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

John Wong, Ph.D.

Johns Hopkins University

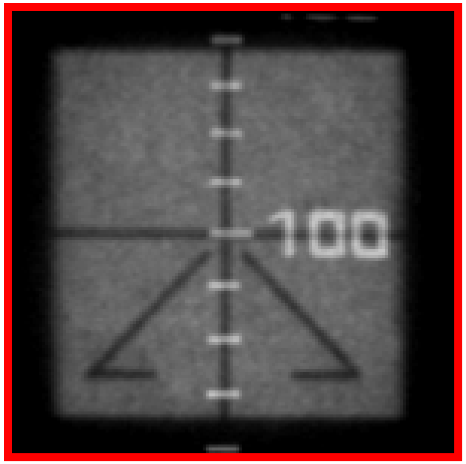
## Acknowledgments

- *Radiation Oncology Physics*
  - T McNutt, E Tryggestad, K Wang, T Roland, ……
- *Radiation Oncology Clinical & Molecular Radiation Sciences*
  - J Herman, P Tran, D Song, H Quon, T DeWeese
- *JHU Computer Science/Robotic Engineering*
  - R Taylor, P Kazanzides, I Iordachita
- *Radiology, Neurosurgery, Neurology, ICMIC, Oncology*
- *JHU Physics & Astronomy*
  - Alex Szalay

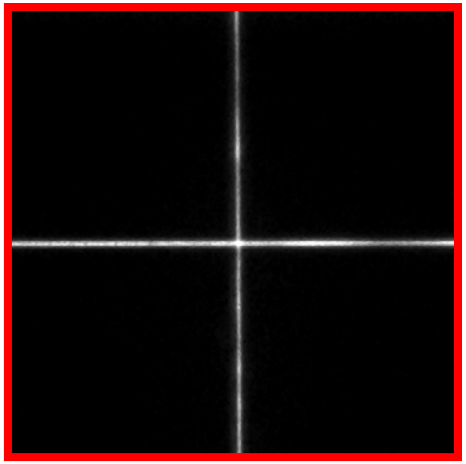
## Disclosure

- *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*

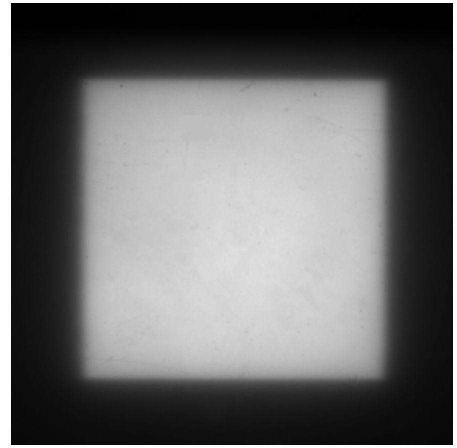
# Technology Challenge: TG 142 QA



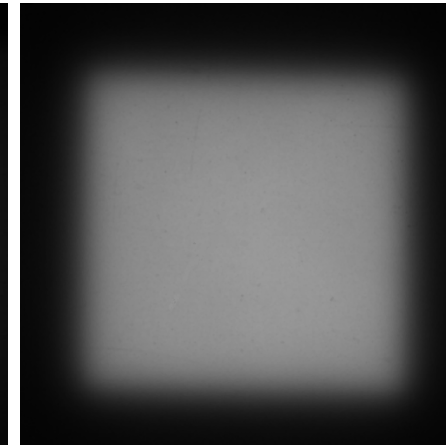

***Light field with ODI***



***Room Lateral Laser***



***6 MV x-ray at dmax***

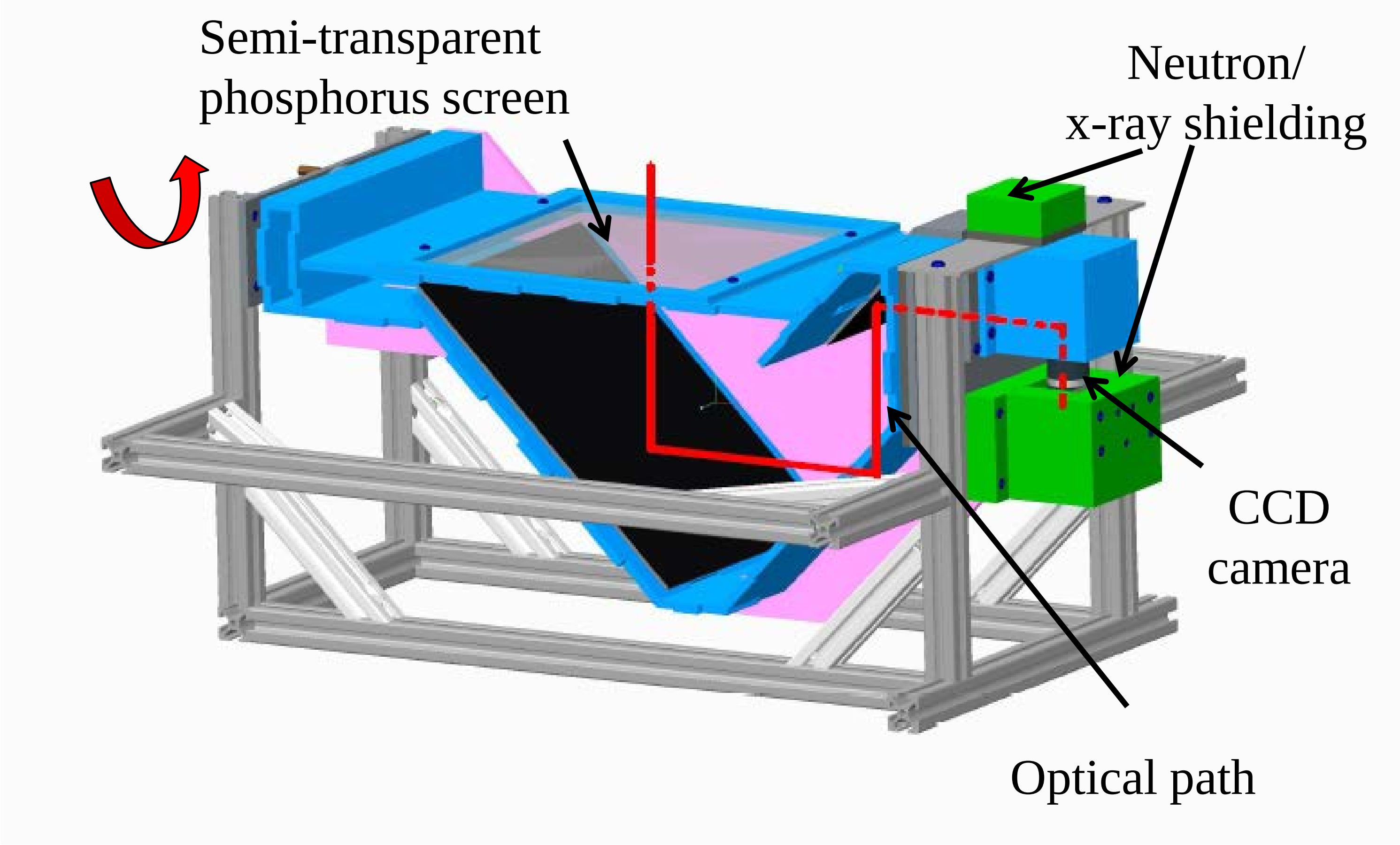


***12 MeV electron at dmax***

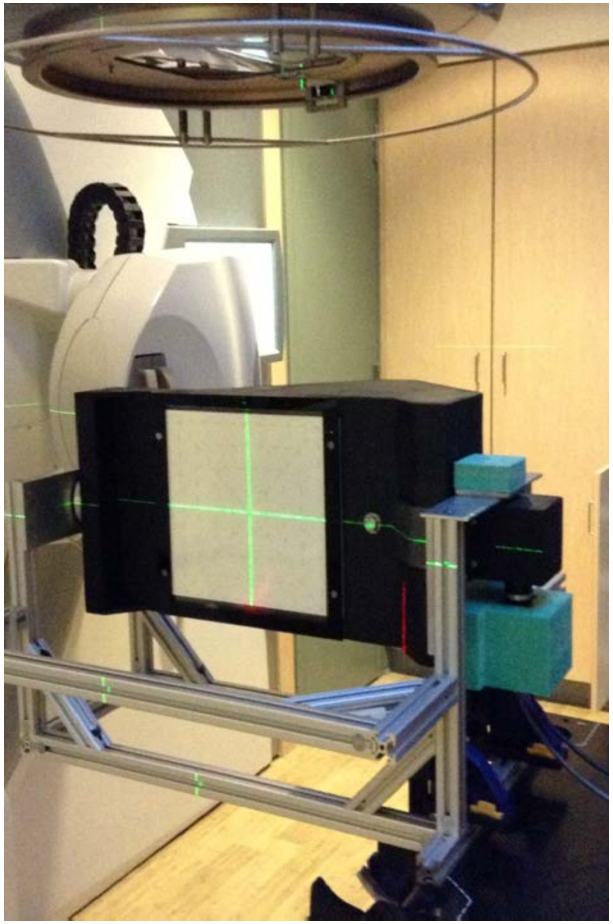
- 1.4 Mpixels, 16-bit, CCD camera to provide 0.2 mm x 0.2 mm per pixel resolution for a 20 cm x 20 cm image
- CCD operates at integration mode
- Optical / Laser imaging *without* buildup on phosphor
- Radiation imaging *with* buildup on phosphor

# An Unified QA System for TG 142

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



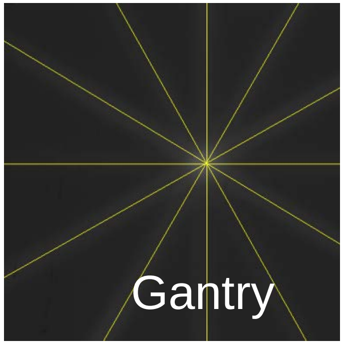
# 1$^{st}$ prototype

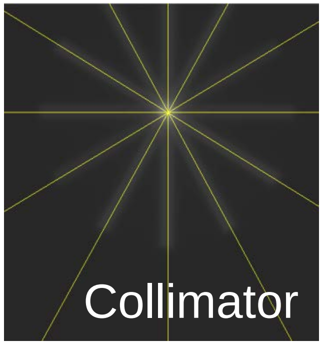


Suspended setup for gantry rotation measurements

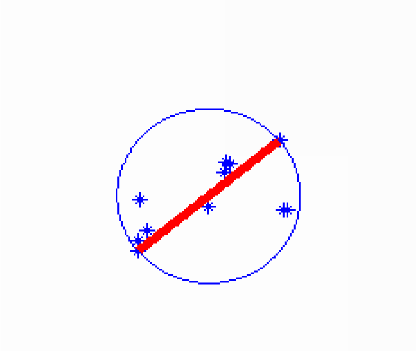
# Radiation Isocenter QA

- 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:

