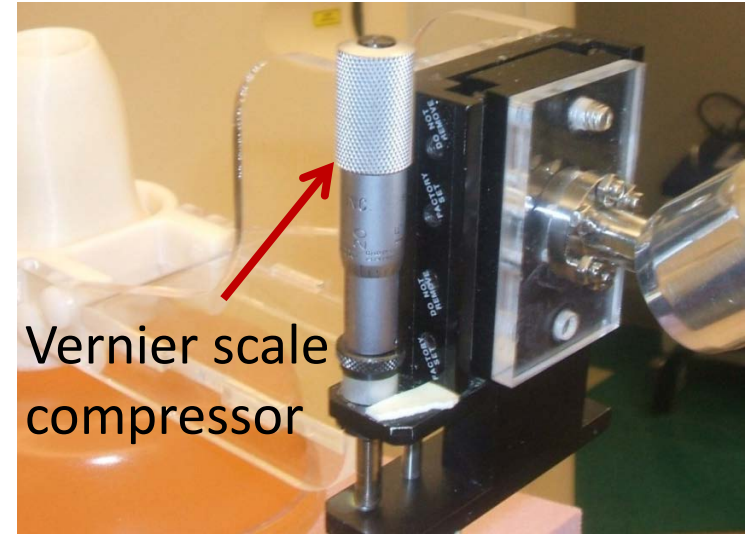
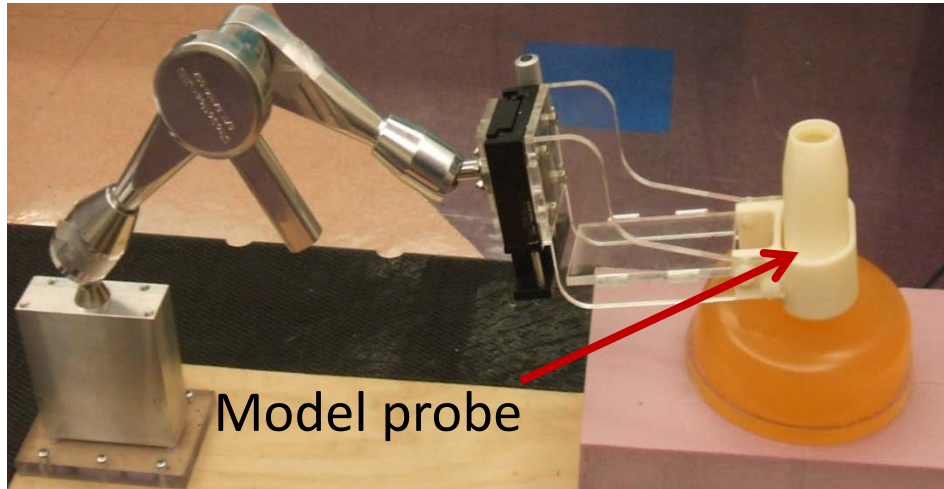
Hypothesis:

- US-CBCT offers a non-ionizing, non-invasive inter- and intra-fraction solution for soft tissue targets
- Prostate, liver, pancreas



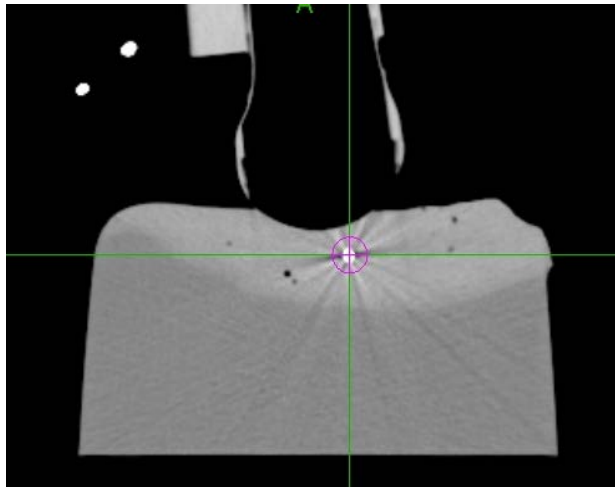
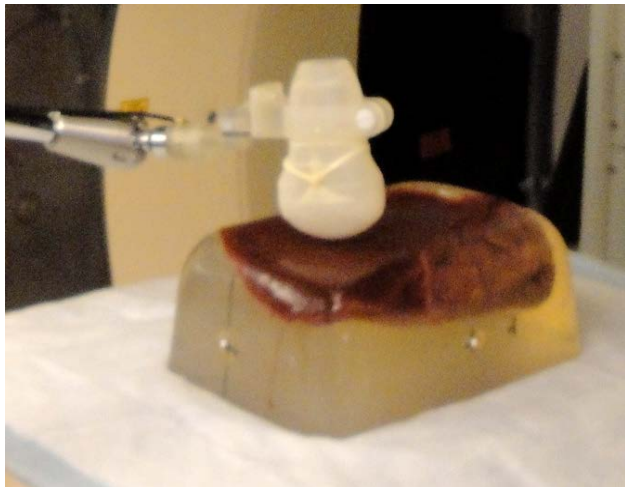
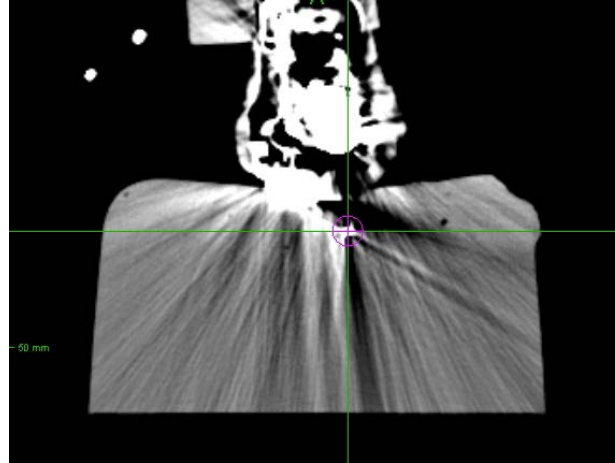
Challenges of US imaging	Solutions
Reproducibility / operator dependence	Robotic placement of a 3D probe
Deformation of anatomy	Keep US probe in place during irradiation while avoiding beams → Intra-fraction monitoring
Soft tissue registration	By definition, auto-fusion of CBCT and real-time US
<i>Require simulation/planning of patient in treatment position with the ultrasound/CBCT system in place</i>	

Passive robotic arm and gel phantom



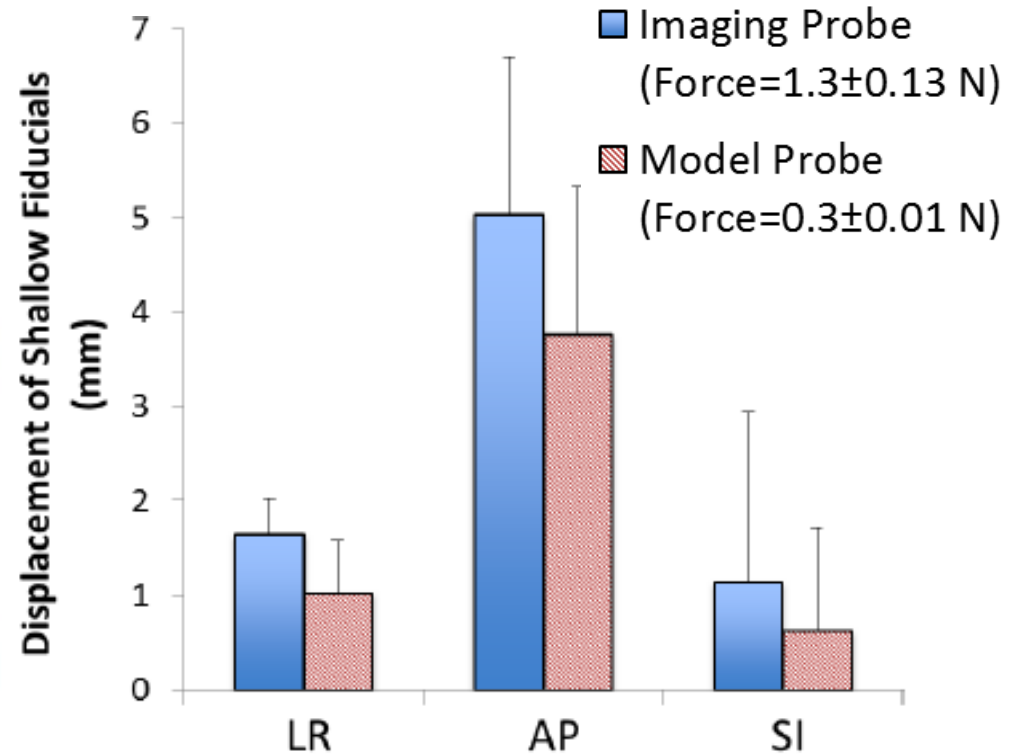
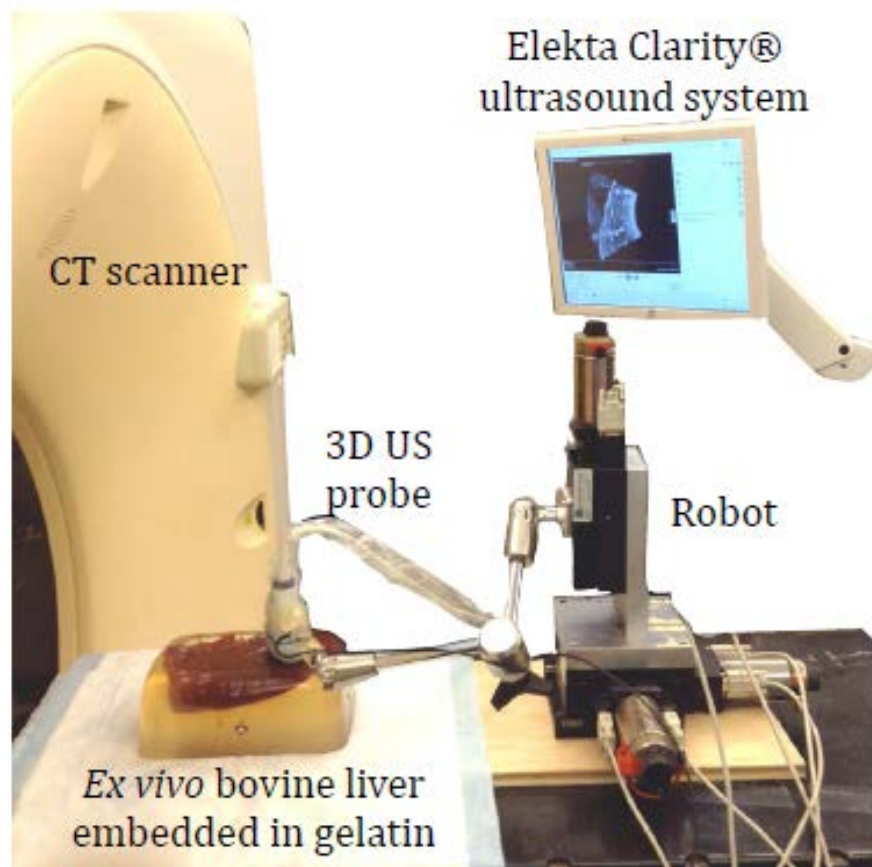
- A passive robotic arm with 1D linear (vernier scale) actuator
- Deformable gel phantoms with embedded 12 PMMA beads (1.2, 2.8, 3.2 mm in diameter)
- CT scans of repeat cycles compress/release to determine reproducibility
- Intra-, inter-fraction reproducibility all within 1 mm

Ex-vivo Bovine Liver in gel phantom



- Gel phantom was overly simplistic with uniform deformation
- A more realistic ex-vivo liver phantom was devised
- Comparison of deformation was made between ultrasound and model probe.

Reproducibility of Deformation



Contact forces lower with model probe
The robotic arm needs to be stiffened

- Significant compression force differences between gel and liver phantom
- Suitability of phantom material is of concern



12/19/2013

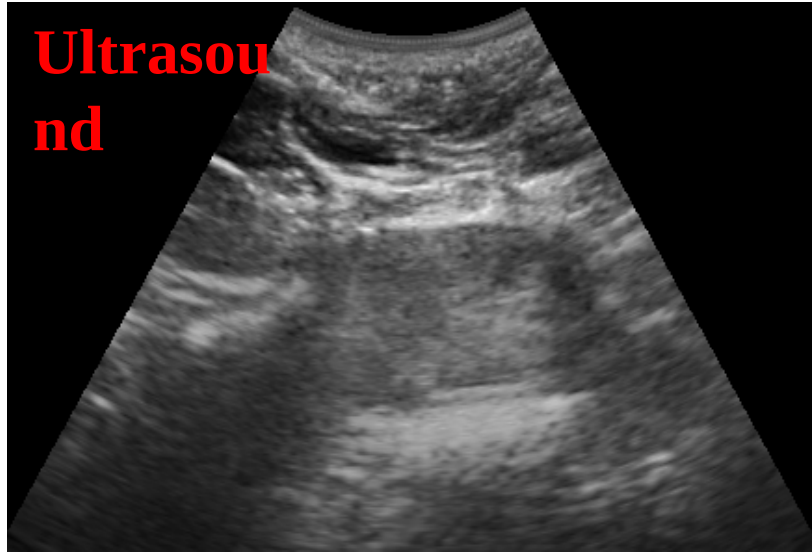
180

Prostate (Force = 14 N)

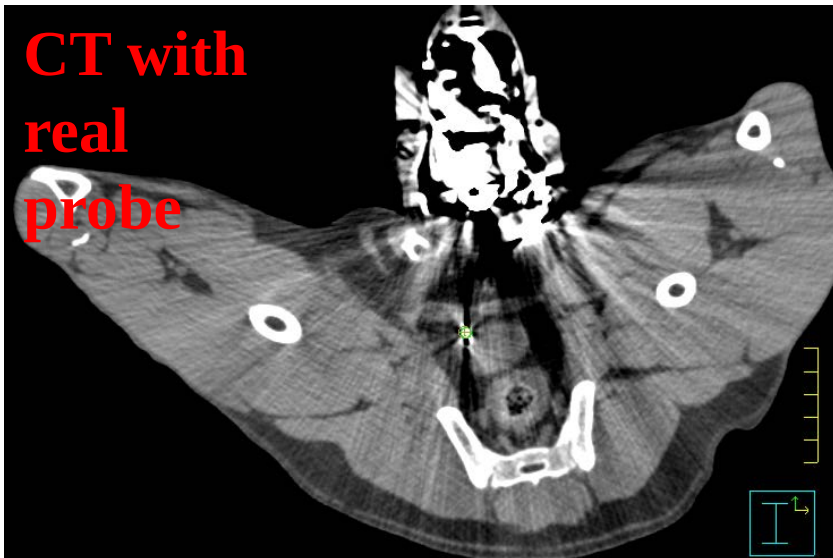


Prostate Images

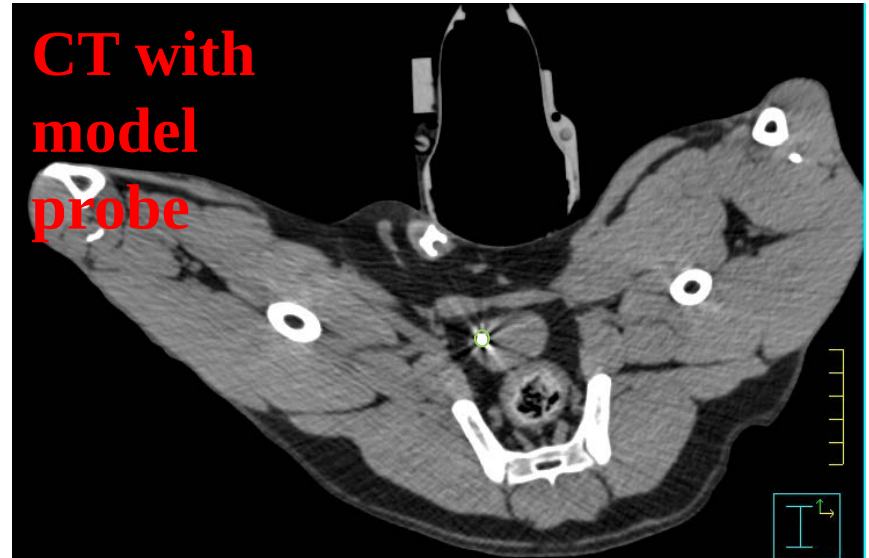
Ultrasound



**CT with
real
probe**

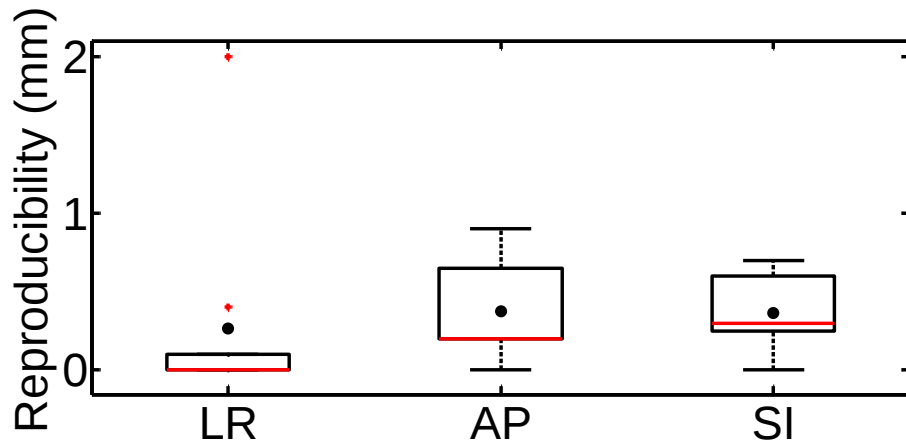


**CT with
model
probe**

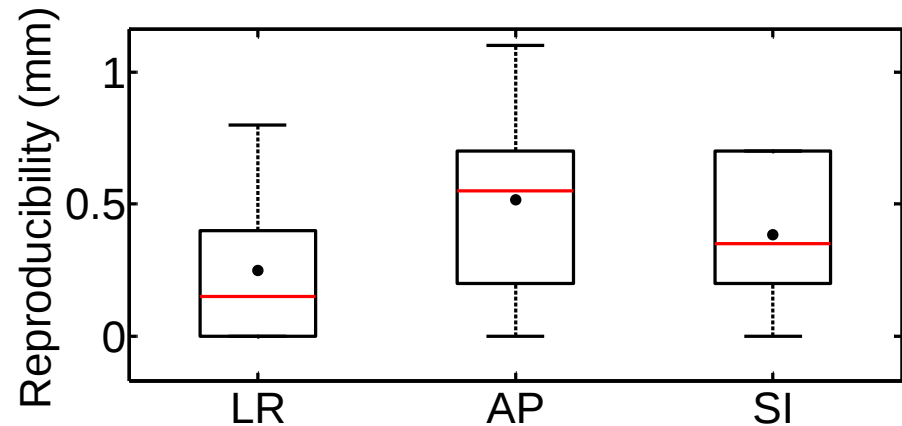


Prostate (Force = 14 N; 10 N ~ 1 kg): Marker Position Reproducibility in Interquartile Range

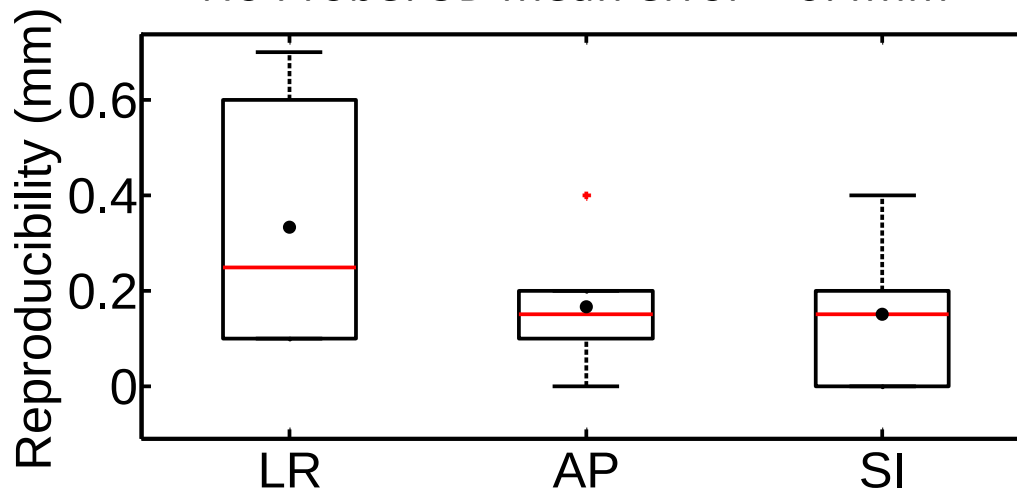
Real Probe: 3D mean error=0.6 mm



Model Probe: 3D mean error = 0.7mm

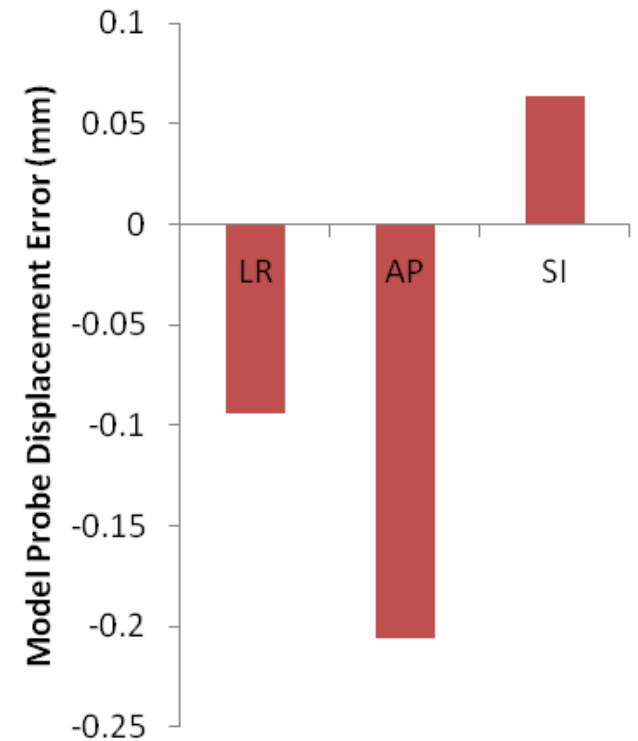
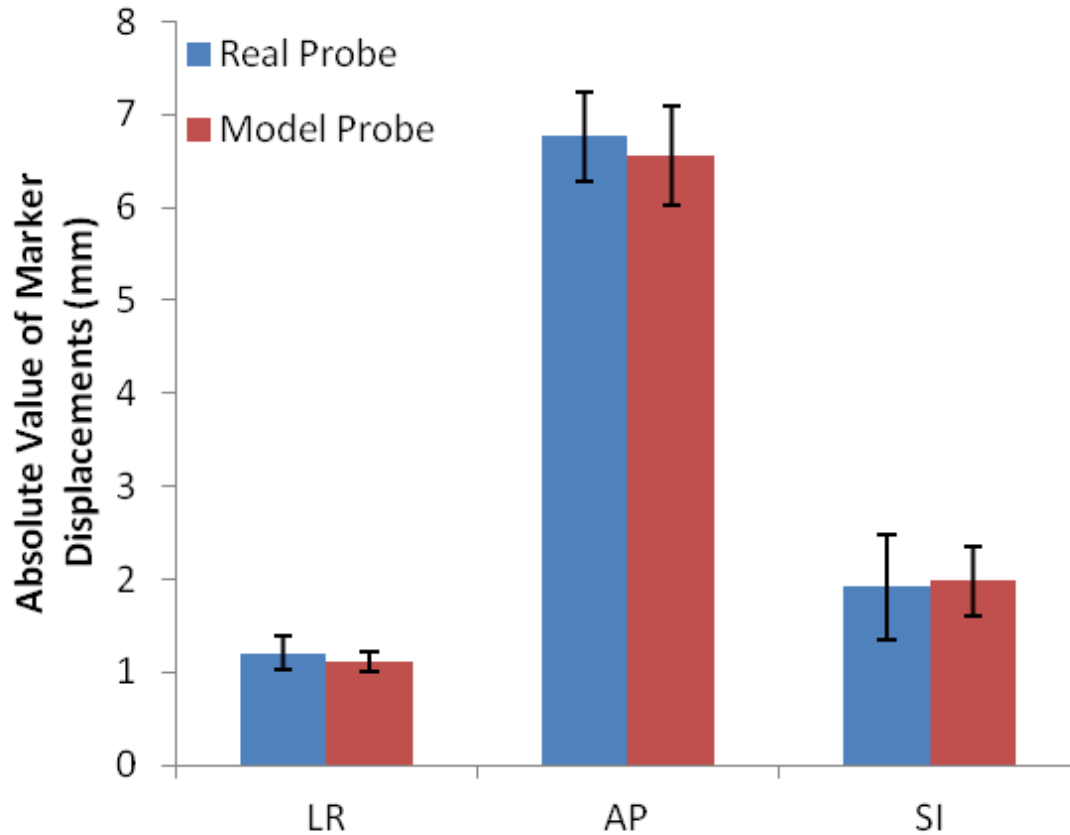


No Probe: 3D mean error = 0.4mm



Prostate:

Probe-Induced Marker Displacement (from no probe)

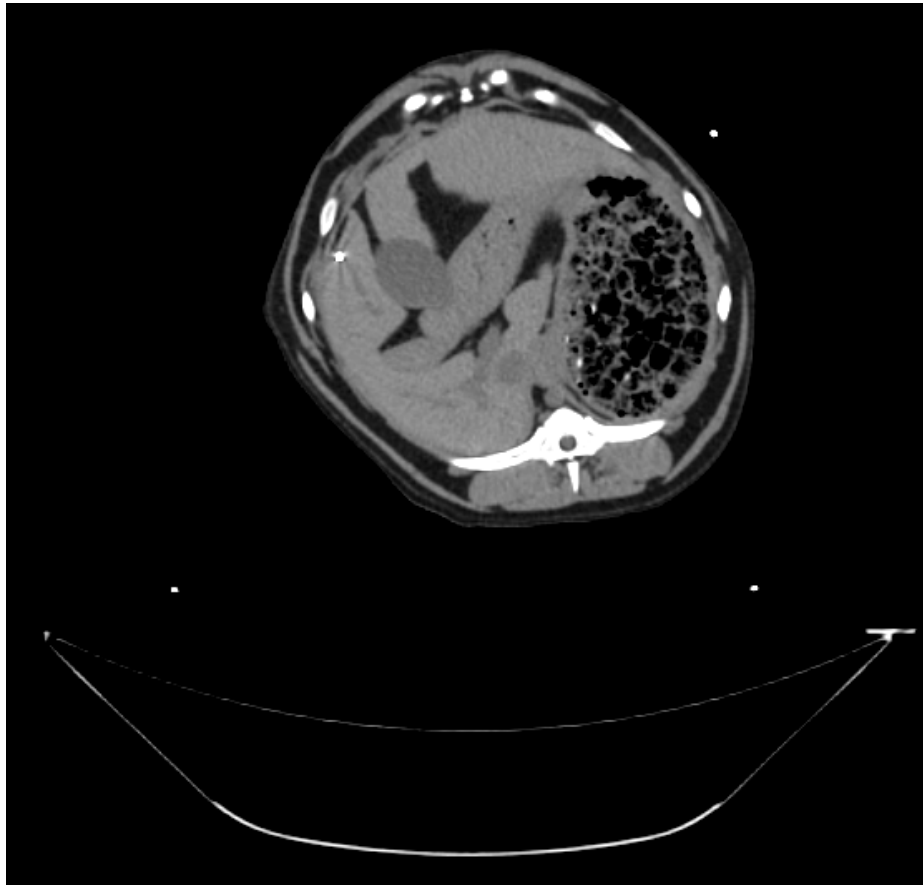


3D mean error
= 0.2mm

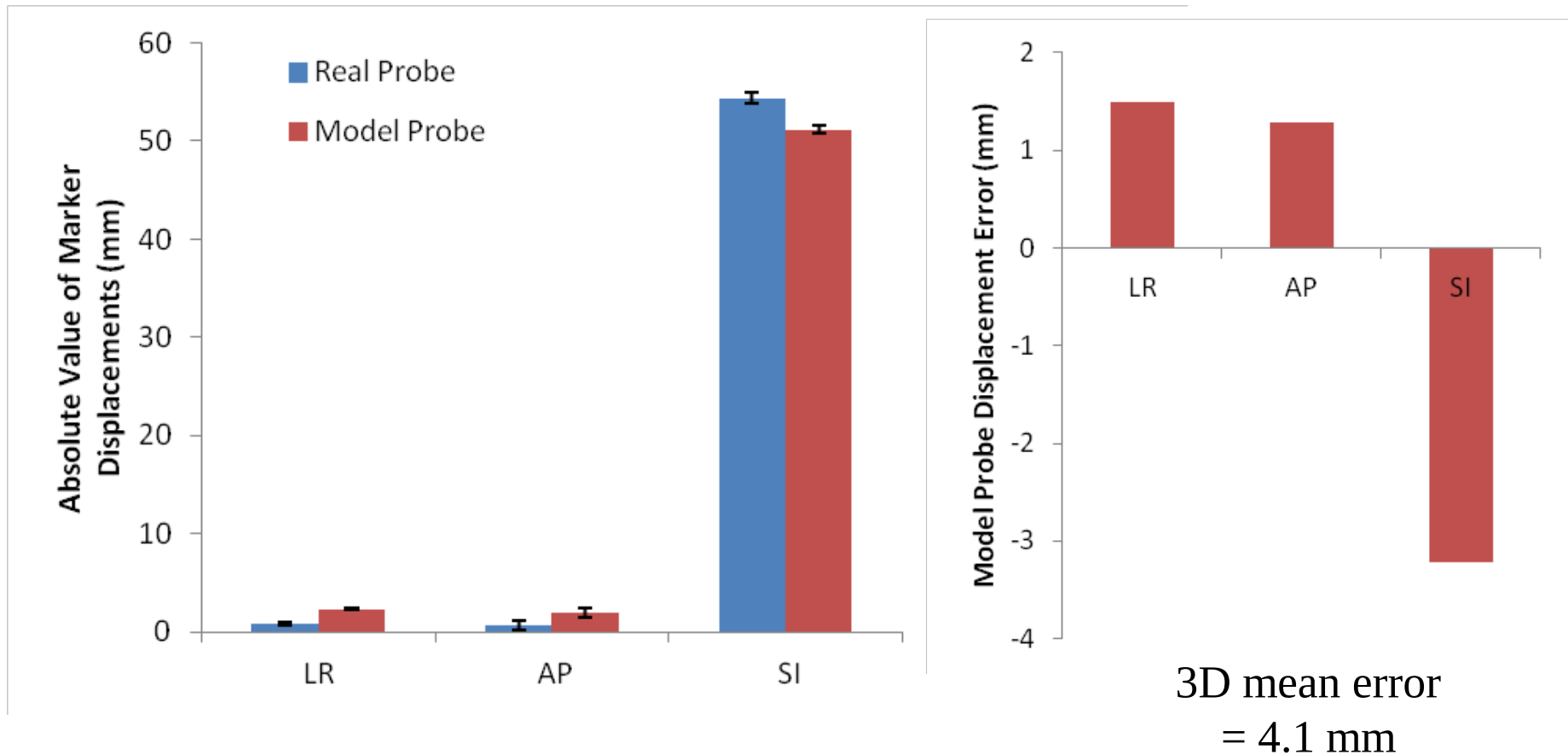
Liver at Breath-hold (Force = 40 N)



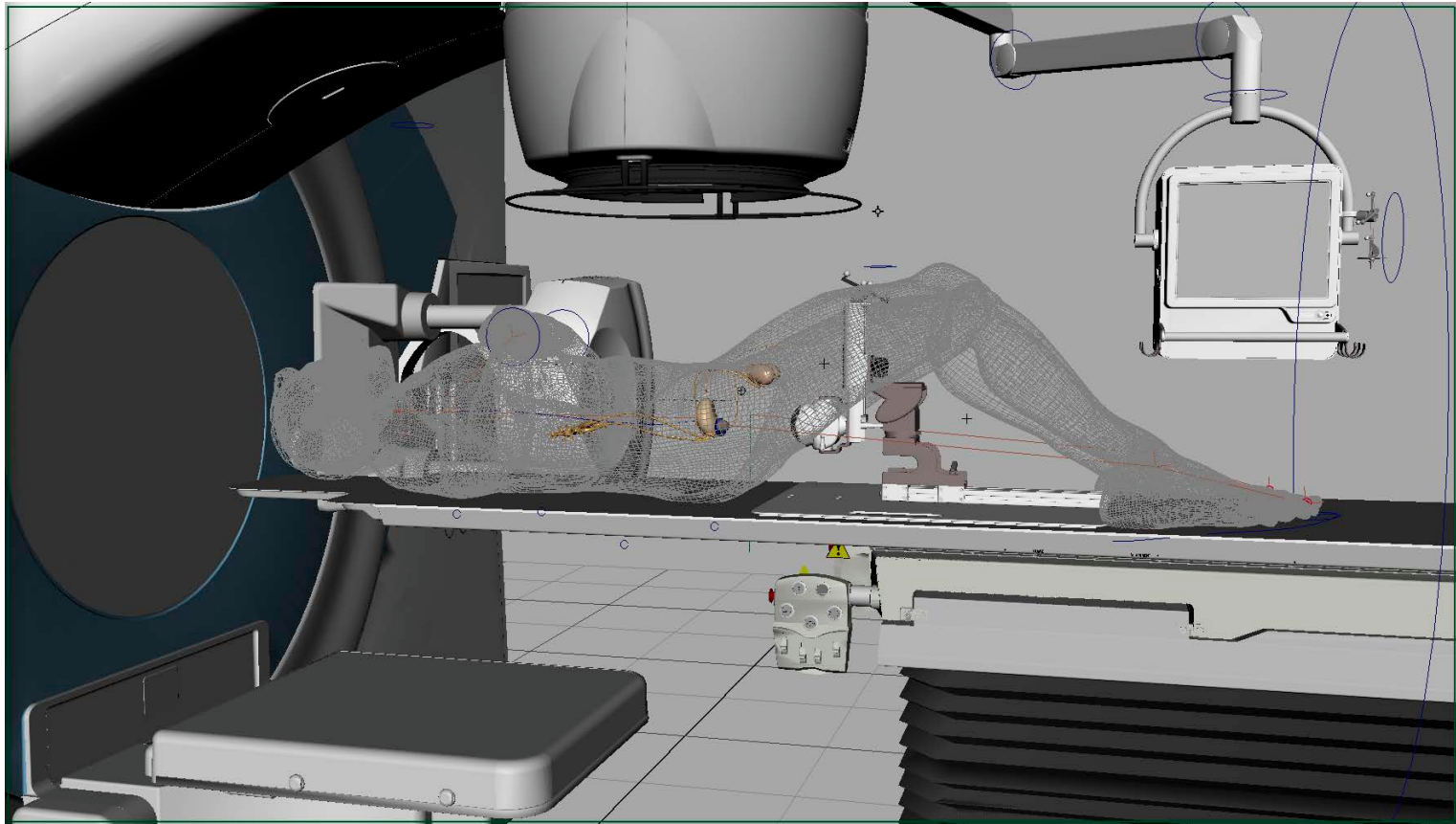
Liver CT and Ultrasound Images

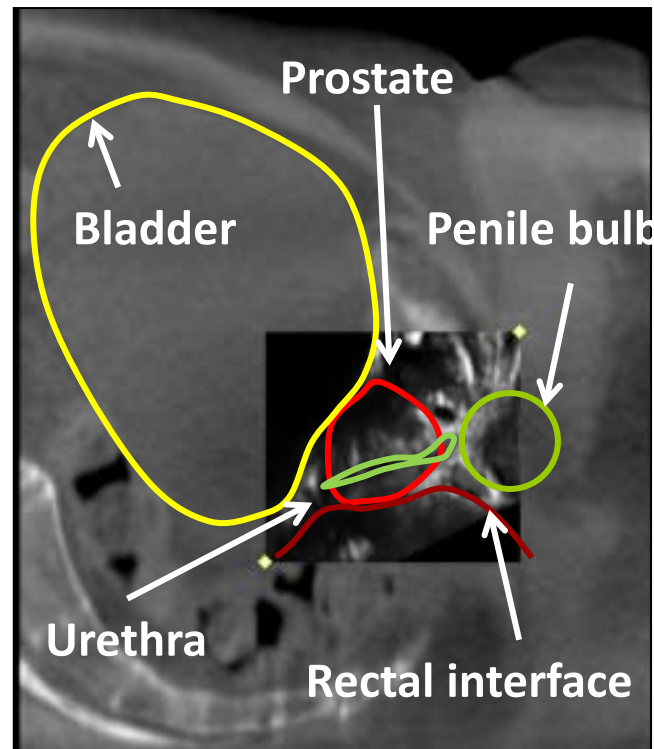
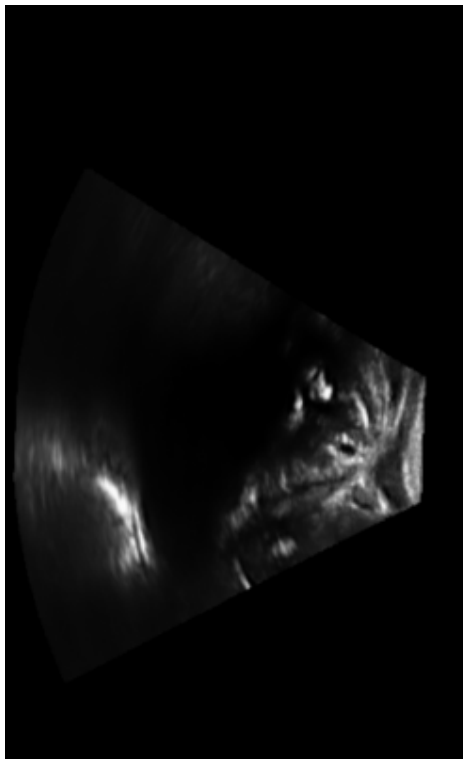
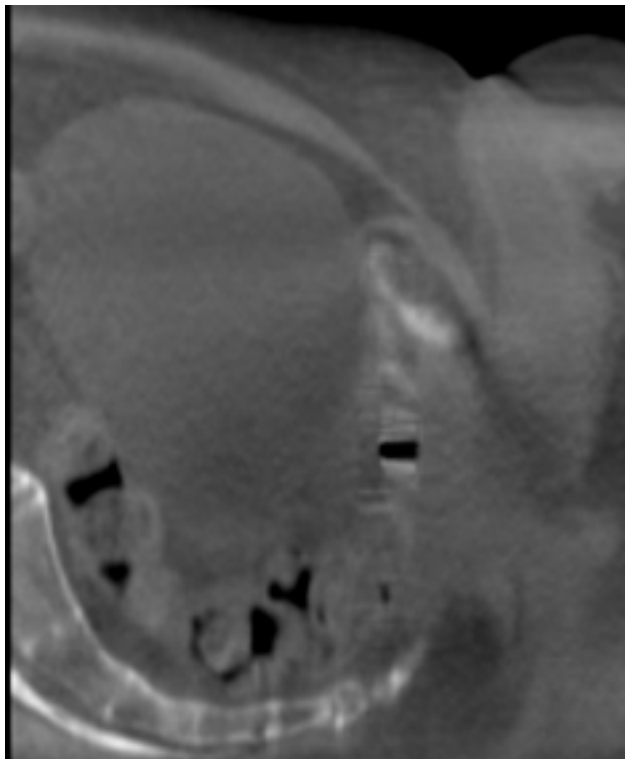