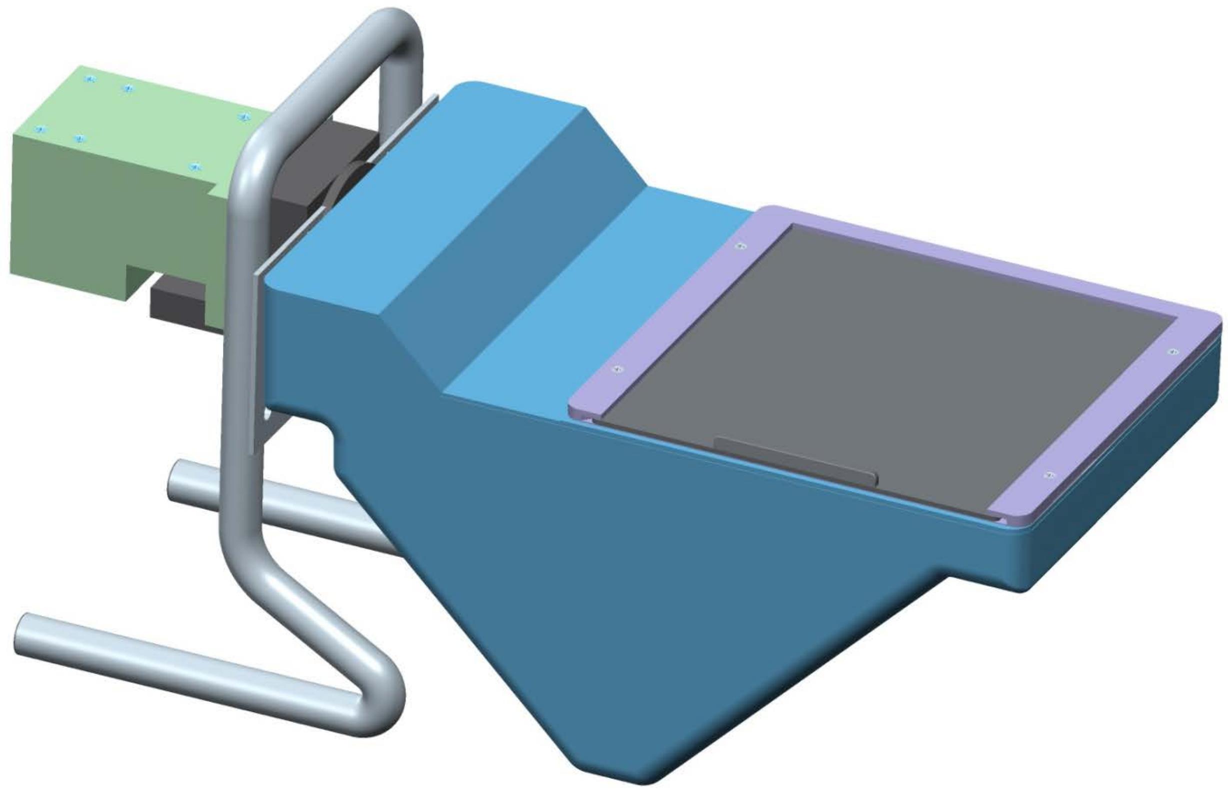


COM diameter = 0.3 mm

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

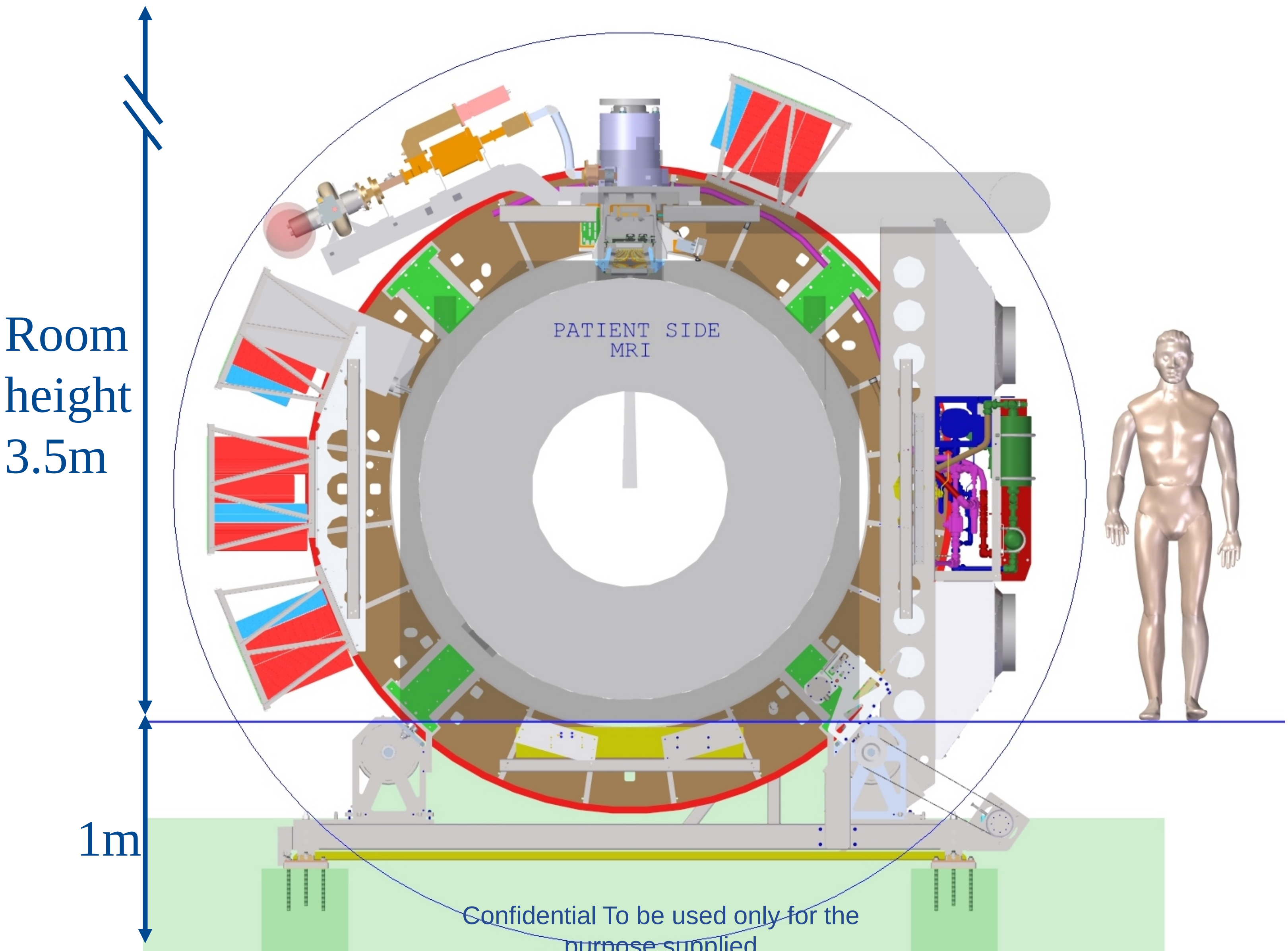
| **Inter-fraction methods: Cone beam CT, MV CT** | | | |
|---|---|---|---|
| **Pros** | Adaptive Radiation Therapy | **Cons** | Ionizing radiation |
| | | | Image Quality |

| **Inter-fraction methods: Intra-modal ultrasound imaging** | | | |
|---|---|---|---|
| **Pros** | Soft tissue information | **Cons** | Snap Shot (at present) |
| | Non-ionizing | | Expertise/operator dependence |

| **Intra-fraction methods: Implanted Markers** | | | |
|---|---|---|---|
| **Pros** | Real-time monitoring | **Cons** | Invasive |
| | Non-ionizing option | | Ionizing radiation |
| | | | Soft tissue surrogate (truth?) |

- Emergence of MRI-Radiation Machines

# Phase 1 Prototype MRI-GRT



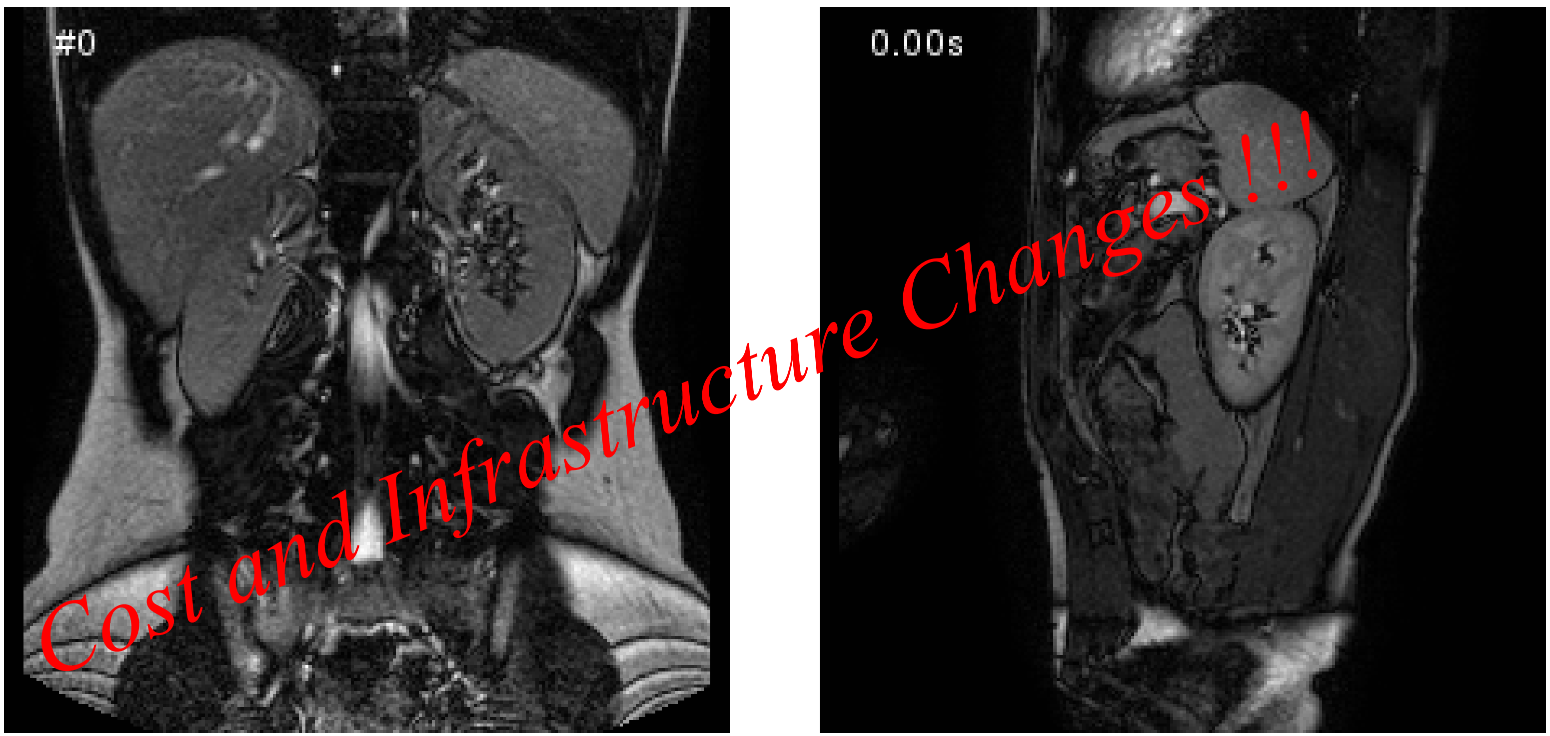
# MRI-GRT project : Current Status

- 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

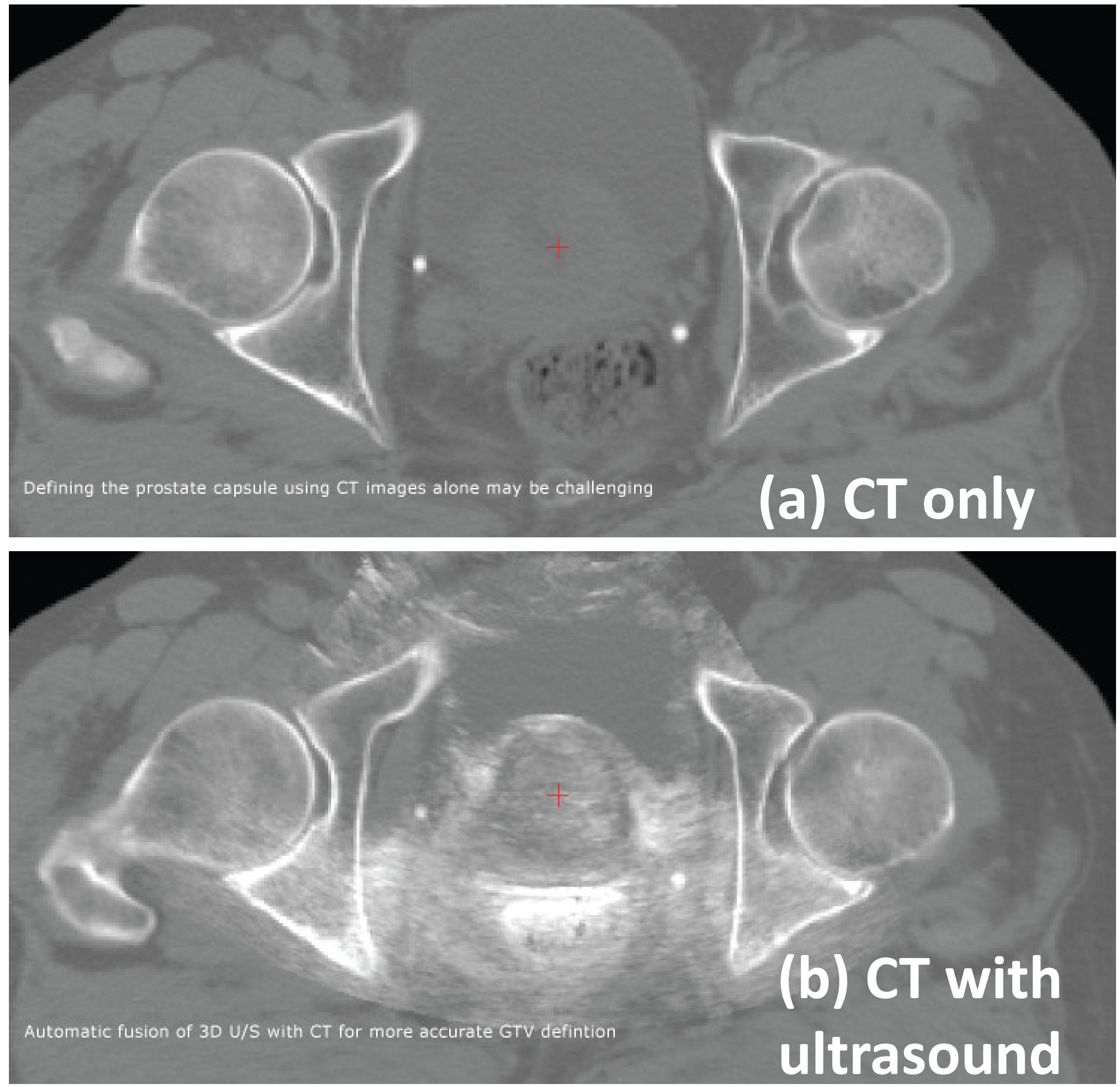



Courtesy UMC Utrecht

# Integrated 3D ultrasound/CBCT imaging  for soft tissue IGRT

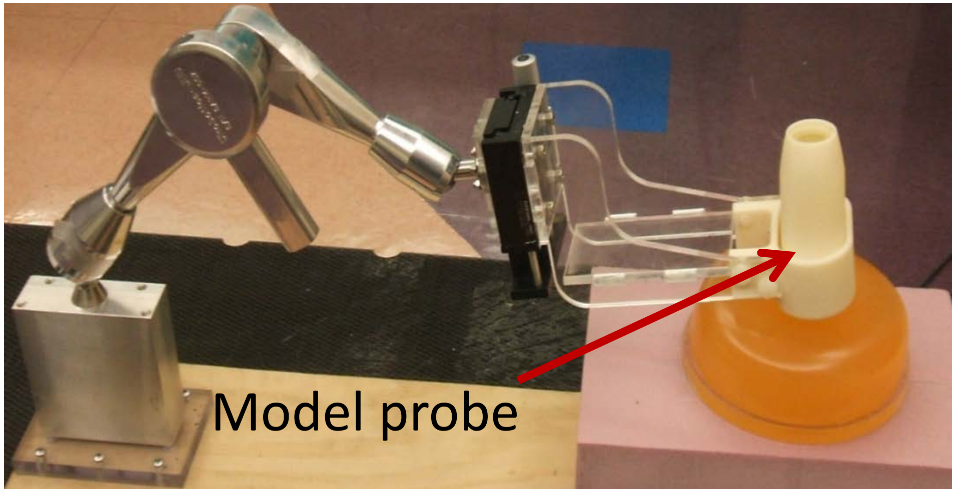
***Hypothesis:***

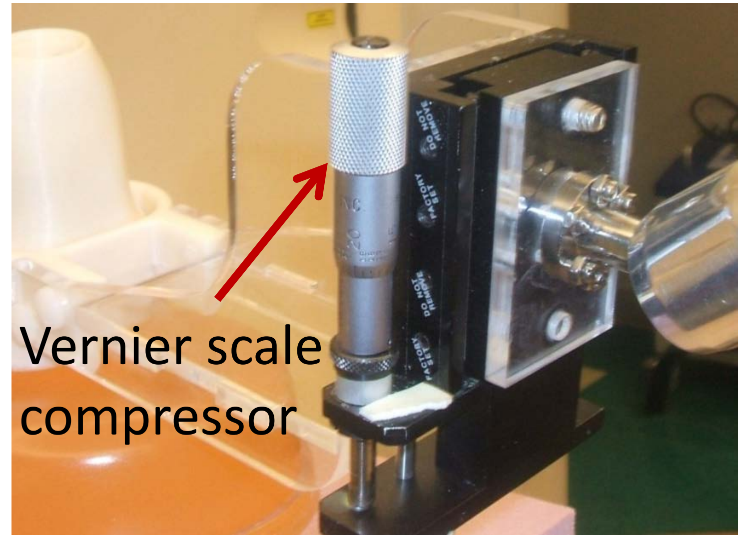
- US-CBCT offers an non-ionizing, non-invasive inter- and intra-fraction solution for soft tissue targets
- Prostate, liver, pancreas



| 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 |
| *Require simulation/planning of patient in treatment position with the ultrasound/CBCT system in place* | |