Liver (at Breath-hold): Probe-Induced Marker Displacement



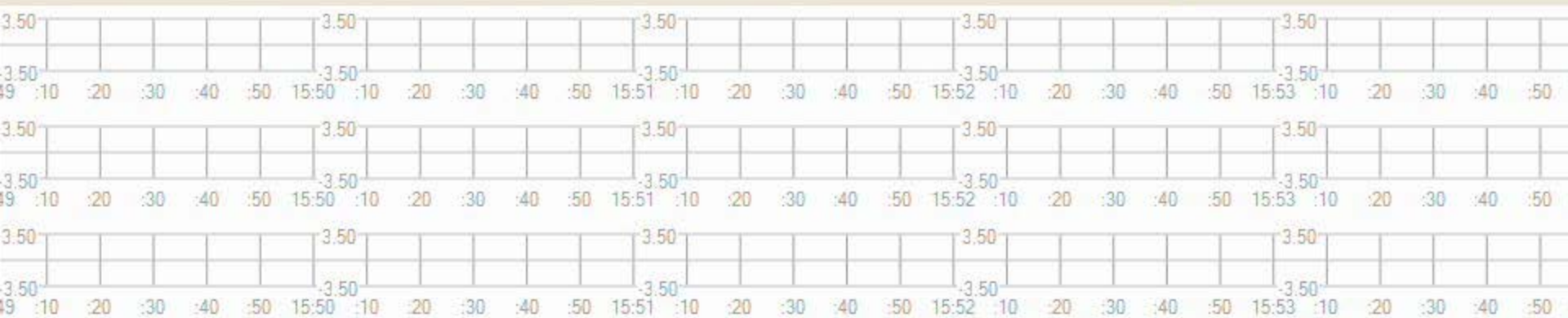
Model of Elekta-Resonant 4D prostate system: Novel transperineal (TPUS) scan





[stop monitoring](#)

Capturing reference volume.



Patient

Scan

Segment

Setup

Position

R&V

Monitoring



Done



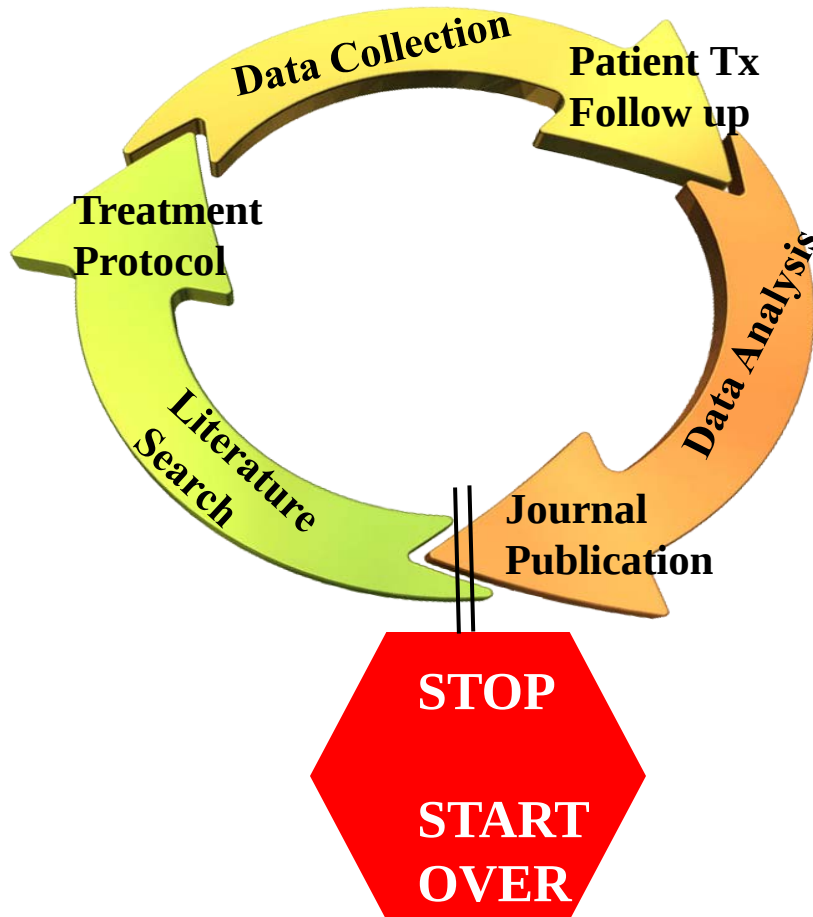


Analytic database for personalized medicine and data sharing in radiation oncology

Radiation Oncology and Molecular Radiation Sciences
Johns Hopkins University

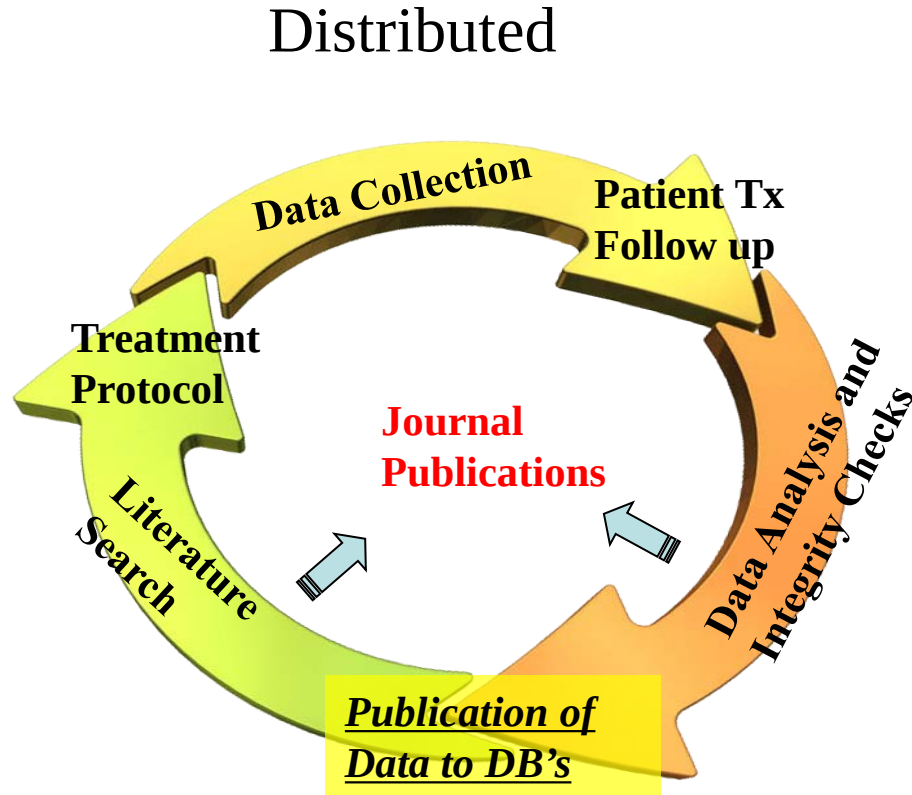
Re-engineering the Cooperative Research Model

Present (RTOG)



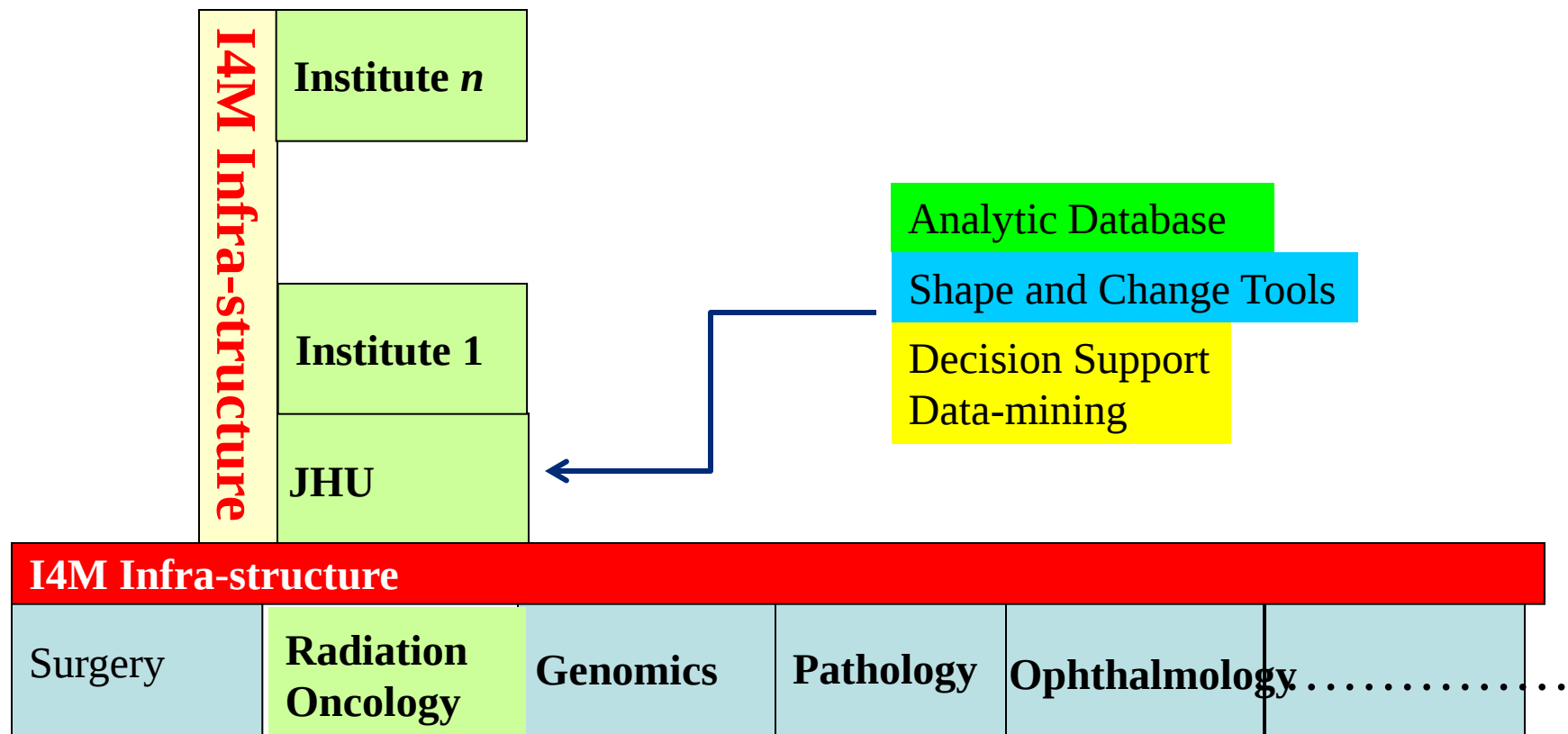
- < 3% of patients treated are enrolled in cooperative clinical trials
- Required data submission for QA and approval – “*big problem*”
- Average duration to complete a clinical trial
 - > 5years
 - outpaced by advances
- No feedback from community practice
- Data limited for re-use
 - Data/Knowledge lost

JHU: Re-engineering the Cooperative Research Model



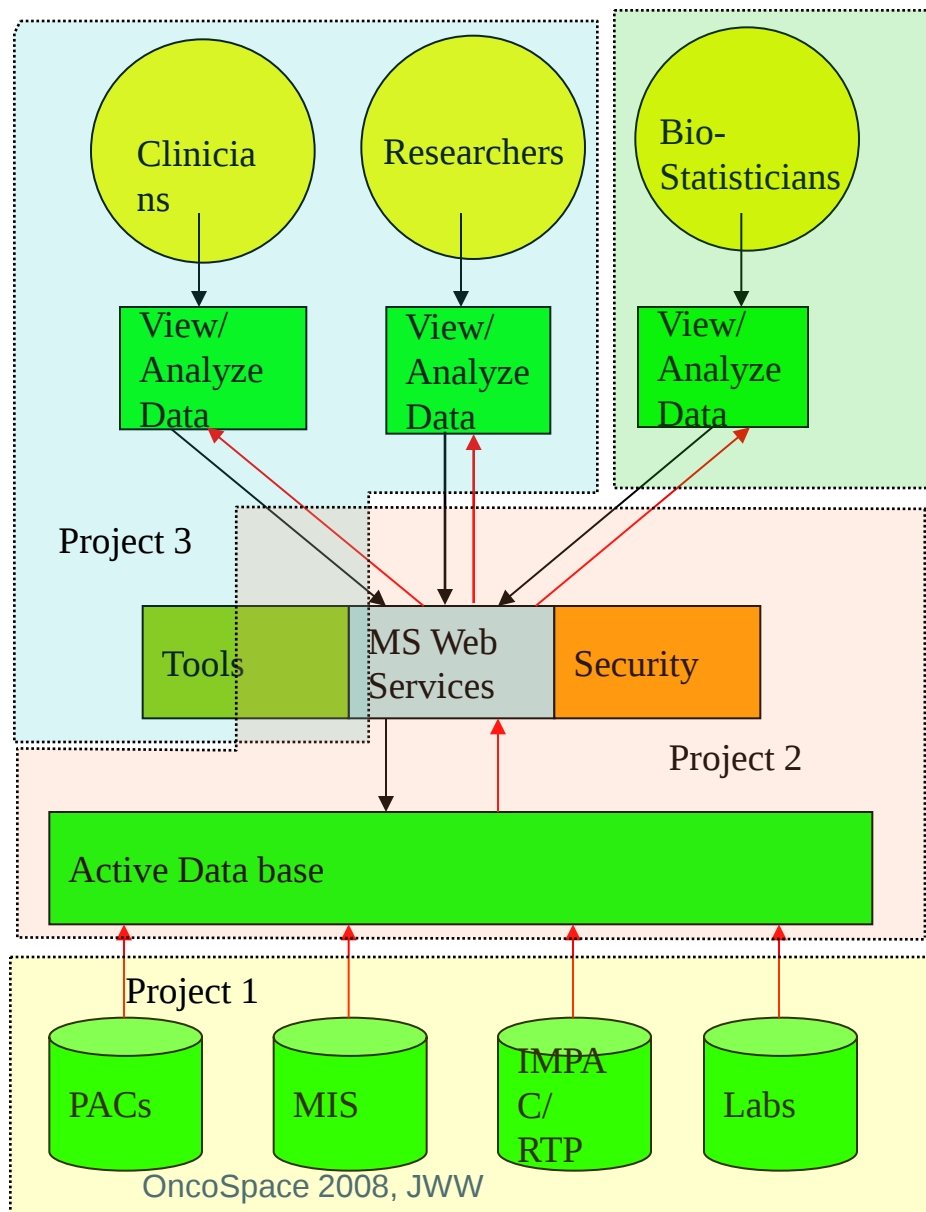
- Keep data local and available in an active database
- Send queries to data, extracting only answers
 - e.g. Validate the PTV margin prescribed for lung SBRT
- Facilitate data-reuse, decision support and education
- Promote data sharing for CER
- *Tools for data capture to populate OncoSpace*

OncoSpace: Radiation Oncology Model for Data Sharing and Decision Support



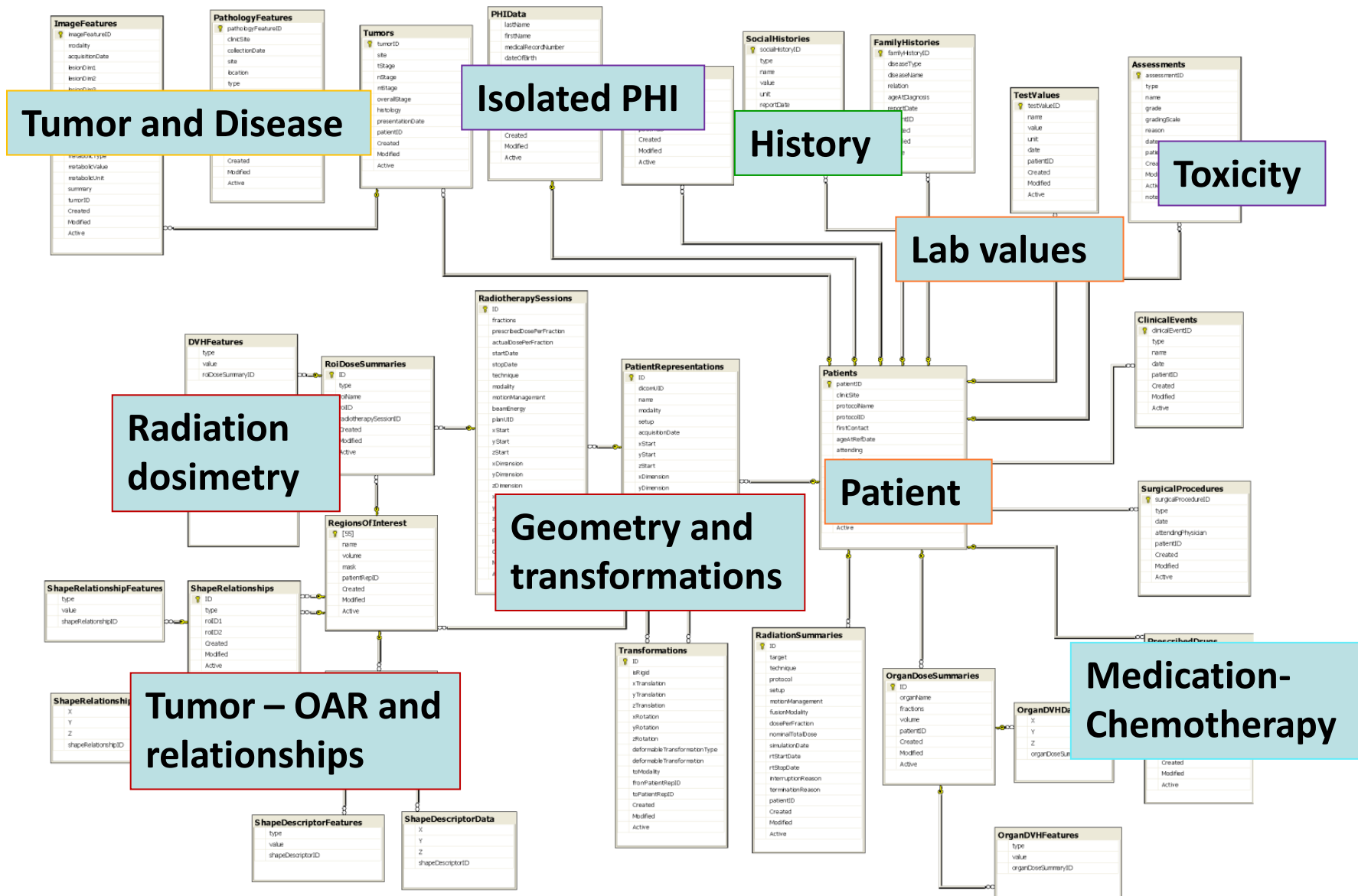
I4M: Integration of Imaging, Information and Intervention in Medicine

Hopkins OncoSpace



1. Integration of clinical workflow with data collection to populate OncoSpace.
 - ***Enable Mosaiq/Aria and TPS to capture data***
2. Optimize database architecture for secured distributed web-access
3. Tools for query, analysis, navigation and decision support
4. Data mining, decision support and bio-statistic research

Database organization



MOSAIQ RO information system



Diagnosis: Soft palate, NOS (excludes nasopharyngeal surface of soft palate t-147.3) [145]
Histology: Squamous cell carcinoma, NOS [80703.00]

Stage: II
MD: Sanguinet

Flowsheet | Clinician Worksheet | Laboratory | Vital Signs | Assessments | Graphs | Pt. Education

View: RO ON

Date	10/02/08	10/09/08	10/16/08	10/22/08	11/07/08	11/12/08
Additional Information						
Rad Dose	1400.00	2200.00	3400.00	4000.00	6400.00	7000.00
Unplanned Breaks						
Unplanned Break Reascn						
Admitted						
Thrush			✓			
PEG			✓			
PO	✓	✓	✓	✓	✓	✓
KPS % Score						
Comfort Alteration						
Fatigue	1	2	2	3	3	3
Pain due to XRT	0	1	1	2	2	2
Larynx						
Cough CTC		0	0	0	0	0
Mucous Membrane Alteration						
Esophagitis/Pharyngitis	1	2	2	3	3	3
Dysphagia, Esophagitis	1	3	3	3	3	3
Xerostomia	2	2	2	2	2	2
Nutrition Alteration						
Nausea	2	3	2	3	3	3
Skin Alteration						
Skin Reaction		0	0	0	0	0
Sensory Alteration						
Hearing Changes	0	0	0	0	1	1
Taste Disturbance (Dysgeusia)	1	2	2	2	2	2
Voice Changes	0	0	0	0	0	0
Physical Findings						
Dermatitis		1	1	1	2	2
Mucositis		2				
Larynx LRM						
Response						
Primary Response	NA	NA	NA	NA	NA	NA
Node Response	NA	NA	NA	NA	NA	NA
Impression / Plan						
Impression	0	0	0	0	0	0
Direct Laryngoscopy						
Instruction						
Notes						
X-Ray Review Check						
Symptoms Management						
Oral Care						
Impression note						
Salt/Soda						
Oral Rinse						
Larry's sol						
Gelclair						
Fluconazole						
Lidocaine						
Mouth care: Other						
Skin Care						
Skin vera nel						

11/12/2008 6:25:52 PM: Pathologic stage I for T1c N0 M0

Configure... OK Cancel

Clinical Trials - JH

View: By Disease Site Find:

Disease Site	Trial Id	Title	Status	Staff	Trial Coordinator	Phone
Breast	J-0805	Partial Breast w/ Various Chem	Active	Kim, Helen C.	410-614-3950	S
Breast	R0413	WBI vs. PBI	Active	Kim, Helen C.	410-614-3950	Z
Breast Cancer	J-0728	Breast Ultrasound	Active	Kim, Helen C.	410-614-3950	Z
Breast Cancer	J-0609	SPECT Analysis	Active	Kim, Helen C.	410-614-3950	Z
Gastric or Gastroesophageal	CALGB80101	CALGB Gastric	Active	Kim, Helen C.	410-614-3950	H
Gastrointestinal Tract	J-0727	UART or WART	Active	Kim, Helen C.	410-614-3950	H
Lung	R-0623	Small Cell Lung Cancer	Active	Kim, Helen C.	410-614-3950	S
Metastatic to the Brain	J-07126	Abbott study	Active	Kim, Helen C.	410-614-3950	KI
Non-lymphoma metastasis	R-0438	Phase I XRT Dose Escalation	Active	Kim, Helen C.	410-614-3950	H
Pancreas	J-0686	Gemox Protocol	Active	Kim, Helen C.	410-614-3950	H
Prostate	R-0518	Zometa	Active	Kim, Helen C.	410-614-3950	S
Prostate	J-0736	C-Arm	Active	Kim, Helen C.	410-614-3950	S
Prostate	J-0859	Hypofractionated Prostate	Active	Kim, Helen C.	410-614-3950	S
Rectal Cancer	J-06109	QOL	Active	Kim, Helen C.	410-614-3950	H

Filter By: ☐ Active ☐ Closed to Accrual ☐ Suspended ☐ Terminated ☐ All

Sequence Num Patient Name DOB Age Treatment Description Status

J0805JHH0		10/21		Other regimens	On Trial, In Follow Up
J0805JHH0		7/31		TCarbo H	On Trial, In Follow Up
J0805JHH0		11/15		TC	On Trial, On Treatment
J0805JHH0		7/23		Dose dense AC	On Trial, On Treatment
J0805JHH0		11/04		Dose dense AC	On Trial, On Treatment

Add Change Delete

Follow-Up Status - 21EX_TEST, QUASAR_CO_G0

Date: 10/25/2008 Type: Lung OK

Status: New Manifestations Cancel

Status: Expired: 10/20/2008 Cause of Death: Dx Related to CA Note

F/U Status: 4 ECOG: 5

Loc: Recurrent Regional: NED Distant: NED

Comment: Patient expired in sleep

Toxicity

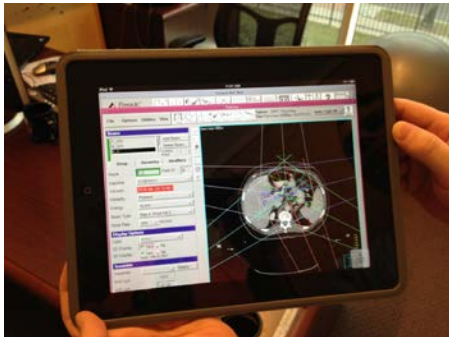
Type	Severity
Type 1: Lung	Severity: 4 Severe
Type 2:	Severity:
Type 3:	Severity:

Next Contact:

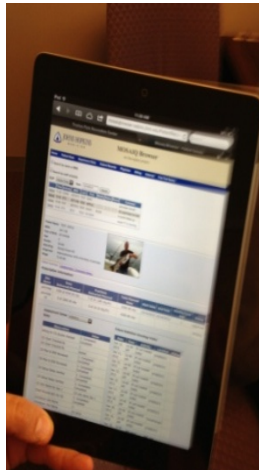
Follow-Up Status Will Be Changed

Mobile devices for specific tasks

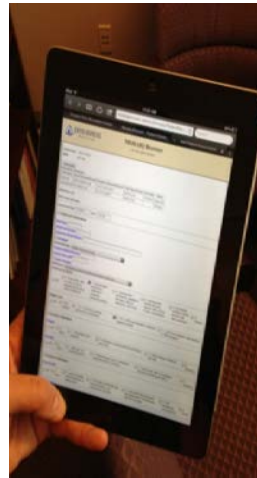
Plan Approval



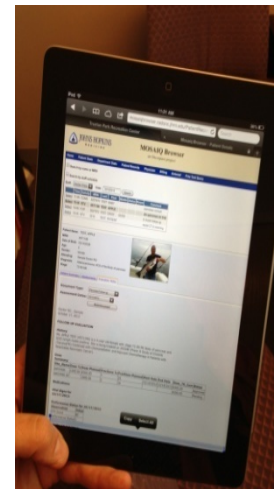
Patient summary



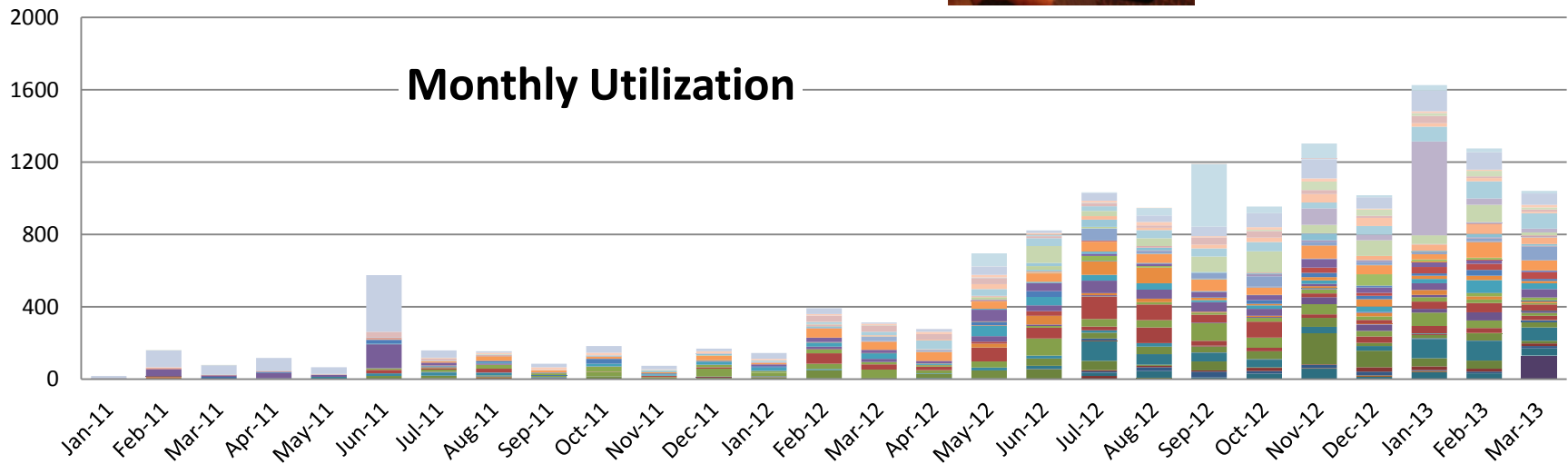
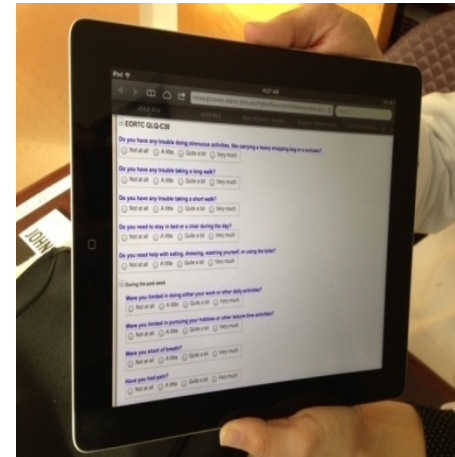
Clinical assessment



Clinical notes



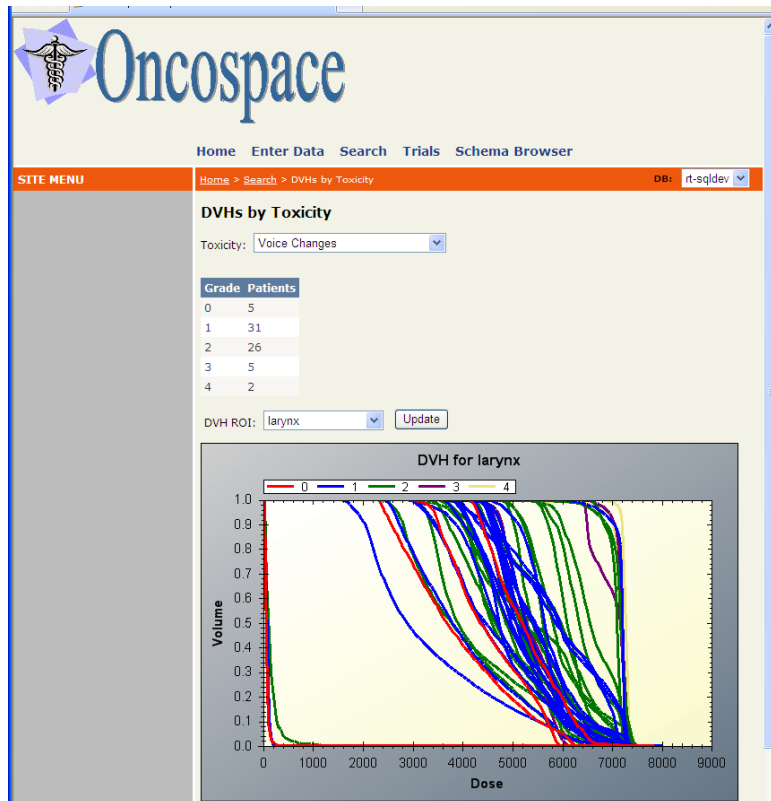
Patient Quality of Life



Safety and Quality

Oncospace: Query & Analysis

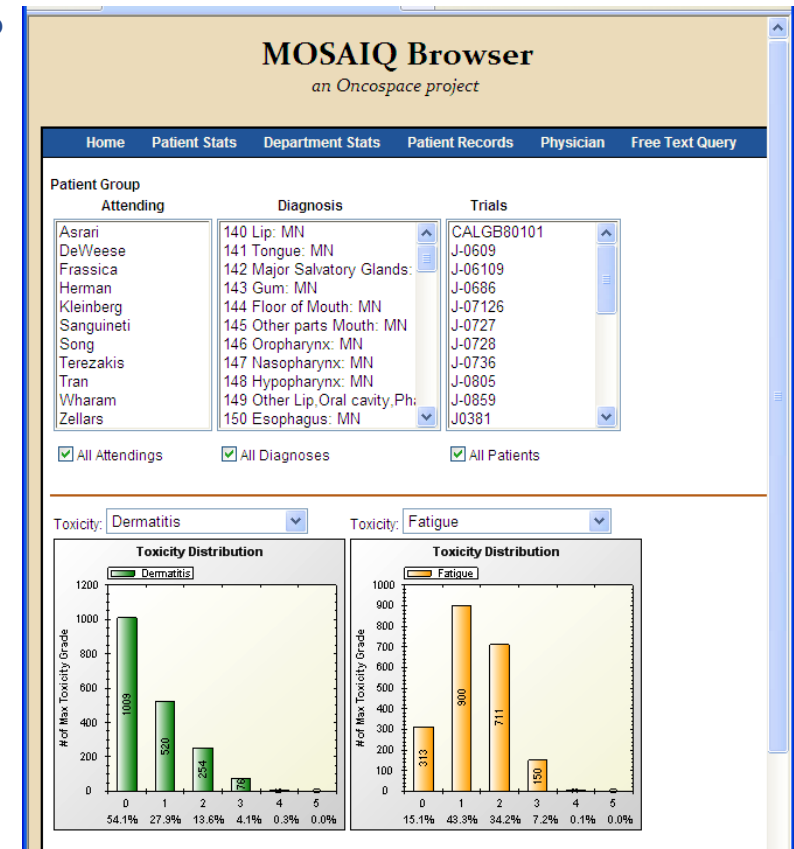
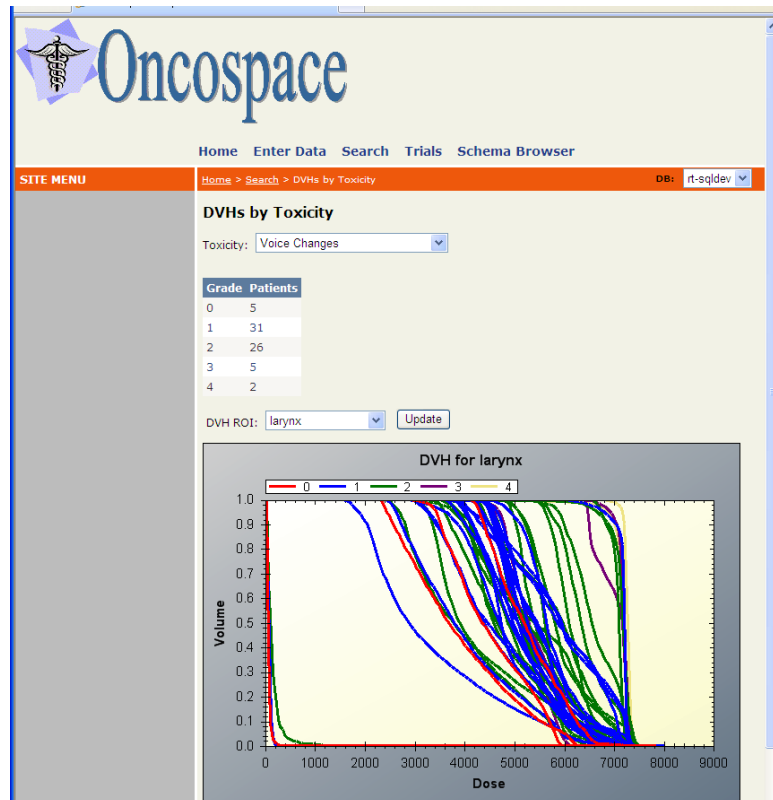
- How to ask questions of the data?
 - Given this DVH, what is the risk of toxicity?