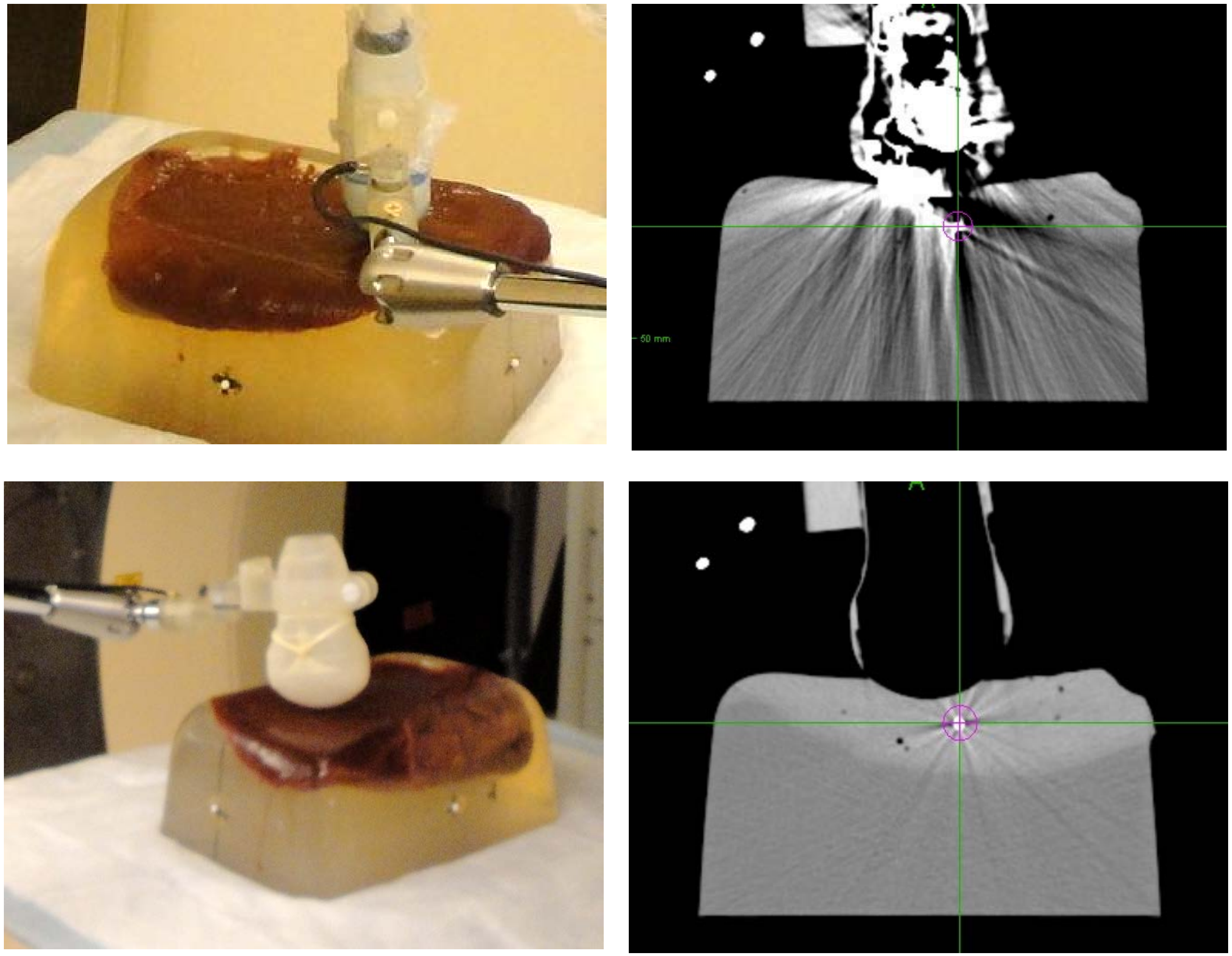
# Passive robotic arm and gel phantom



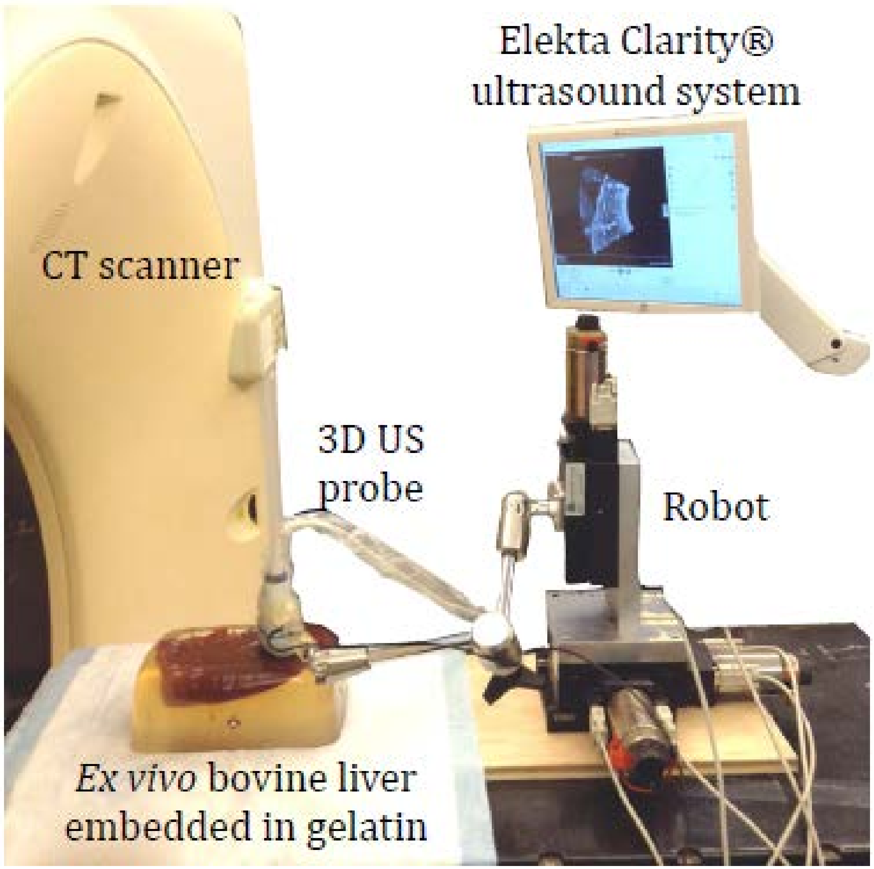

- A passive robotic arm with 1D linear (vernier scale) actuator
- Deformable gel phantoms with embedded 12 PMMA beads (1.2, 2.8, 3.2 mm in diameter)
- CT scans of repeat cycles compress/release to determine reproducibility
- Intra-, inter-fraction reproducibility all within 1 mm