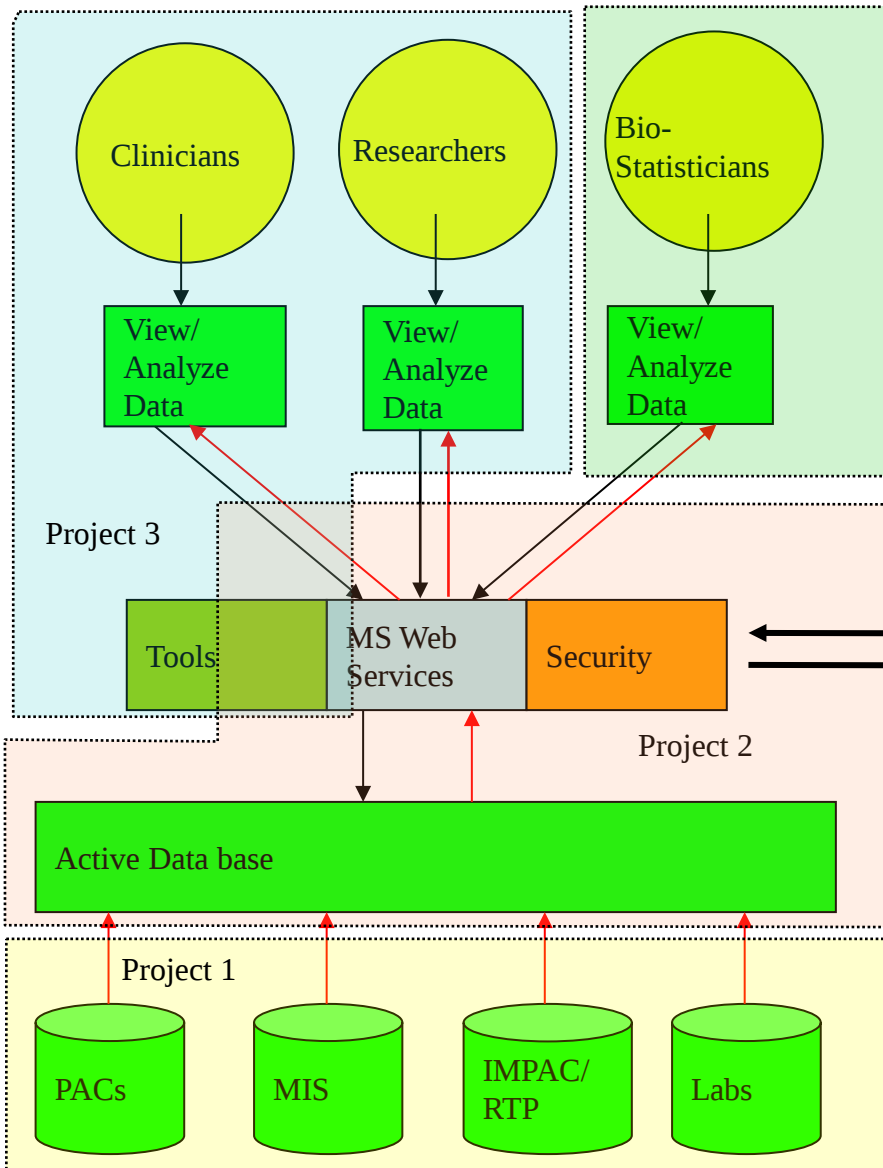
Safety and Quality

Oncospace: Query & Analysis

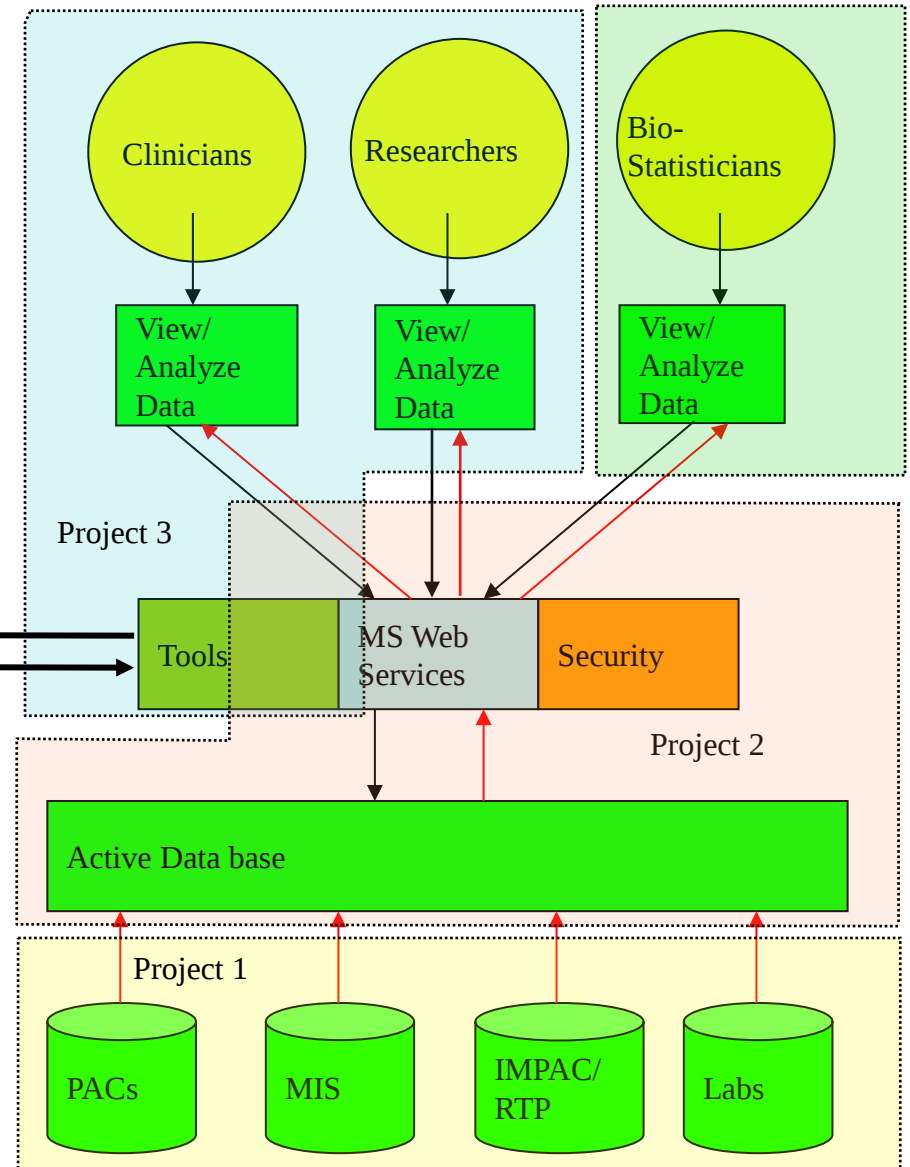
- How to ask questions of the data?
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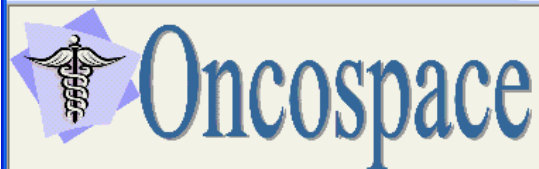


Hopkins



Institution 1,...n (6)





Home Enter Data Search Trials Schema Browser

SITE MENU

- Enter Data
- Search
- Trials
- Schema Browser

Home > Search > DVHs by Toxicity

DB: local

DVHs by Toxicity

Selected Patient: 120

Toxicity: Xerostomia

Grade Patients

0	1
1	5
2	43
3	20

DVH ROI: rt_parotid

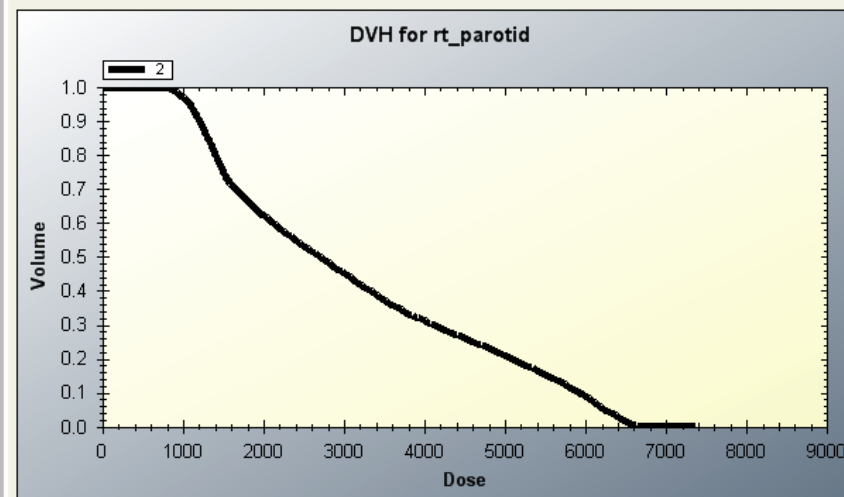
Update

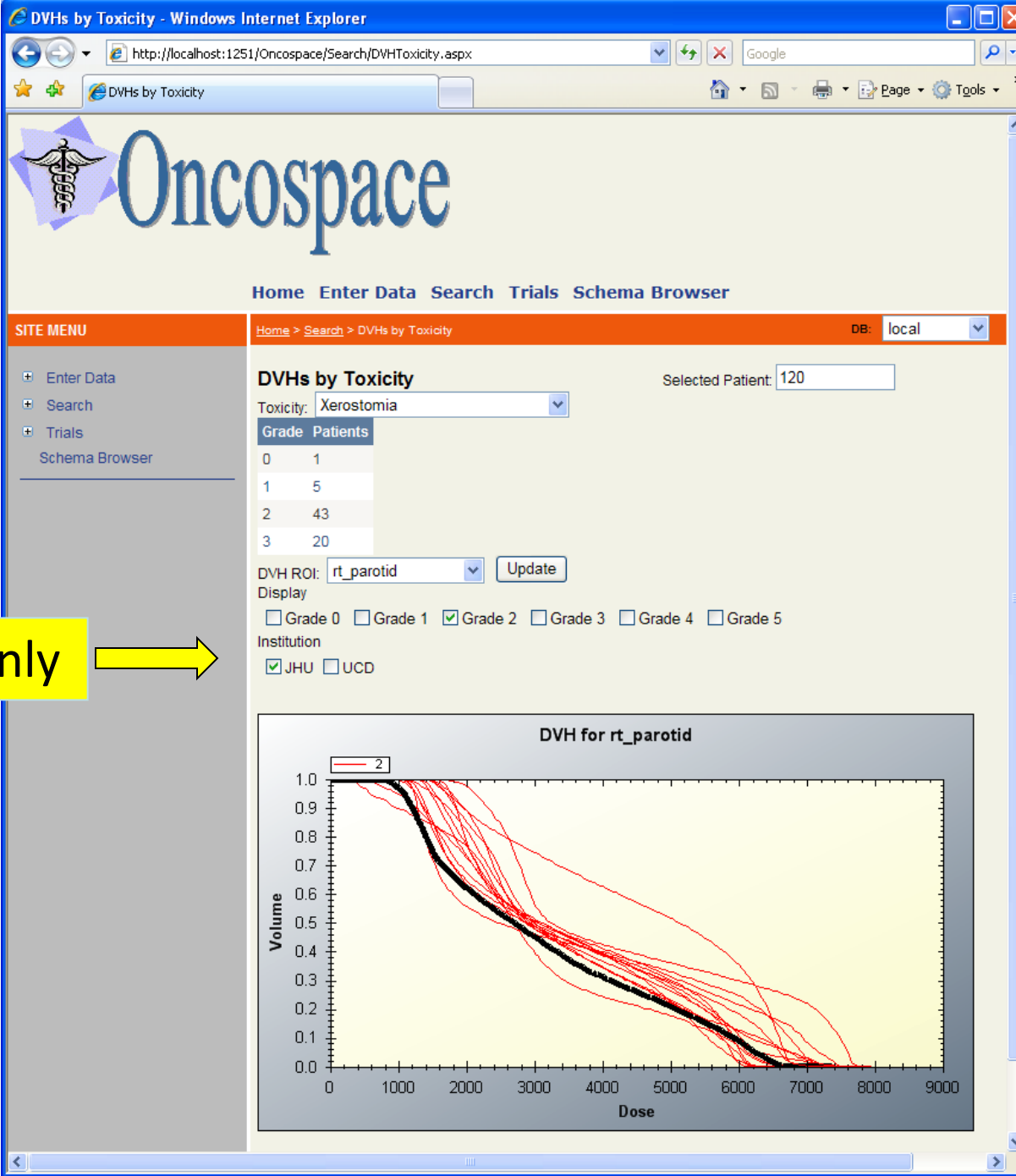
Display

☒ Grade 0 ☒ Grade 1 ☒ Grade 2 ☒ Grade 3 ☒ Grade 4 ☒ Grade 5

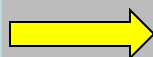
Institution

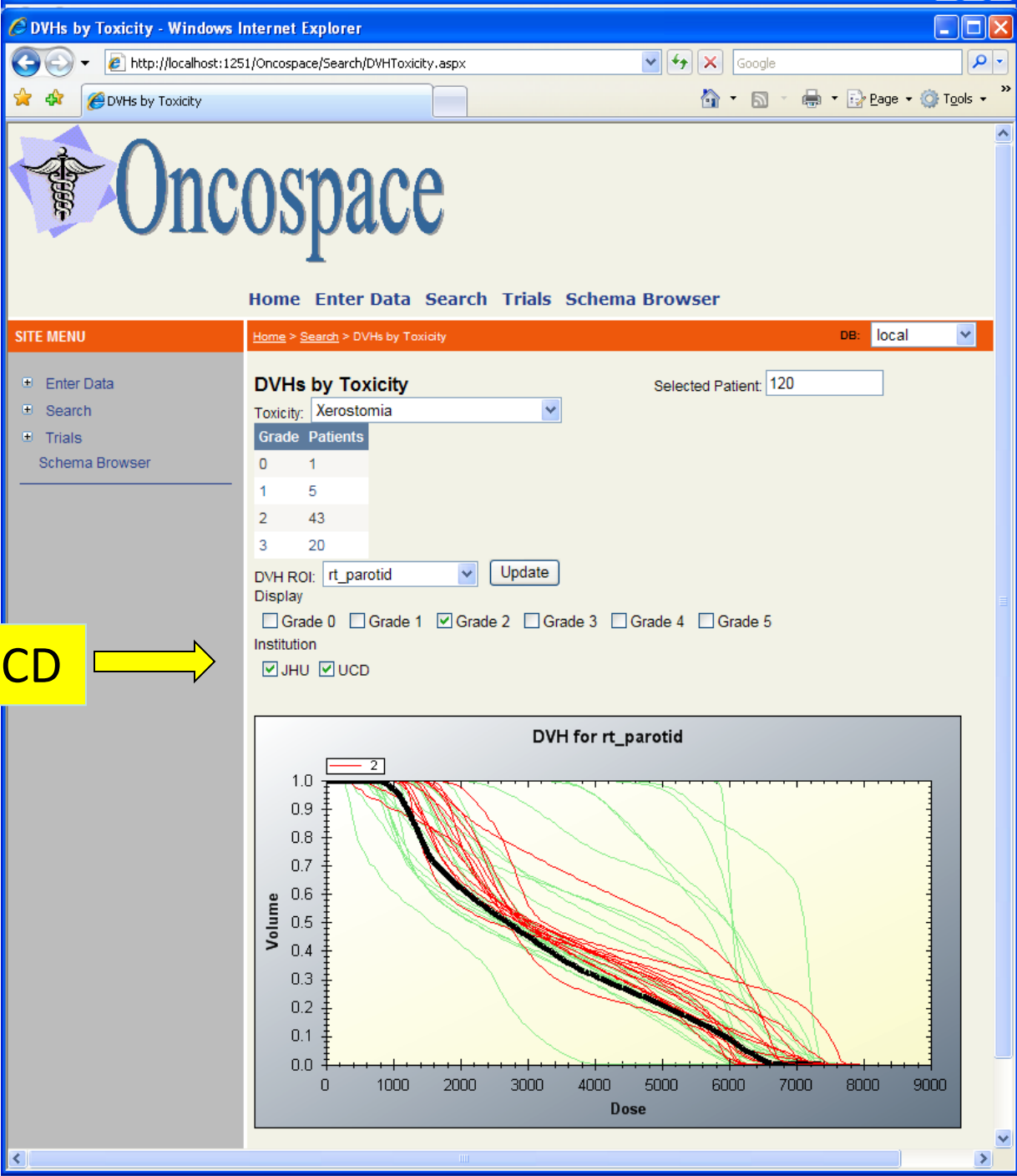
☐ JHU ☐ UCD



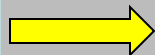


JHU Only





JHU & UCD



Physics to engage Biology in Radiation Therapy

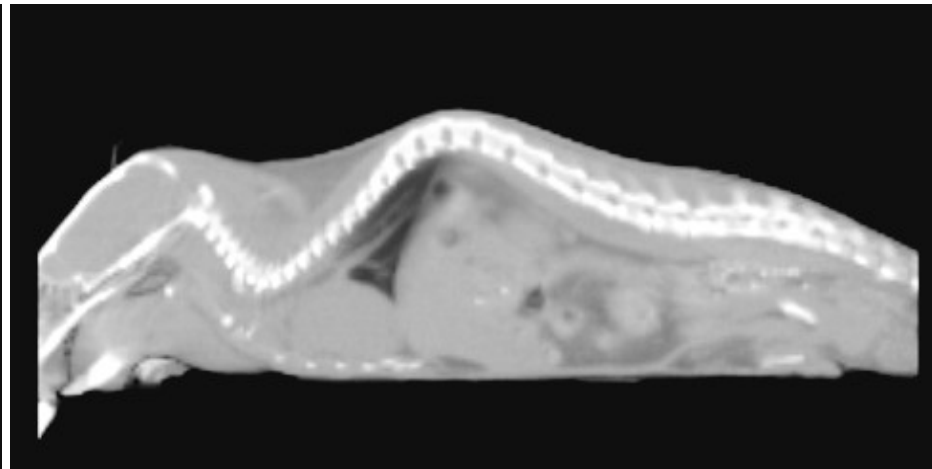
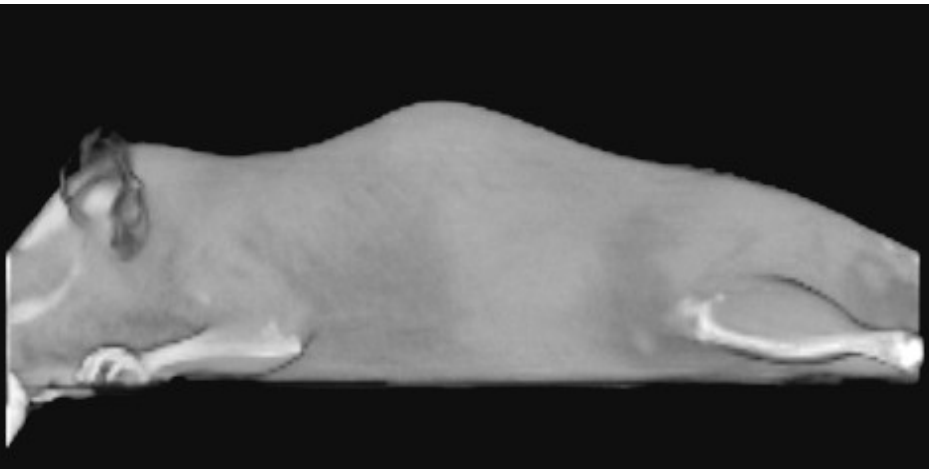
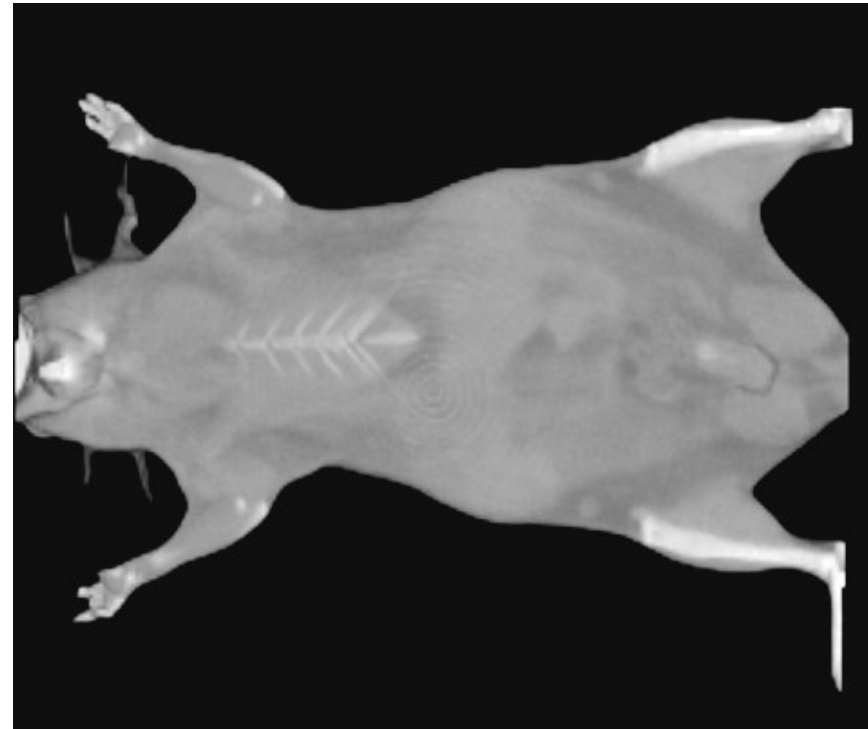
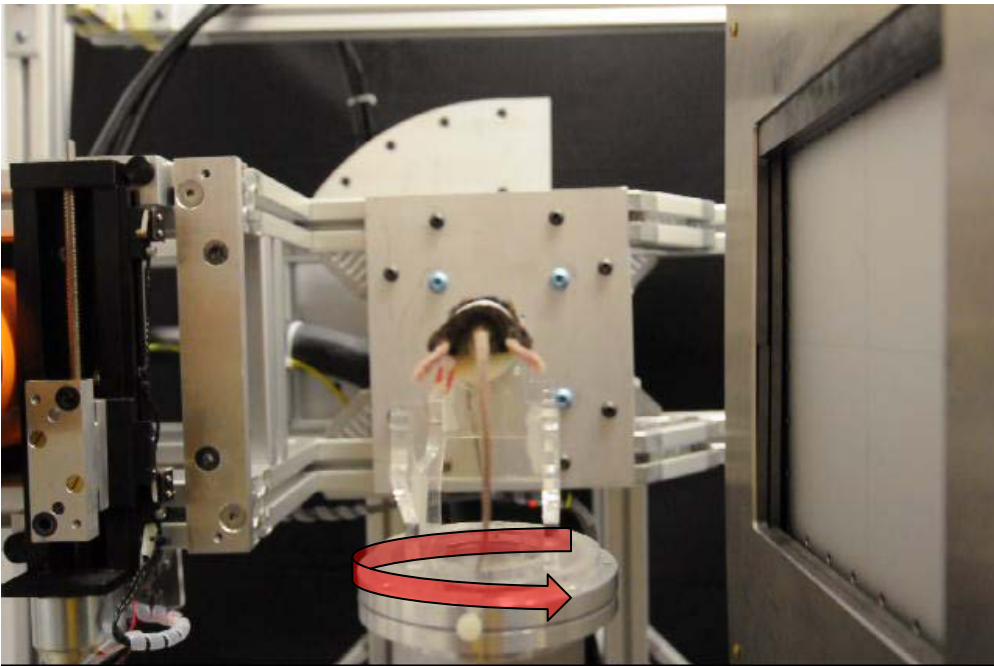
- Questions and Challenges:
 - The validity of EUD, NTCP,
 - Validation and optimization of biological image guided or molecular targeted radiation therapy
 - Others questions: biological target volume???
- Present small animal radiation research methods bear little resemblance to human treatment
- A pressing need to down-size human treatment to bridge small animal laboratory research

Small Animal Radiation Research Platform



- Hopkins-Xstrahl partnership
- Integrated 3D-Slicer-GPU based treatment planning system
- Computer controlled
 - 360° gantry rotation
 - Non-coplanar delivery

SARRP CBCT: “Pancake” geometry



Small Animal Treatment Console

The image displays the Small Animal Treatment Console interface, which is divided into several sections:

- SARRP Control Interface:** This section contains a menu bar (File, View, Robot, Cone Beam CT, XIS Detector, XrayBox Camera, ImageJ, Delivery, Help) and a control panel. The panel includes a table for axis positions, checkboxes for "Motors Enabled" and "Comm OK", and buttons for "Move!", "STOP!", "3D Slicer", "New Patient", "CBCT Acquisition", and "View CBCT".
- 3D Slicer Version 3.6:** This section shows the 3D Slicer software interface. It includes a menu bar (File, Edit, View, Window, Help, Feedback) and a toolbar. The main window displays a 3D model of a rat, with a "Rat Panel" and "Portal Image" section below it. The "Rat Panel" shows a top-down view of the rat, and the "Portal Image" shows a cross-sectional view. The "3D Slicer" window also includes a "Help & Acknowledgement" section and a "Treatment Planning" section.
- 3D Model of a Rat:** A 3D model of a rat is shown in the center of the interface, with a "Rat Panel" and "Portal Image" section below it. The "Rat Panel" shows a top-down view of the rat, and the "Portal Image" shows a cross-sectional view.

The "SARRP Control Interface" section includes the following table:

Axis	X, mm	Y, mm	Z, mm	Theta, degrees	Gantry, degrees
Iso	0.34	0.58	1.24	0.00	0.00
Goal	0.34	0.58	1.24	0.00	

The "3D Slicer" section includes the following table:

Fiducial Name	X	Y	Z
SARRPClient-P	-5.41	18.05	0.00

SARRP Slicer- 3D RTP: GPU Dose – CBCT Engine

3D Slicer Version 3.6.3

File Edit View Window Help Feedback

Modules: SarrpGUI

Search modules

3DSlicer

Prescribed dose: 100 cGy

Dose (cGy): 100

Entry	B.W.	Target	Collim.	G.A.	C.A.	G.E.	C.E.	Time
bea...	33.3	IsoC	3x3 mm	0	0	N/A	N/A	0.05
bea...	33.3	IsoC	3x3 mm	45.0	0	N/A	N/A	0.05
bea...	33.3	IsoC	3x3 mm	90.0	0	N/A	N/A	0.05

Isocenter: IsoC Collimator: 3x3 mm

Beam Mode: Arc

Gantry Angle: 90

Couch Angle: Set Gantry, Couch angle

Compute Dose

Treatment Plan Execution

Execute Plan STOP

Manipulate Slice Views

Manipulate 3D View

Set Iso Assign Wt

3 x 3 collimator

SARRPClient SARRPDose 105 4.57

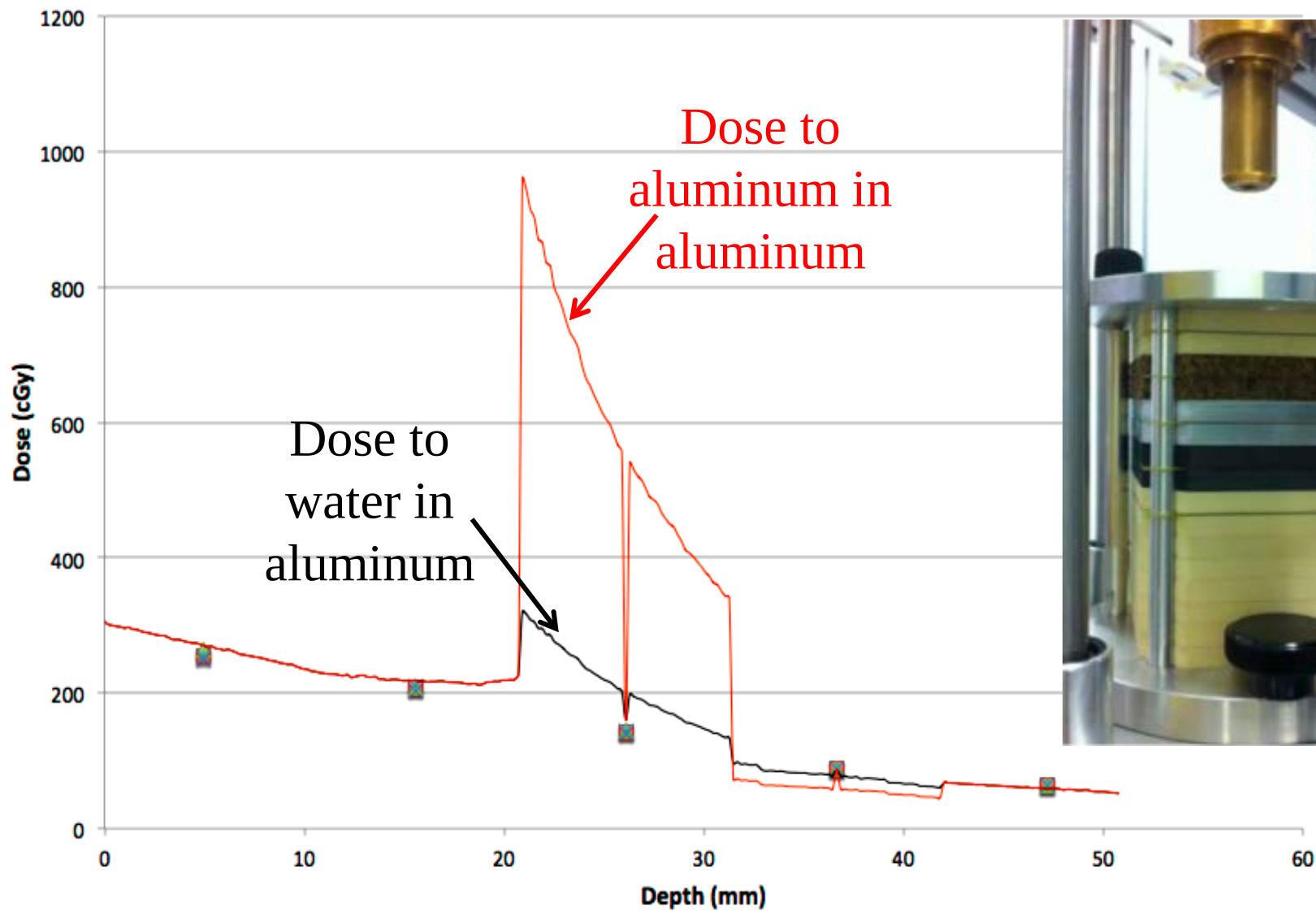
Sagittal SARRPClient SARRPDose 123 -1.1395

Coronal SARRPClient SARRPDose 108 -17.028

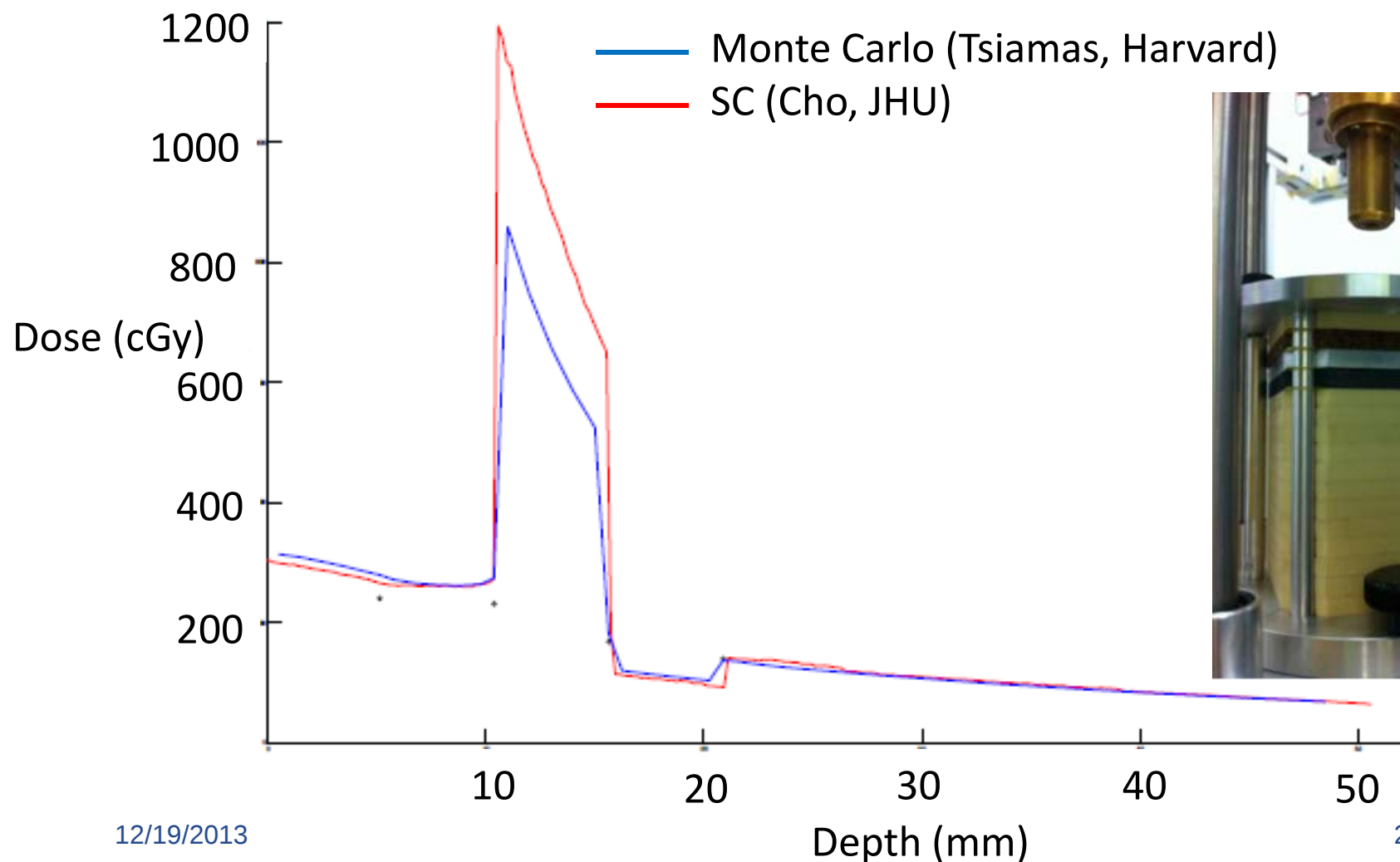
cGy

130.0
124.0
118.0
112.0
106.0
100.0
94.0
88.0
82.0
76.0
70.0

Depth dose (SET2, double)

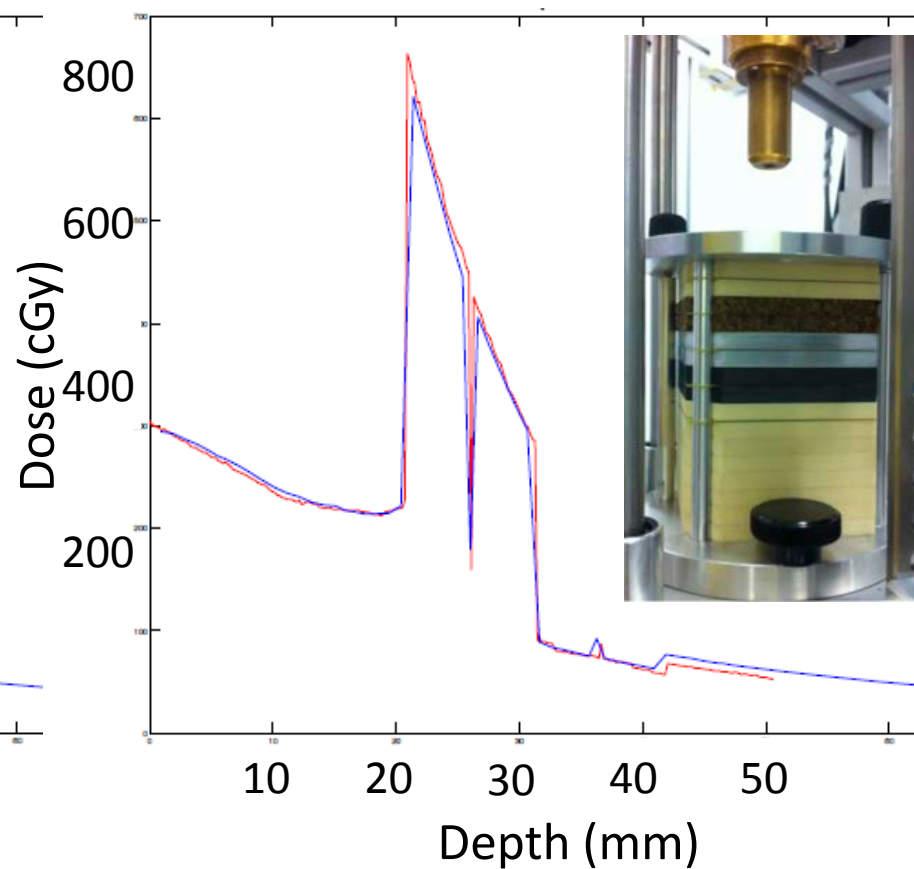
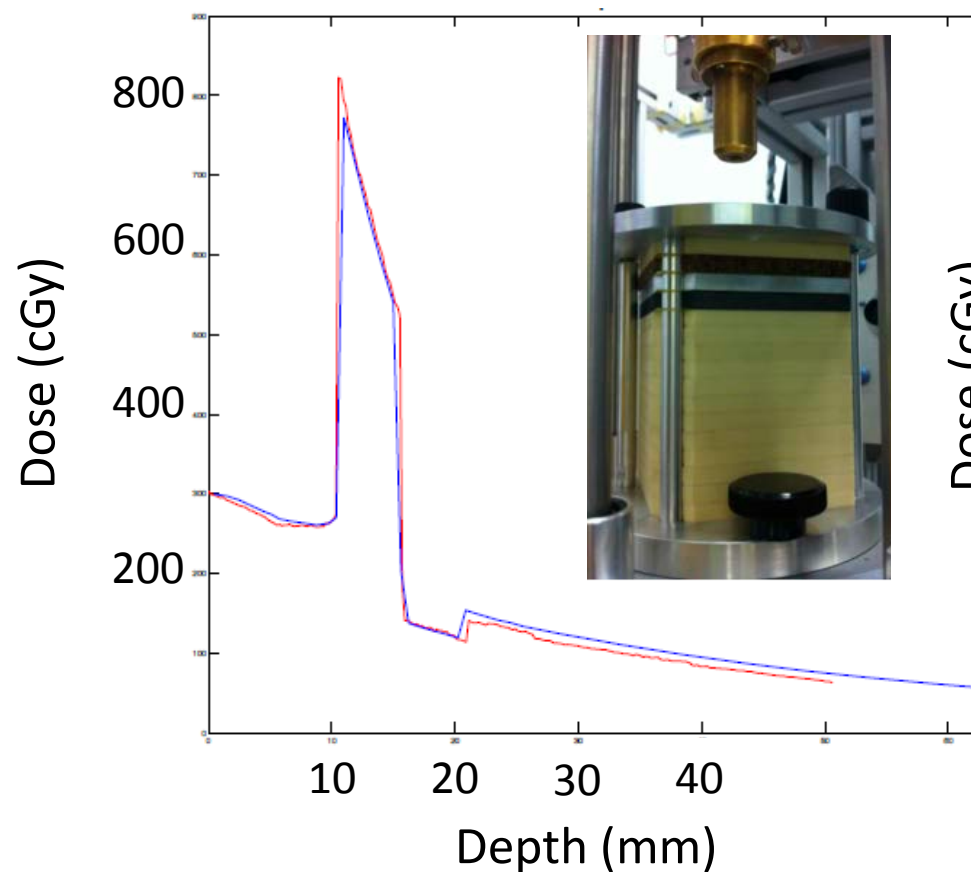