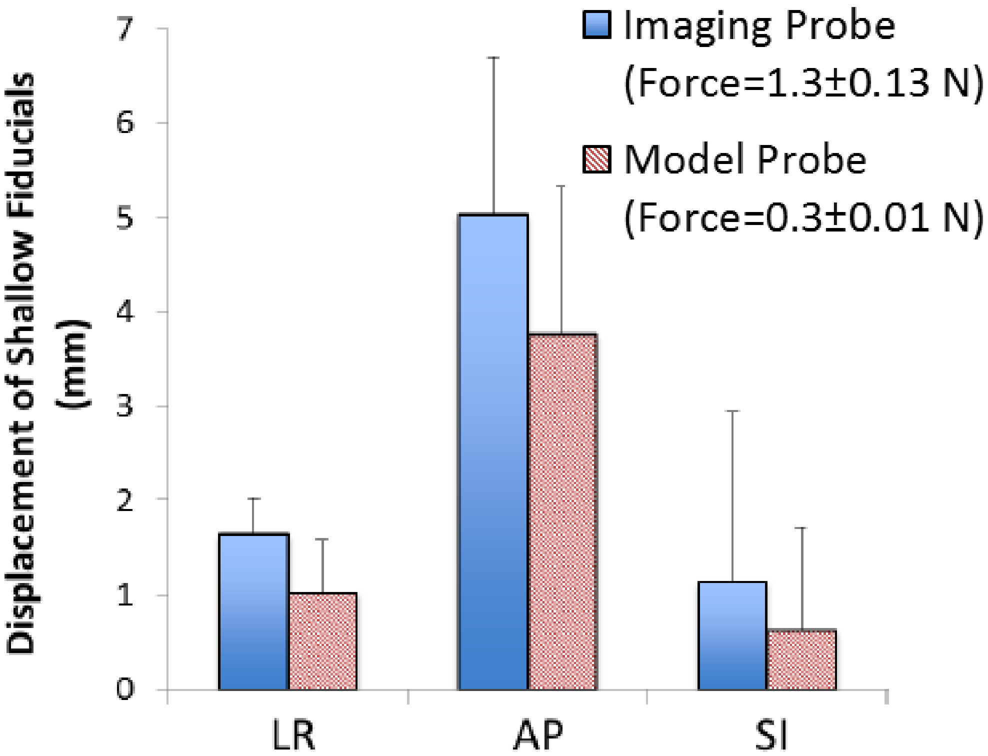
# Ex-vivo Bovine Liver in gel phantom



- 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



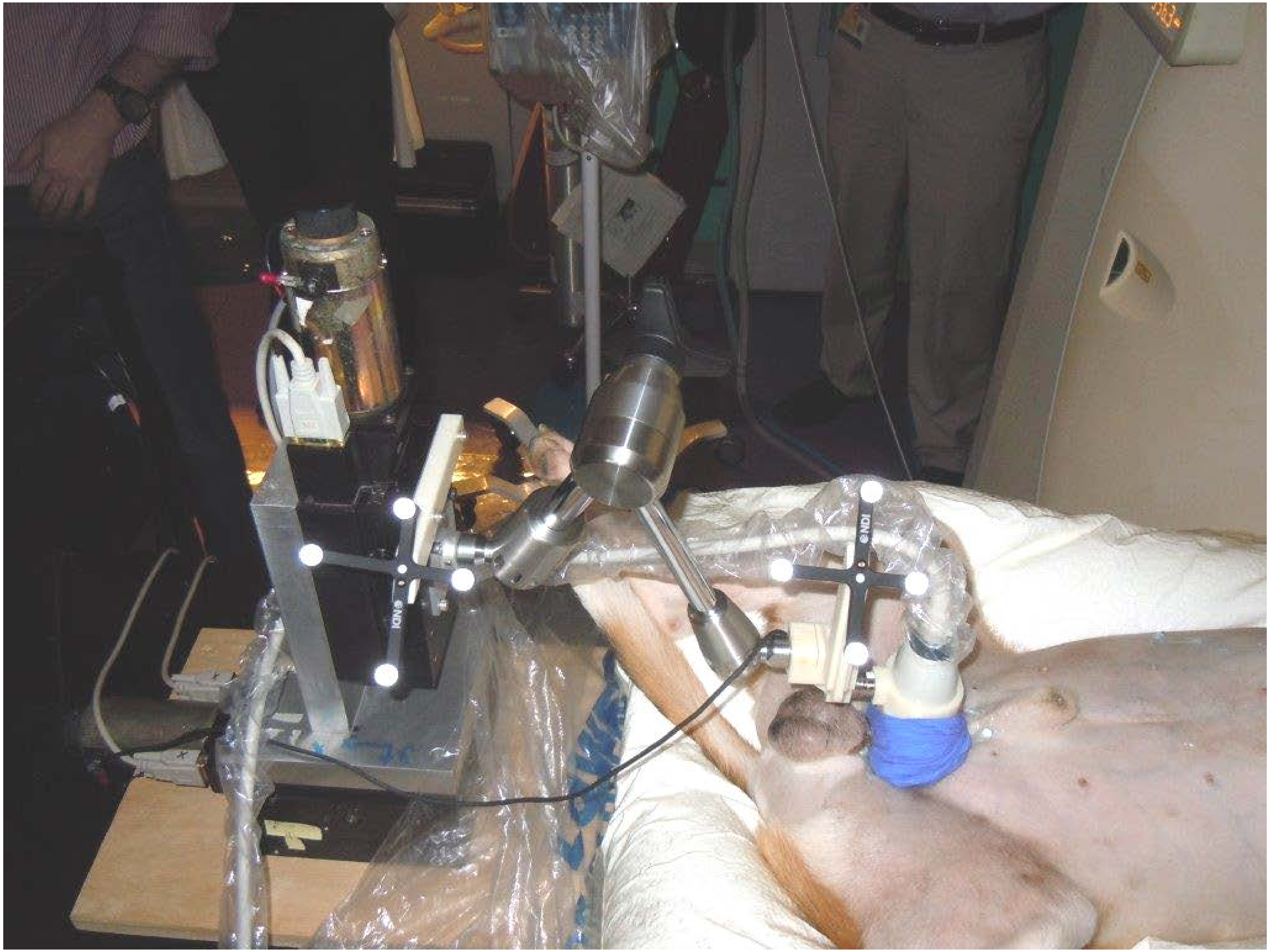




**Contact forces lower with model probe**
**The robotic arm needs to be stiffened**

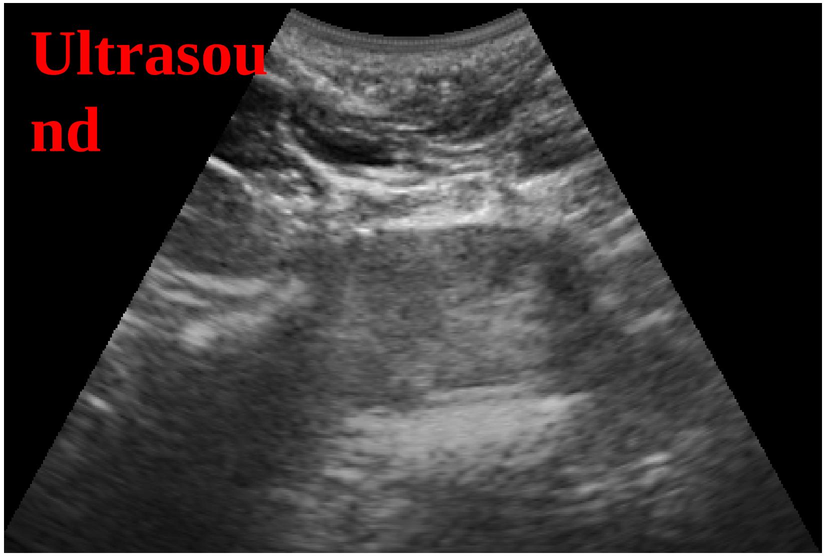
- Significant compression force differences between gel and liver phantom
- Suitability of phantom material is of concern

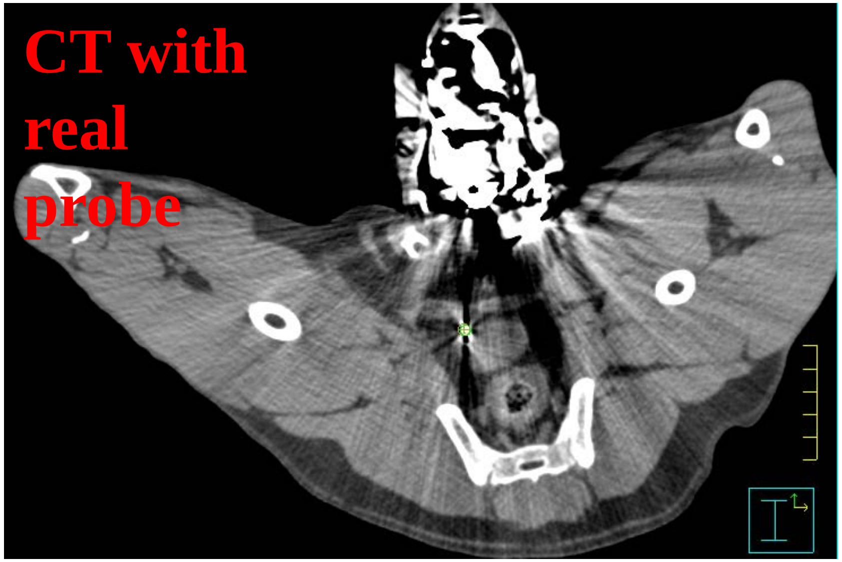

PHILIPS

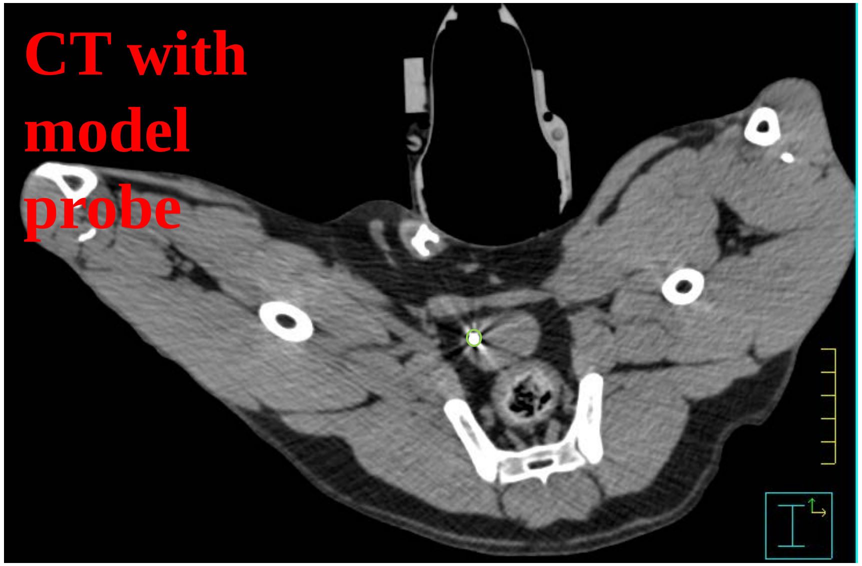
# Prostate (Force = 14 N)



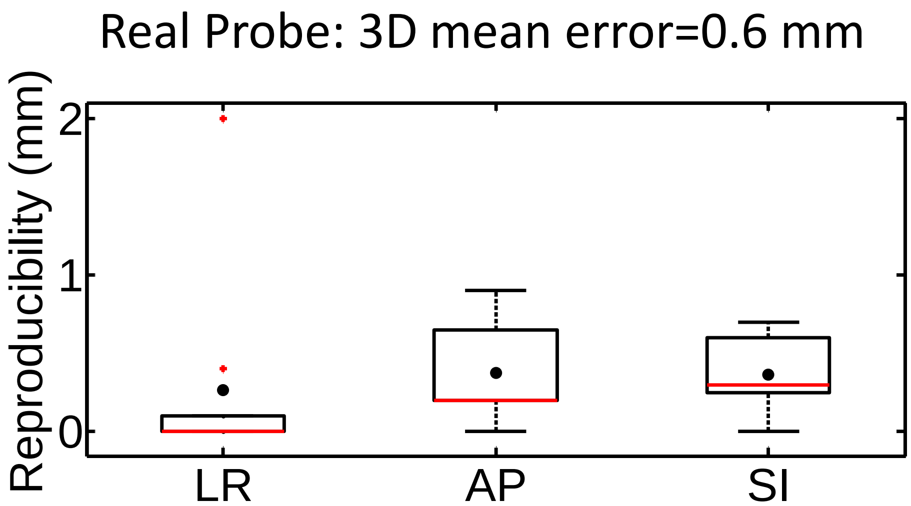
# Prostate Images

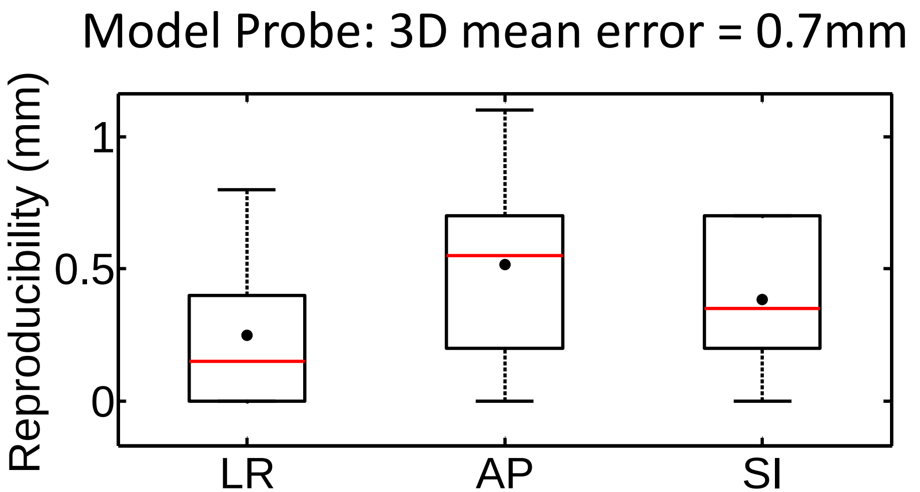


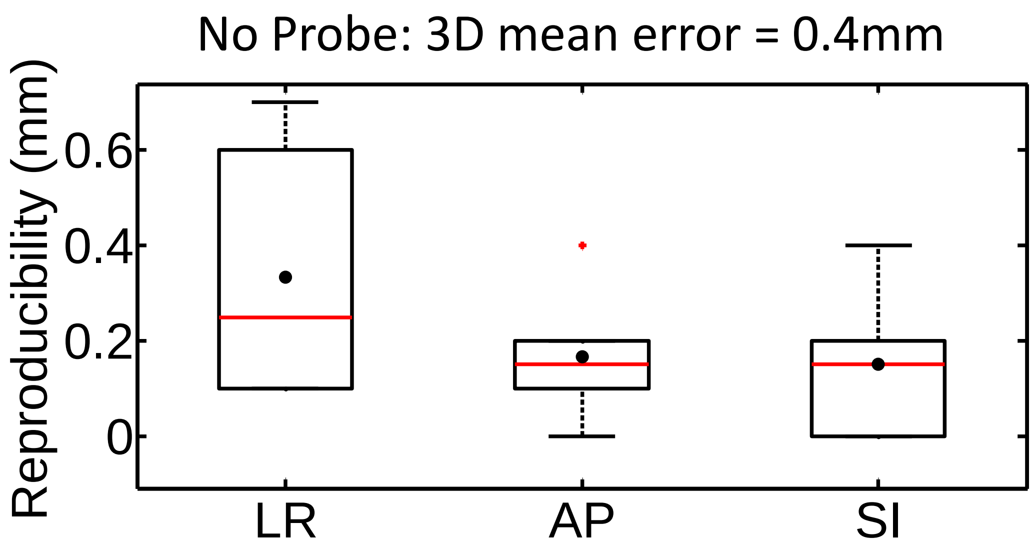



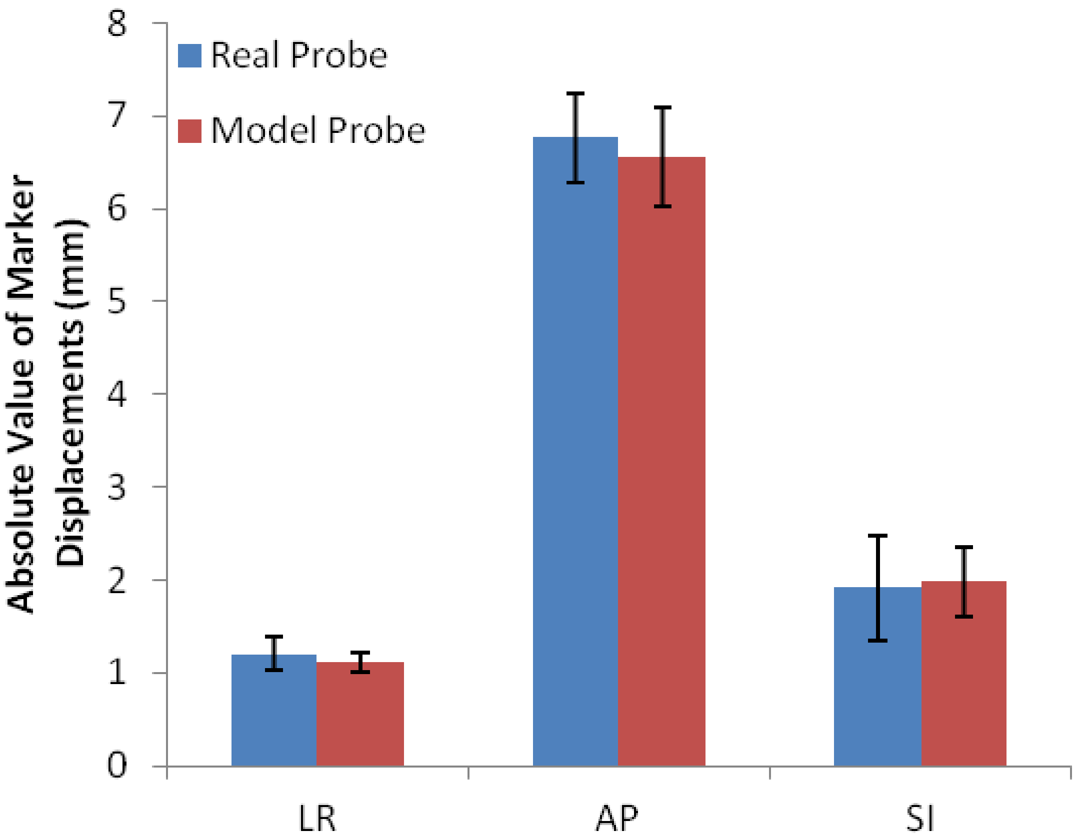
# Prostate (Force = 14 N; 10 N ~ 1 kg): Marker Position Reproducibility in Interquartile Range