Comparison of SC to Monte Carlo

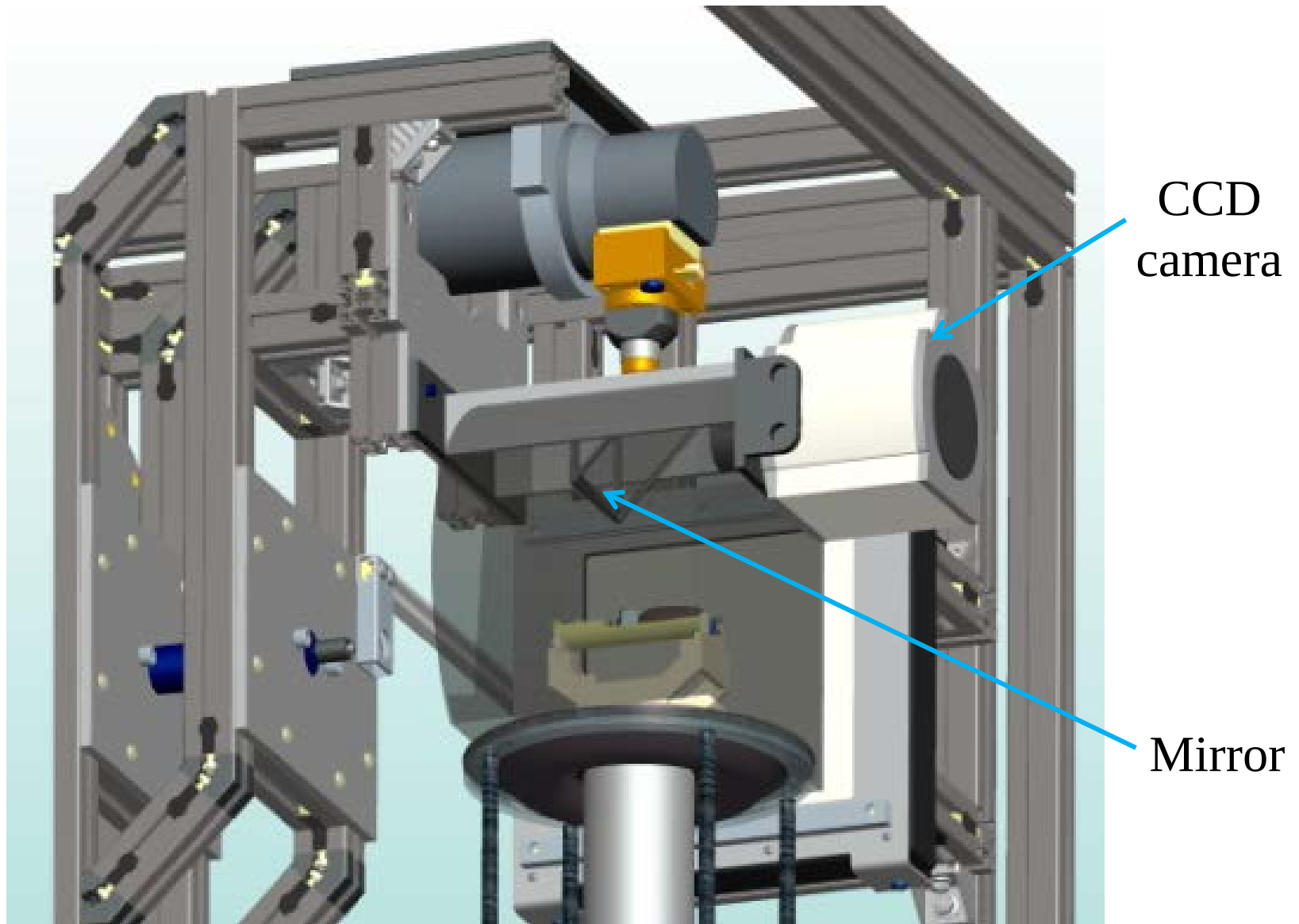


Comparison of SC with MC

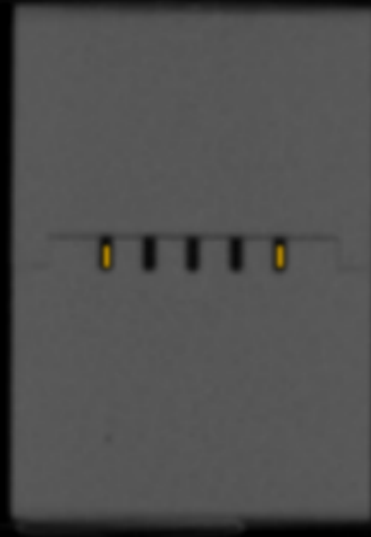
Correcting for density scaling



On-board BLI/BLT for Beam's Eye View Irradiation with the SARRP (R01 CA158100)



CBCT

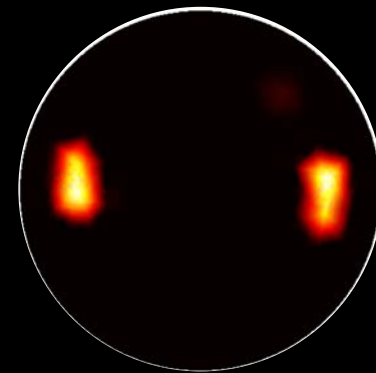


Coronal



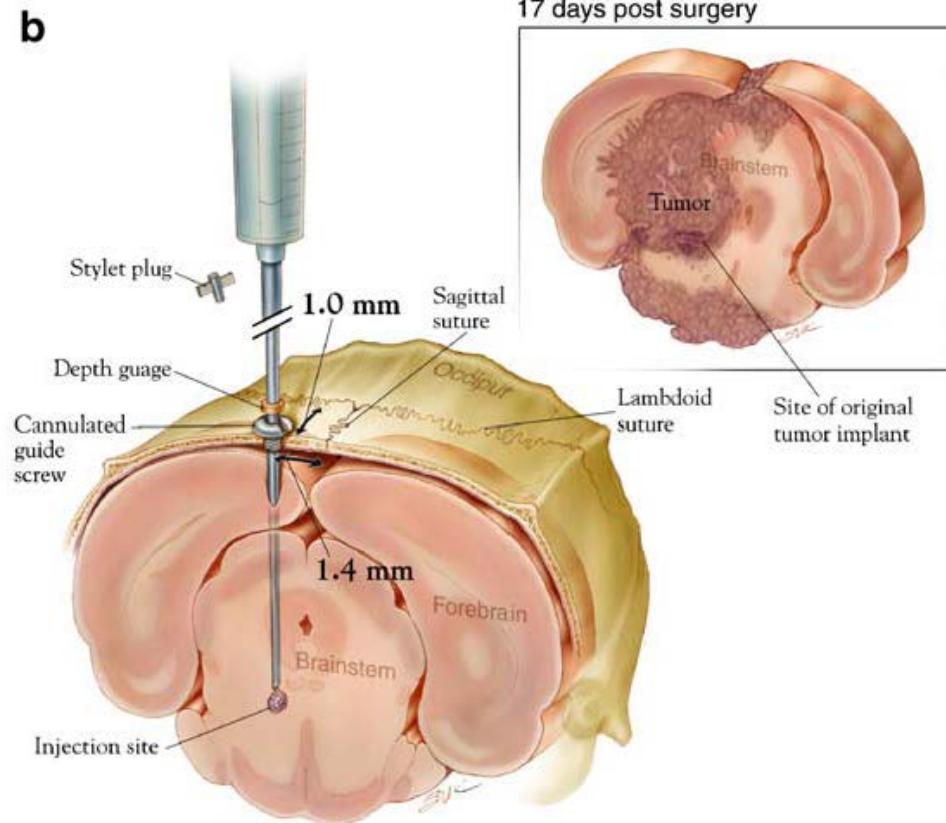
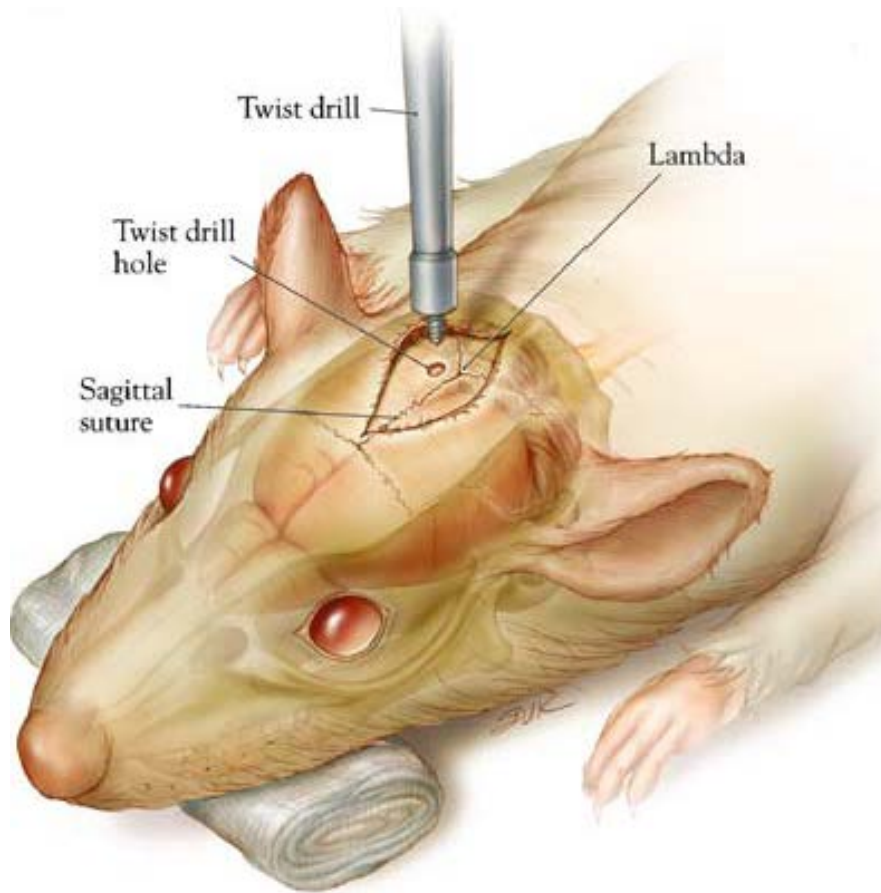
Transverse

BLT



BLT Reconstructed with only one wavelength (630nm). accurate in vertical position, but 1-2mm error along axial direction. Multi-spectral recon would improve the accuracy.

Combining Stereotactic Radiation and Anti-PD1 Therapy in an Orthotopic Mouse Glioma Model (Zeng et al)



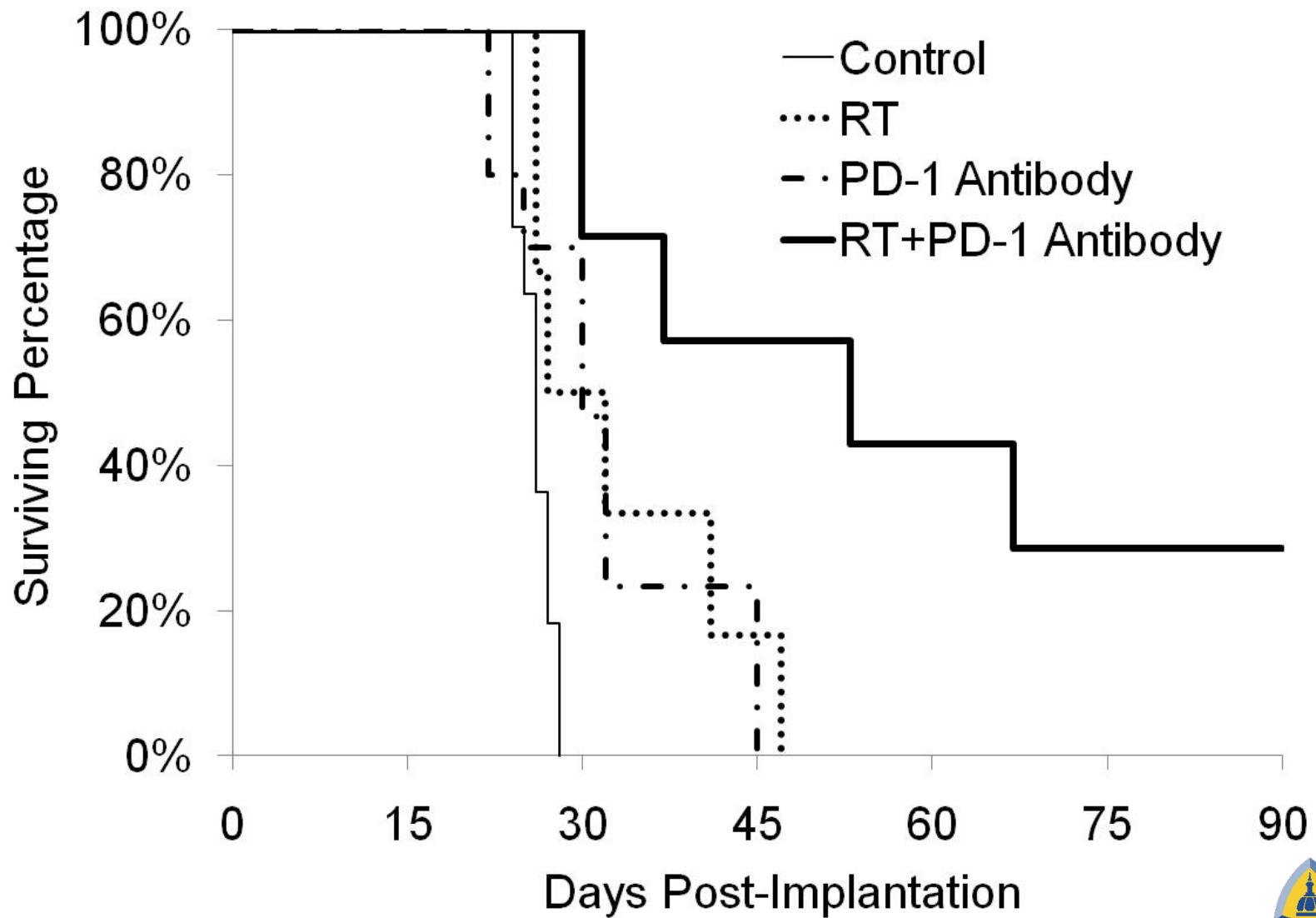
Experimental Design

Day	No Tx	RT only	PD-1 only	RT+PD-1
0	Tumor Implantation			
7	Bioluminescent Imaging			
10		Radiation	1 st antibody dose	Radiation; 1 st antibody dose
11				
12			2 nd antibody dose	2 nd antibody dose
13				
14			3 rd antibody dose	3 rd antibody dose
21	Bioluminescent Imaging			