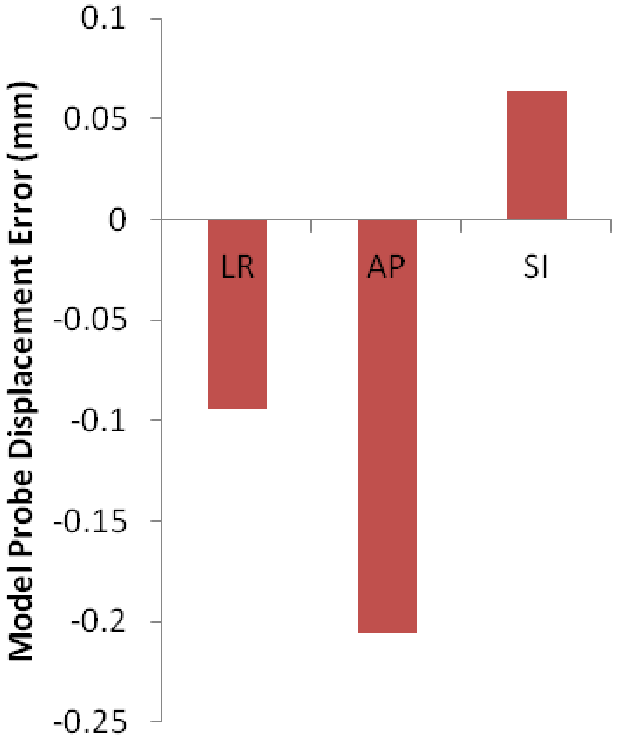


# Prostate:
# Probe-Induced Marker Displacement (from no probe)

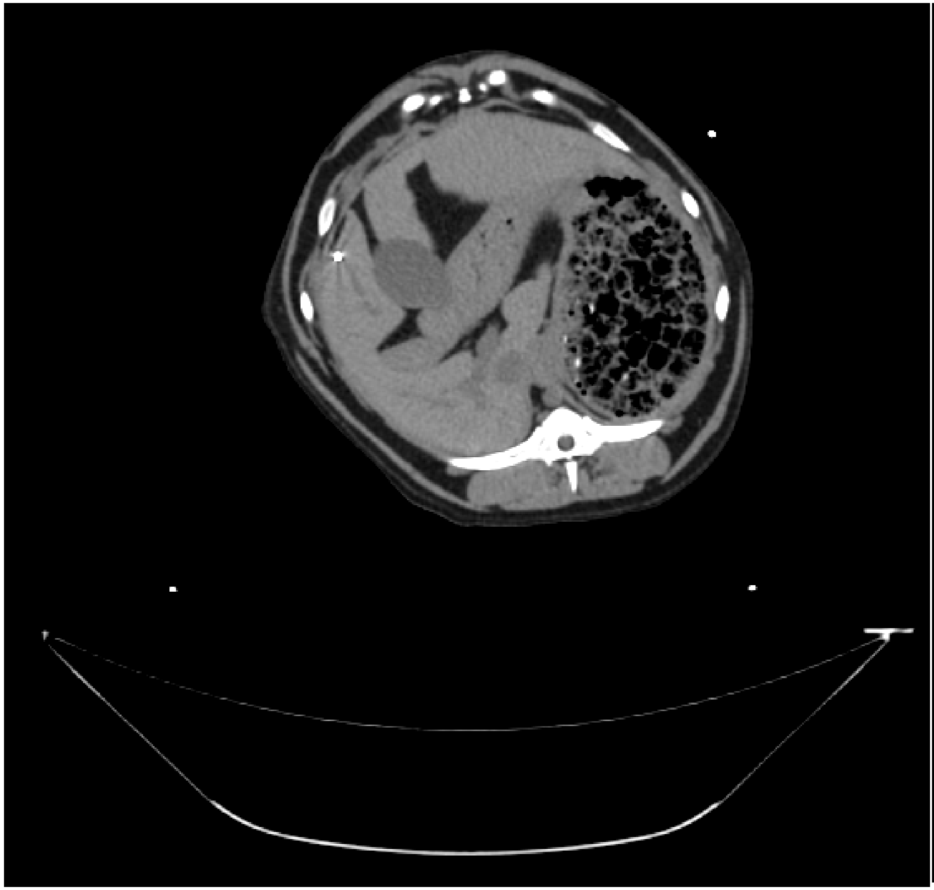


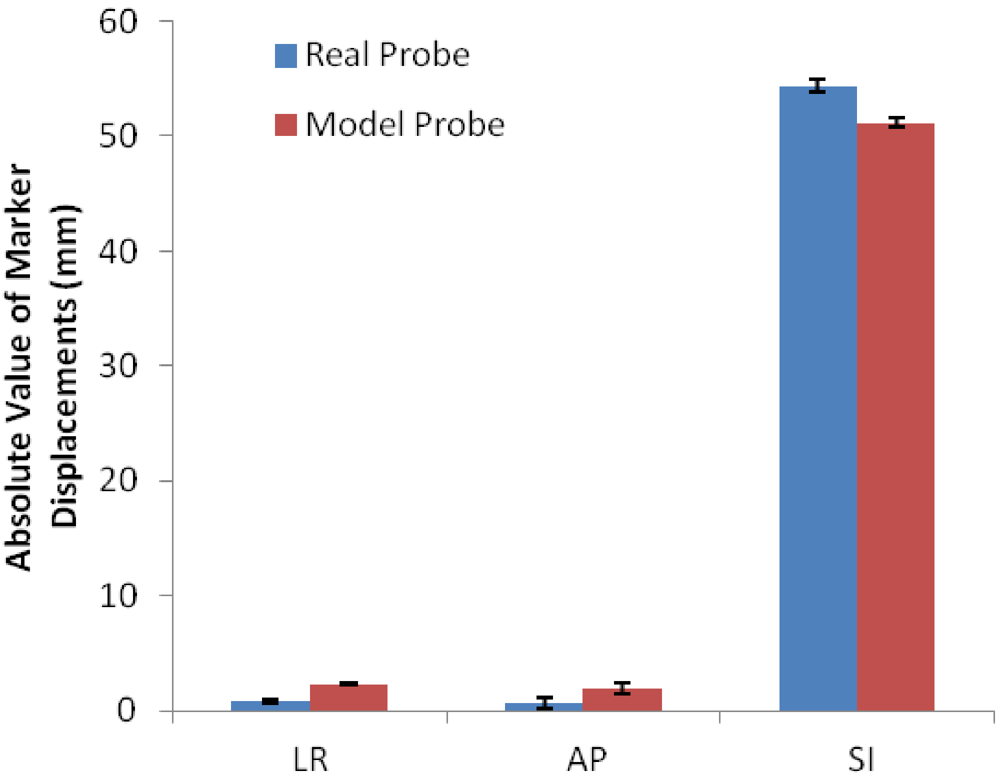

3D mean error
= 0.2mm

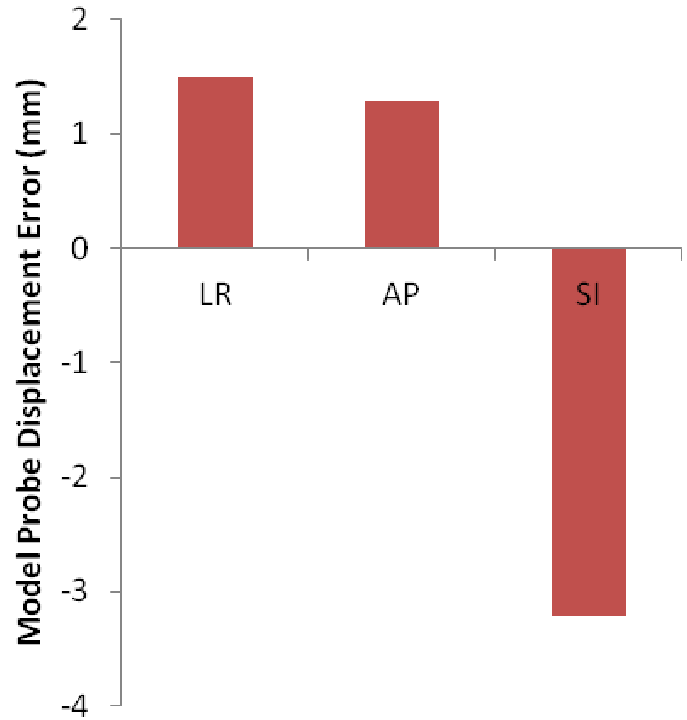
# Liver at Breath-hold (Force = 40 N)

# Liver CT and Ultrasound Images



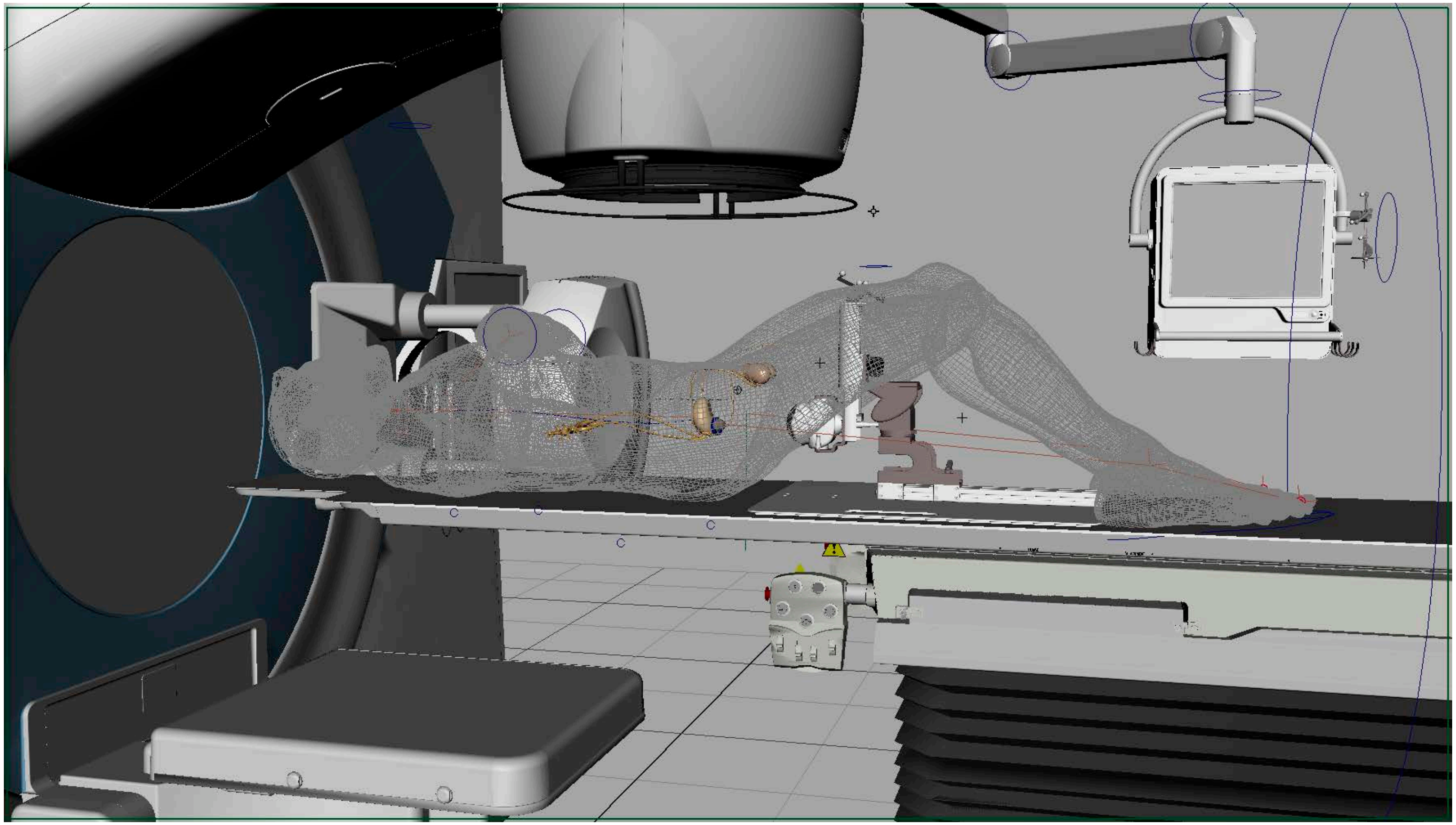
# Liver (at Breath-hold): Probe-Induced Marker Displacement