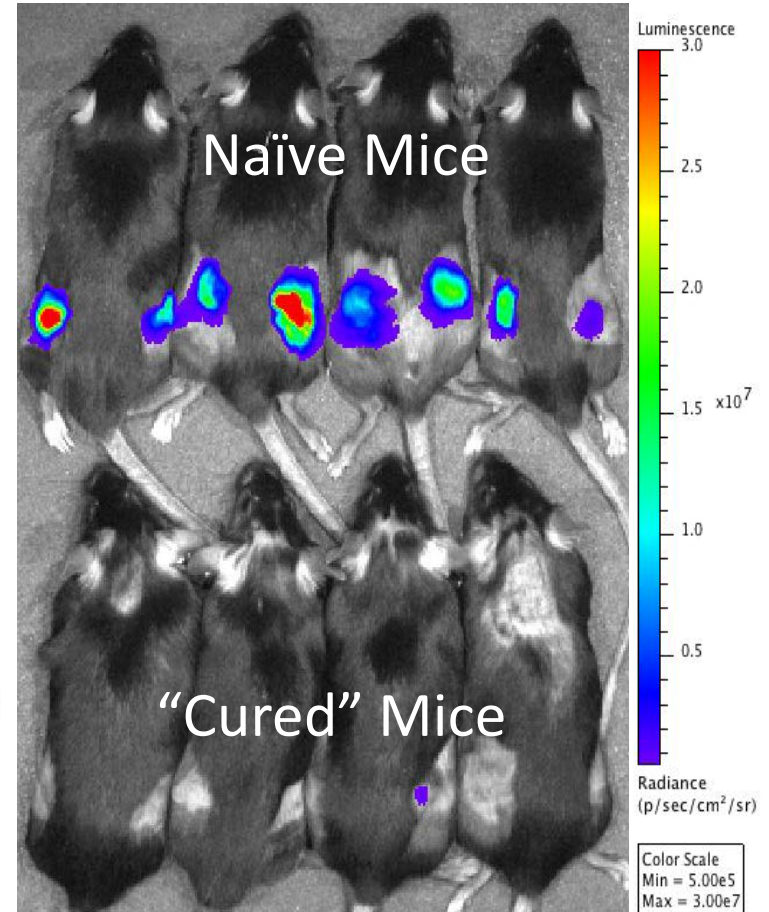
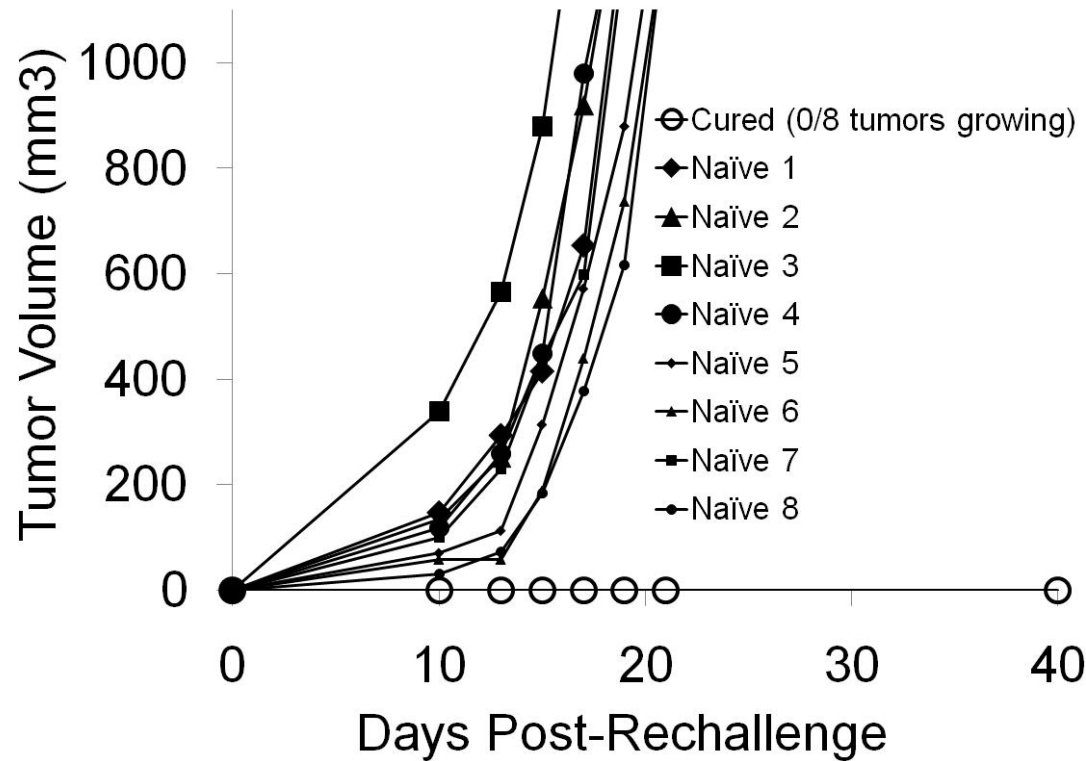
Radiation = 10 Gy in 3 mm beam

Antibody = anti-PD-1 antibody, 200 µg/mouse

Survival Outcome



Flank Re-challenge



What do we do for the next 5 years?

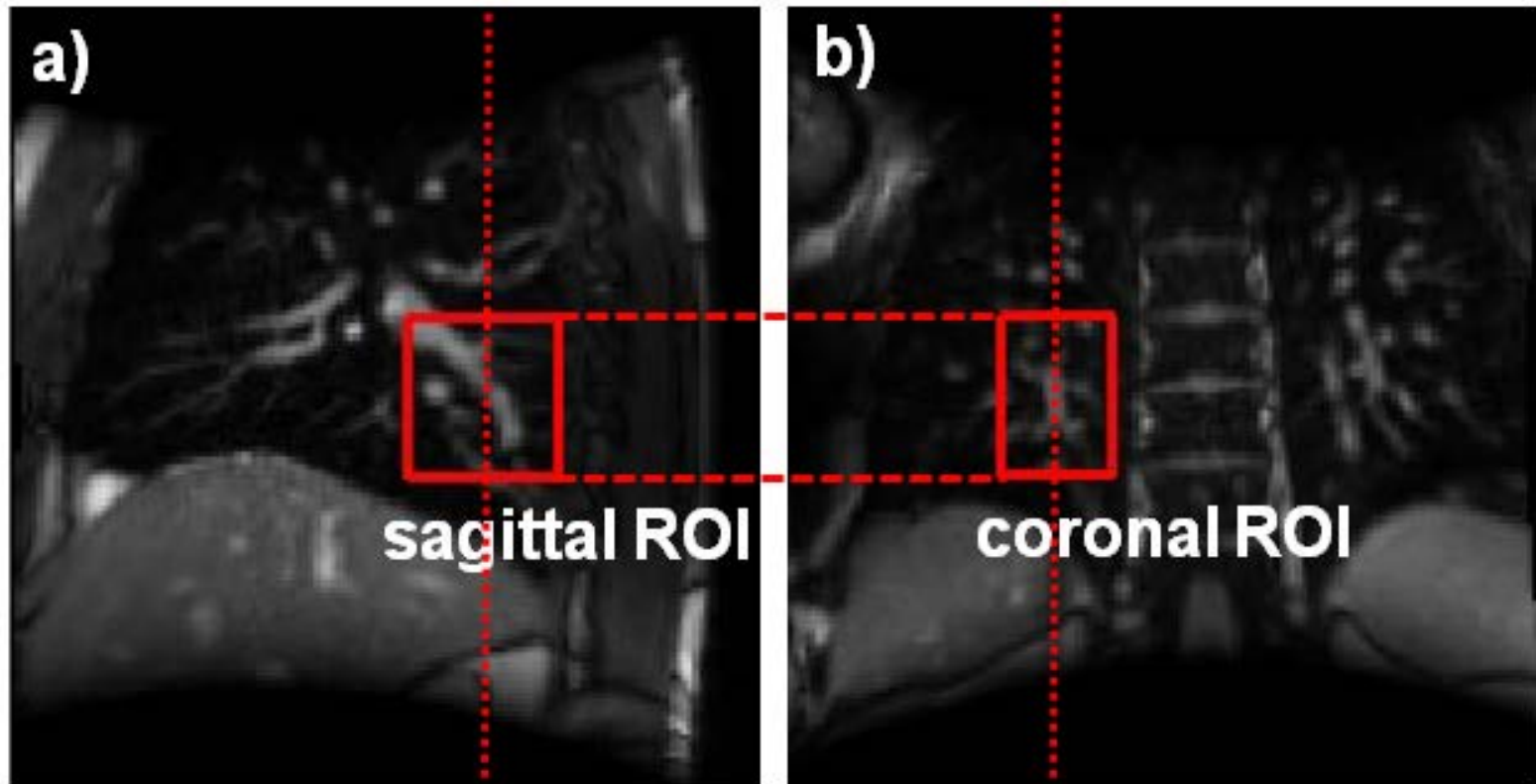
- Medicine (and radiation oncology) is undergoing tremendous changes driven by technologies and information
- Treatment strategies will employ multiple therapeutic agents with radiation
- Personalized medicine will be based on genetics, treatment response, functional/anatomic
- Physics need to expand beyond technologies:
 - *Technology, Informatics, Biology,.....*
 - *We must innovate*

4D MRI (JHU/Siemens)

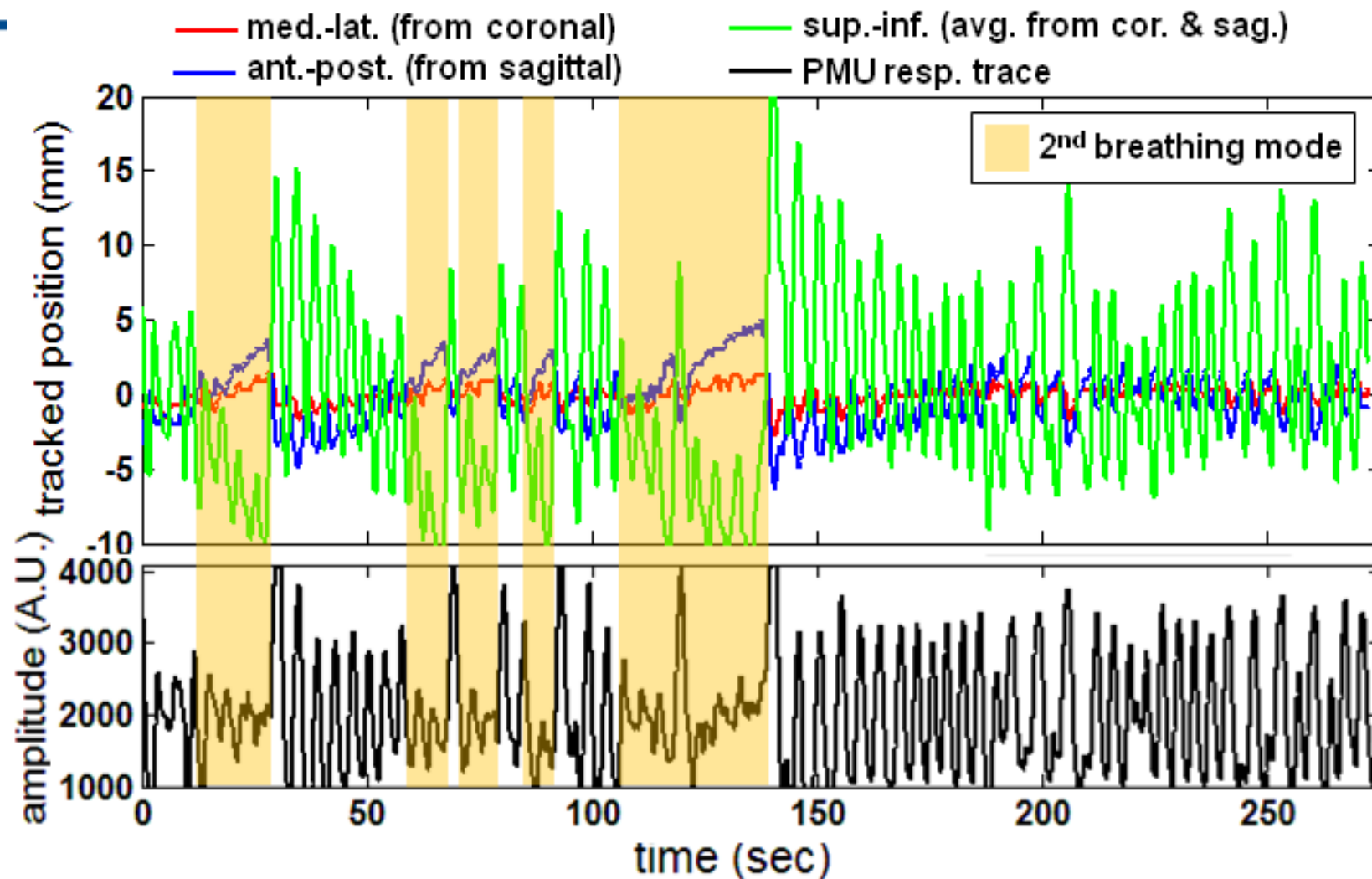
- 4D CT is a 2 min snapshot, not often re-evaluated
- Long duration (15 – 30 min) MRI to represent treatment



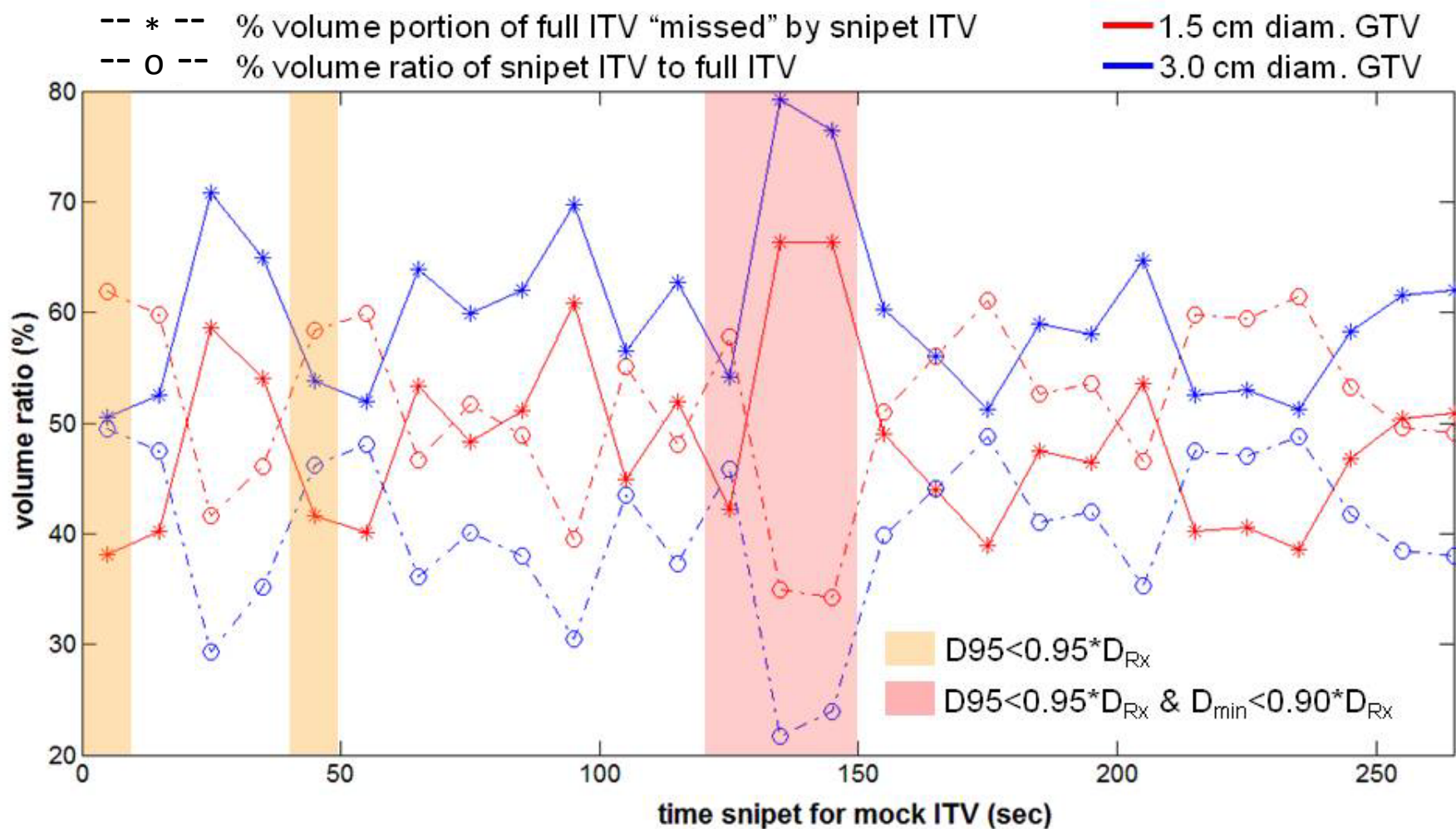
4D MRI – Tracked Motion



4D MRI – Characterization of Motion



4D MRI – Characterization of Motion



Motion Management: A case for Breath-hold

- Breath hold imaging is the gold standard
- *Breath-hold and gating are not mutually exclusive*
- Active Breathing Control for reproducible breath-hold
 - Integrate the ABC process to maximize compliance
 - Short, normal or deep inspiration BH (ABC/gating)
 - Gate the accelerator with the ABC device

Diagnosis vs Prescription

Home Patient Stats Department Stats Patient Records Physician Billing External Free Text Query

185 Prostate: MN
186 Testis: MN
187 Penis & Male Genital Or
188 Bladder: MN
189 Kidney & Other Urinary C
190 Eye: MN
191 Brain: MN
192 Other parts Nervous Sys
193 Thyroid Gland: MN
194 Endocrine Glands & Stru
195 Other/III-Defined Sites: M

Summary
Toxicities
Toxicity Progression
Weekly Stats
Patients and Zip Codes
Offset Predictions
Offset Trends
Offset Raw Data
Rx Frequency
Rx Charting

☒ Select morphology

Acute leukemia, NOS
Adenocarcinoma, metastatic, NOS
Adenocarcinoma, NOS
Adenoid cystic carcinoma
Adenosquamous carcinoma
Astrocytoma, anaplastic type (T-191. __)
Astrocytoma, NOS (T-191. __)
Carcinoma, metastatic, NOS
Carcinoma, NOS
Carcinomatosis
Carcinosarcoma, NOS

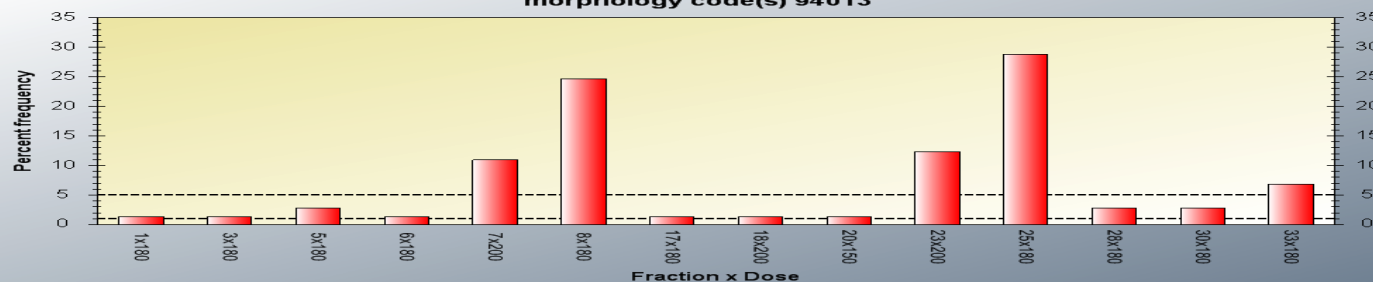
☒ Order by fraction, dose ☐ Order by dose, fraction ☐ Order by frequency ☐ Order by total dose

☒ Absolute value ☐ Percent frequency

Include all

☐ Ignore fractions/doses used less than 1 times(s)

Fraction x Dose Frequency for diagnosis code(s) 191
morphology code(s) 94013



Showing 73 treatment(s) with 14 distinct

Fraction x Dose

OncoSpace: Adapting the SkyServer Approach

Sloan Digital Sky Survey / SkyServer



- SDSS is a collaborative effort to map 25% of the sky
- SkyServer publishes data from the SDSS
- >> 100's of new discoveries in astrophysics
- Increased scale and scope for research
- Shared resources
 - Methodology
 - Software
 - Expertise
 - Experience
- New opportunities
 - Analysis
 - Visualization
 - User experience
- Skyserver.sdss.org