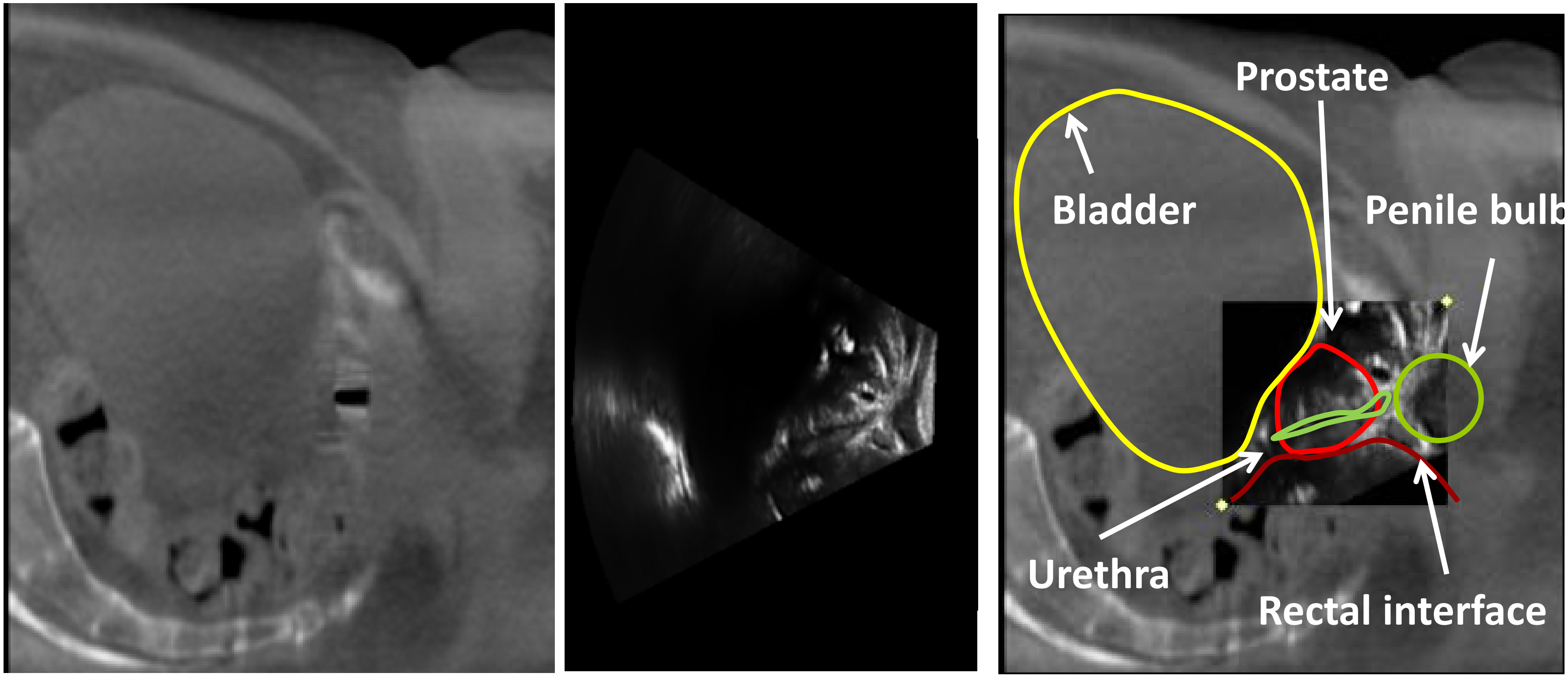


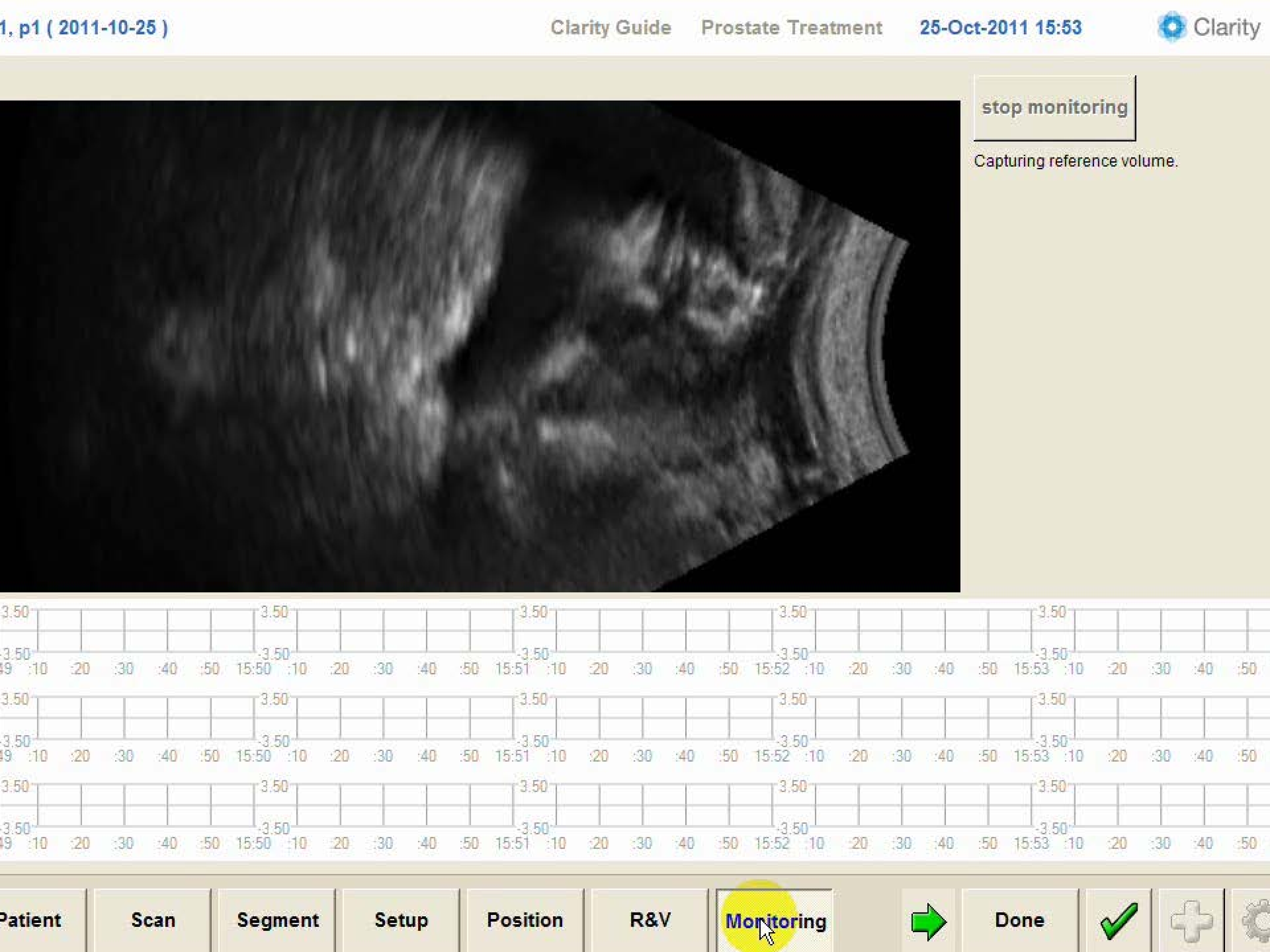

3D mean error
= 4.1 mm

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





Prostate
Bladder
Penile bulb
Urethra
Rectal interface

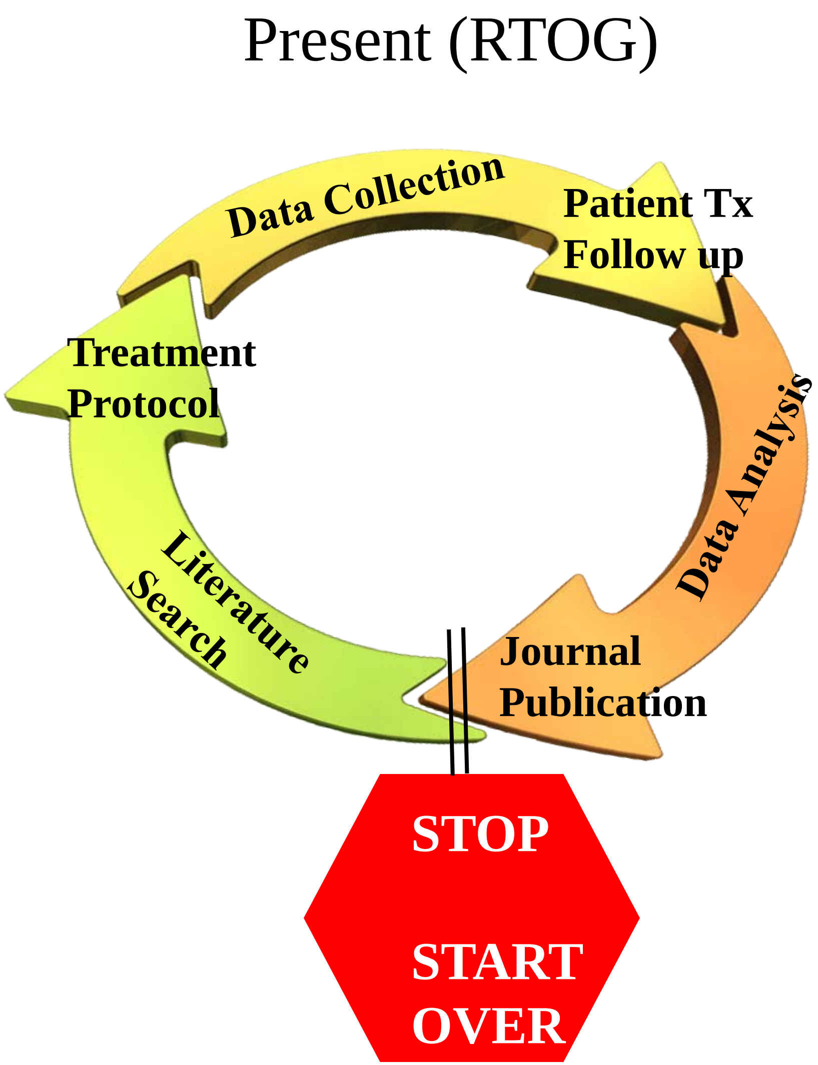


1, p1 ( 2011-10-25 )
Clarity Guide
Prostate Treatment
25-Oct-2011 15:53
Clarity
stop monitoring
Capturing reference volume.
3.50
-3.50
:10 :20 :30 :40 :50 15:50 :10 :20 :30 :40 :50 15:51 :10 :20 :30 :40 :50 15:52 :10 :20 :30 :40 :50 15:53 :10 :20 :30 :40 :50
Patient
Scan
Segment
Setup
Position
R&V
Monitoring
Done

# Analytic database for personalized medicine and data sharing in radiation oncology

Radiation Oncology and Molecular Radiation Sciences
Johns Hopkins University

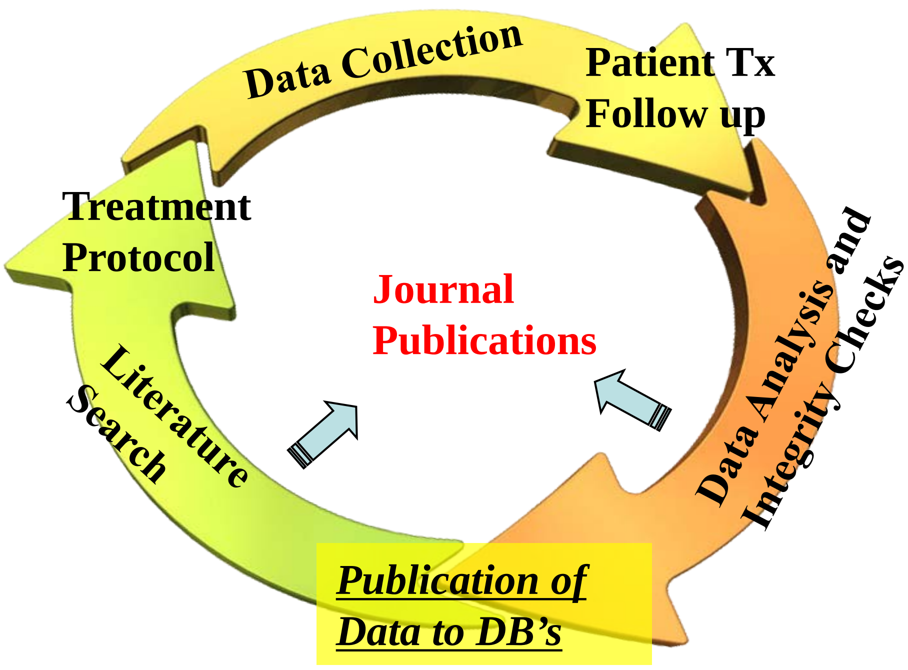
# Re-engineering the Cooperative Research Model




- < 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

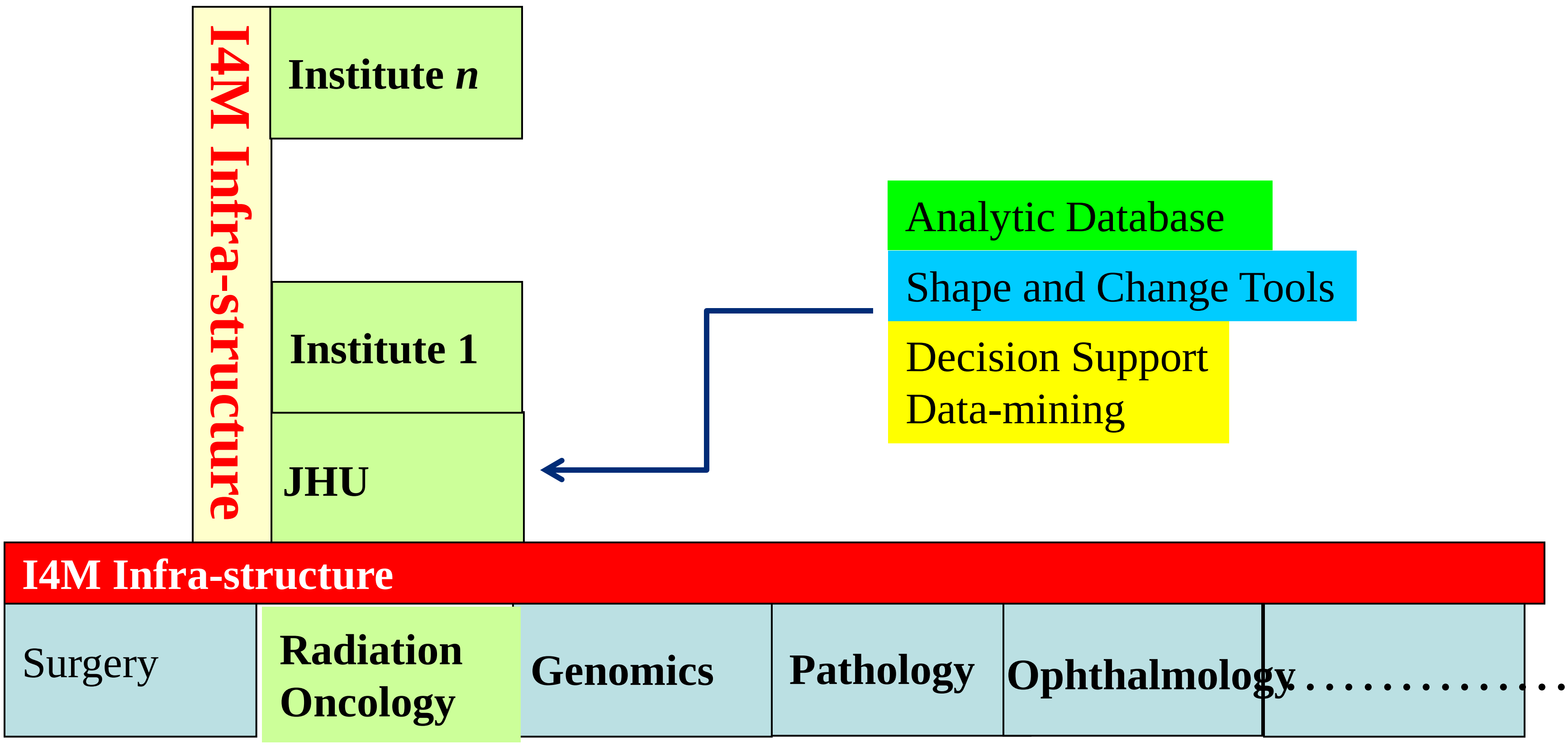
# JHU: Re-engineering the Cooperative Research Model

Distributed



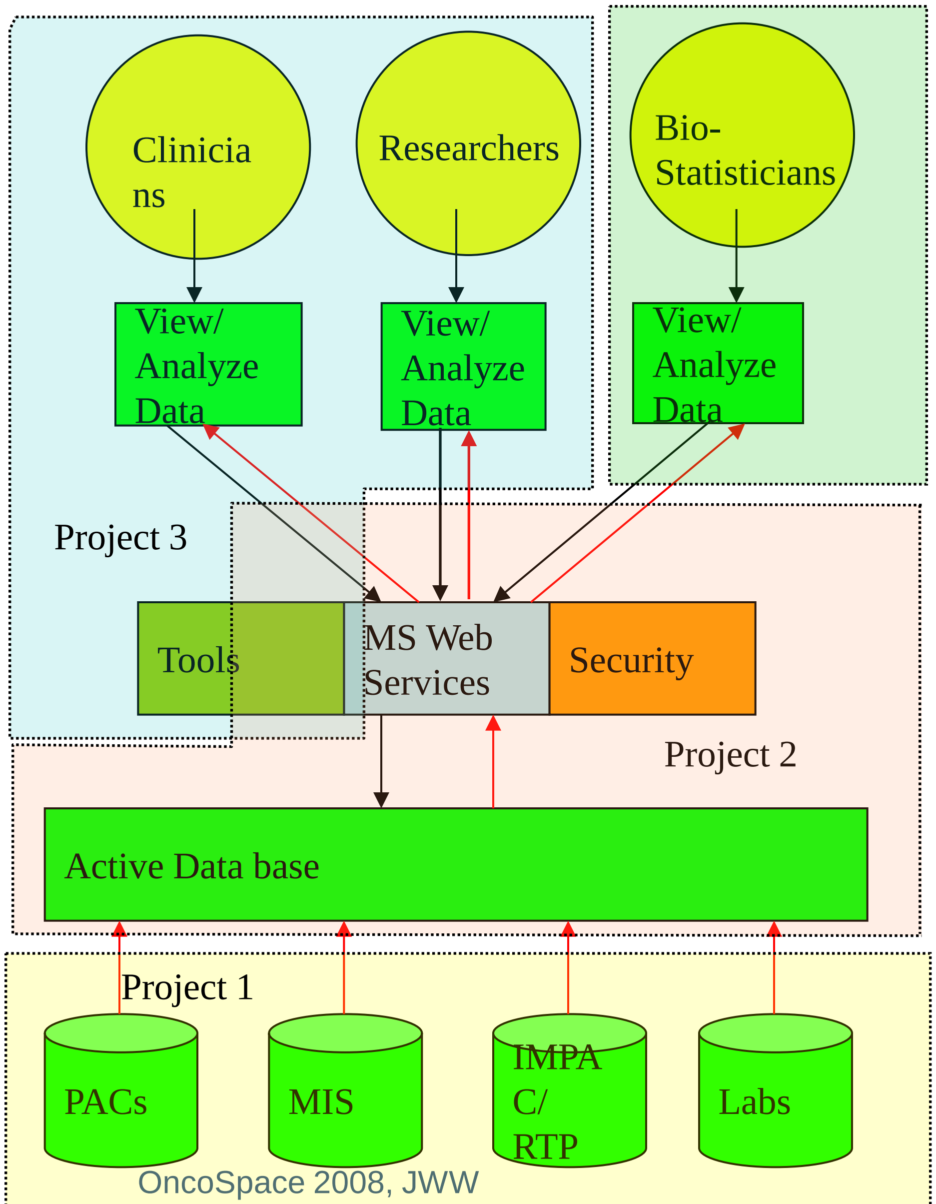

- Keep data local and available in an active database
- Send queries to data, extracting only answers
  - e.g. Validate the PTV margin prescribed for lung SBRT
- Facilitate data-reuse, decision support and education
- Promote data sharing for CER
- *Tools for data capture to populate OncoSpace*

# OncoSpace: Radiaton Oncology Model for Data Sharing and Decision Support



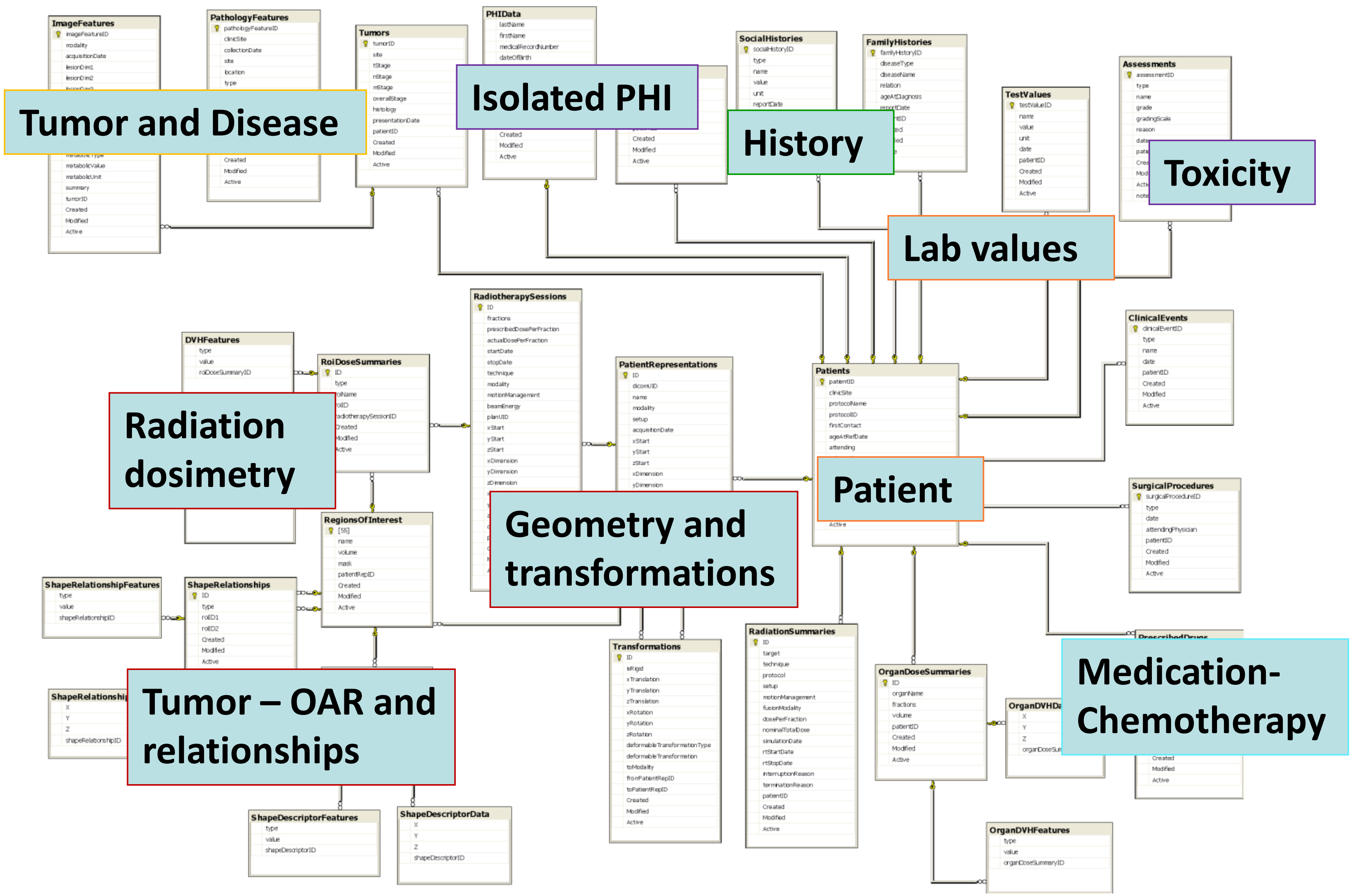

*I4M: Integration of Imaging, Information and Intervention in Medicine*

# Hopkins OncoSpace

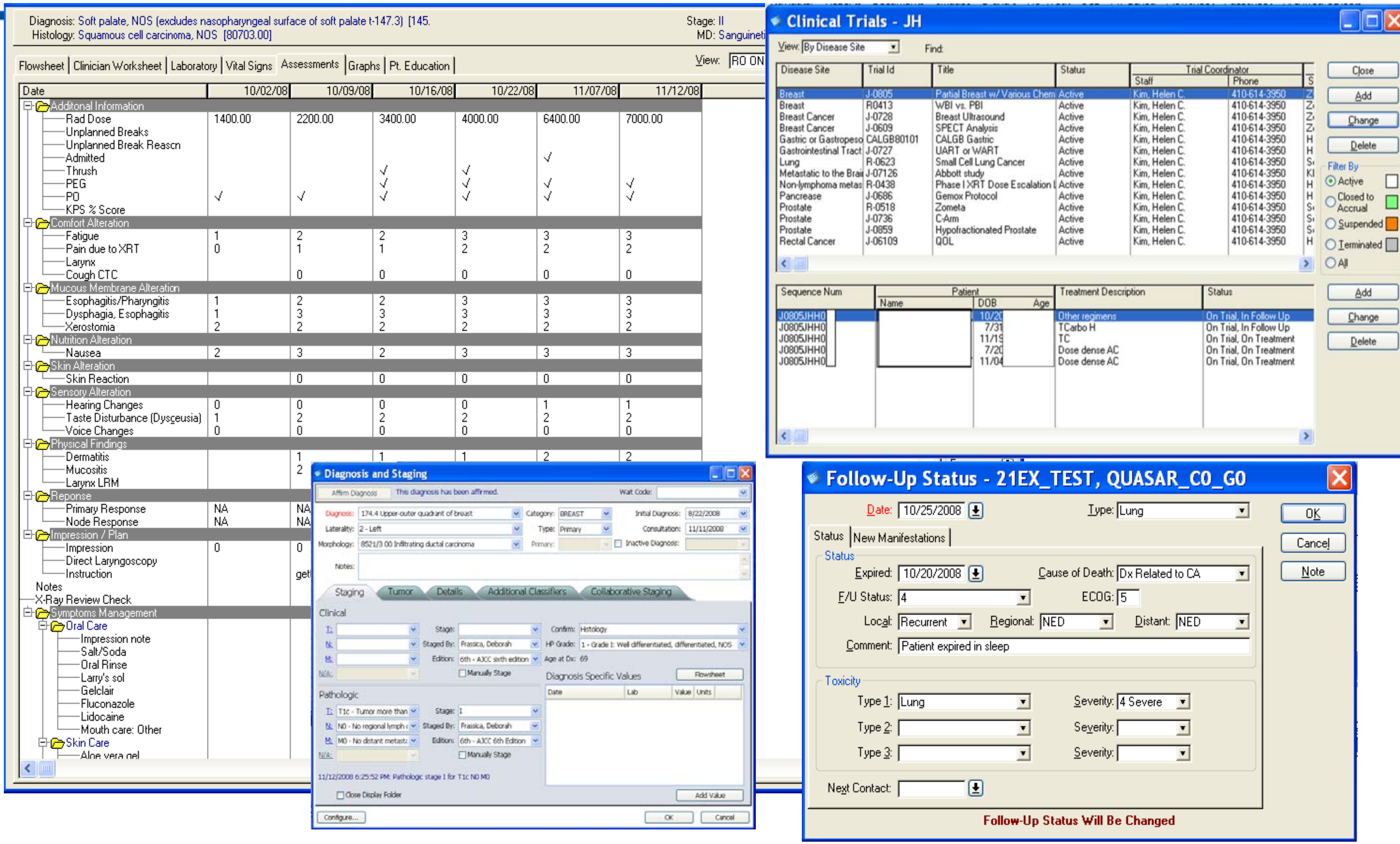



1. Integration of clinical workflow with data collection to populate OncoSpace.
   – ***Enable Mosaiq/Aria and TPS to capture data***
2. Optimize database architecture for secured distributed web-access
3. Tools for query, analysis, navigation and decision support
4. Data mining, decision support and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

# Database organization

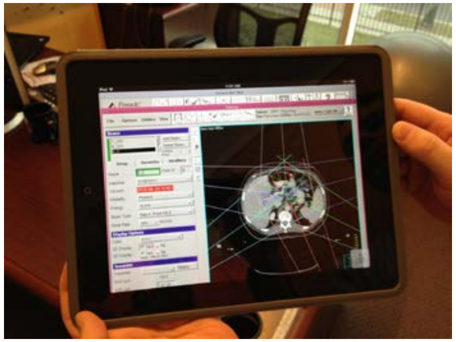


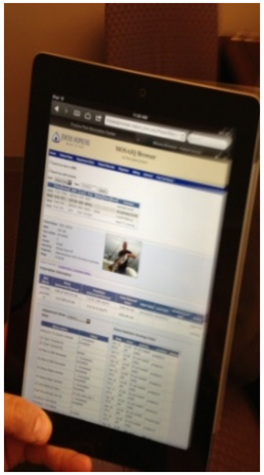
# MOSAIQ RO information system

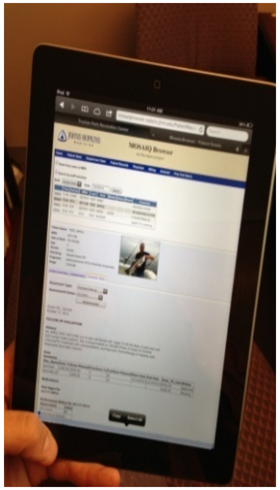


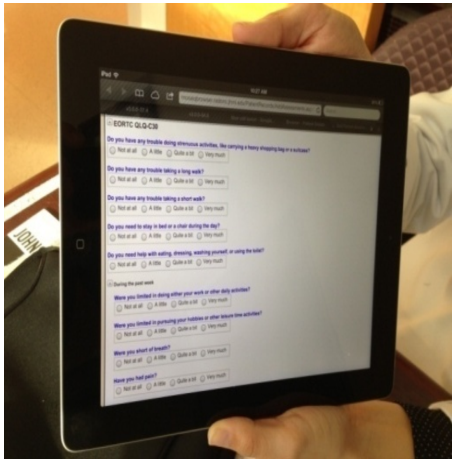
# Mobile devices for specific tasks

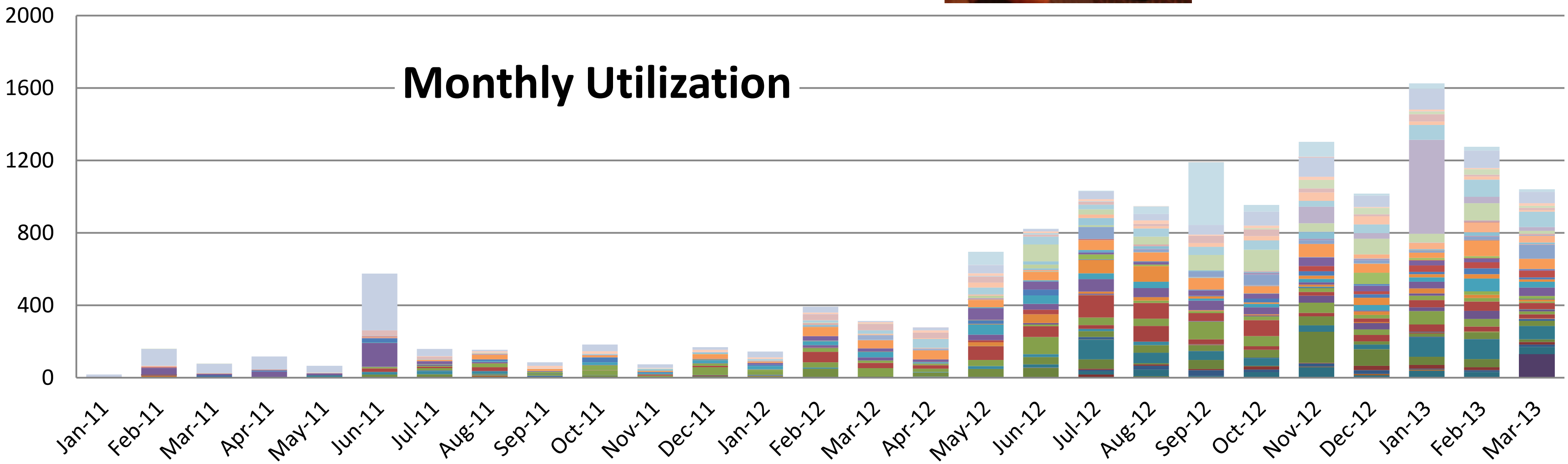
| Plan Approval | Patient summary | Clinical assessment | Clinica l notes | Patient Quality of Life |
|---|---|---|---|---|





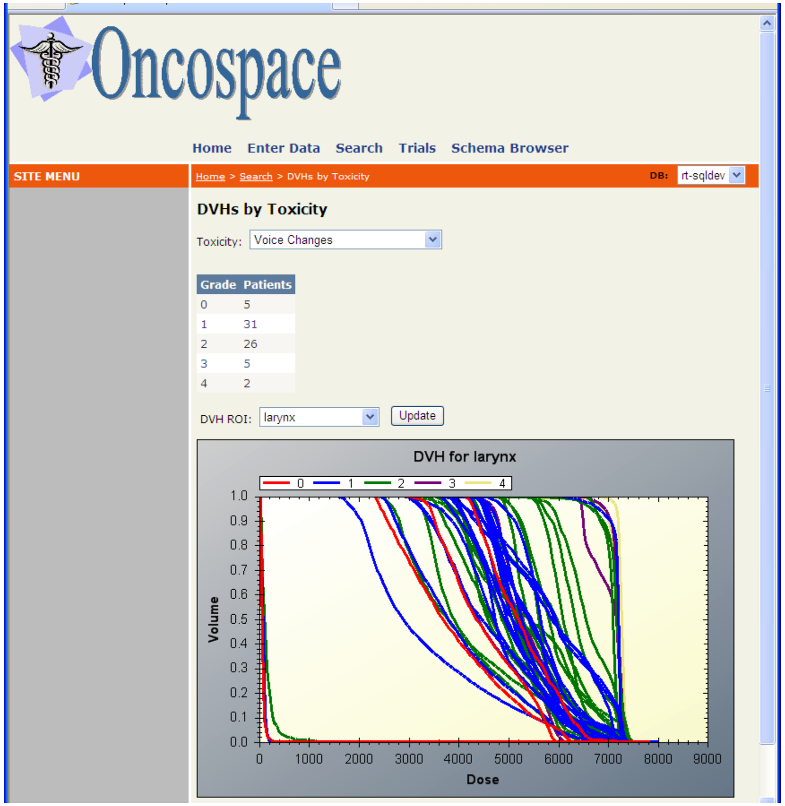






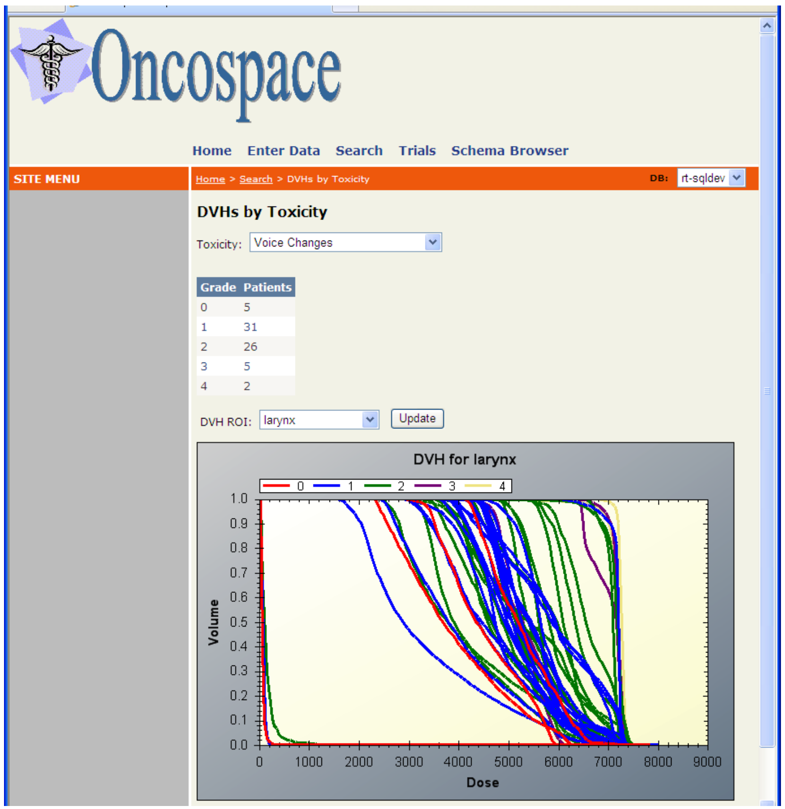
# Safety and Quality
# Oncospace: Query & Analysis

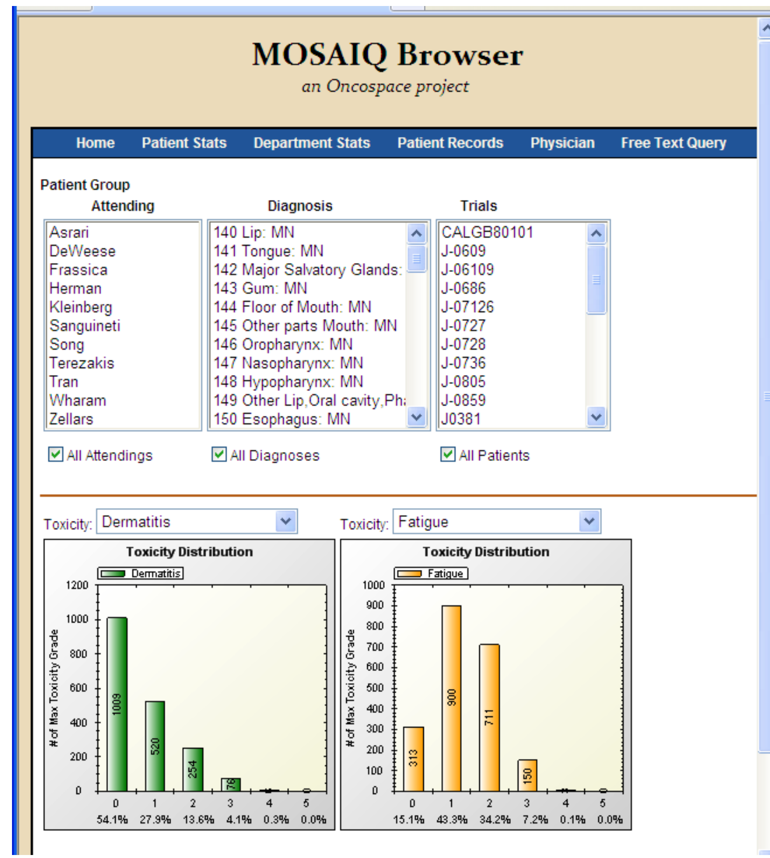
- How to ask questions of the data?
  - Given this DVH, what is the risk of toxicity?

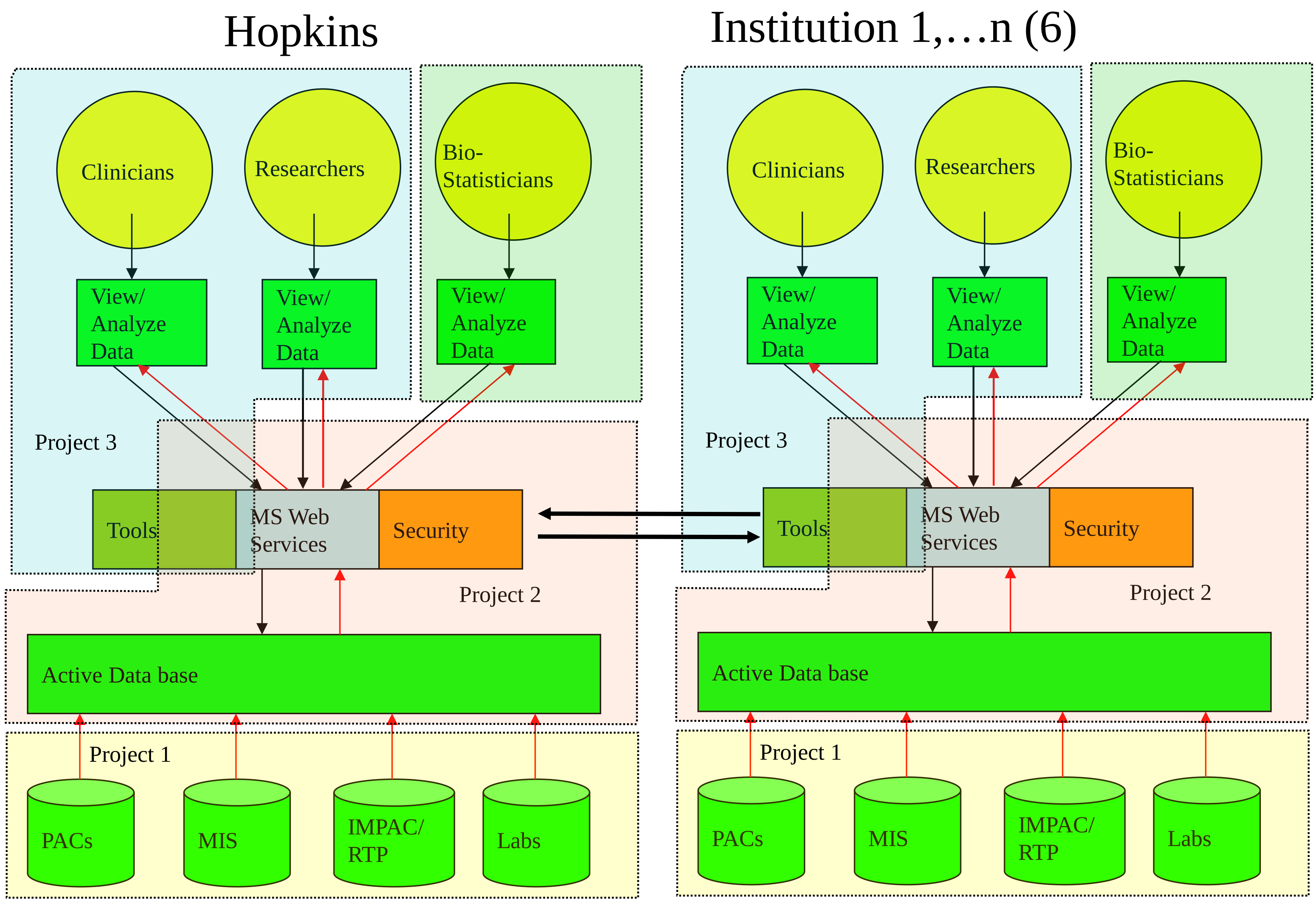


# Safety and Quality
# Oncospace: Query & Analysis

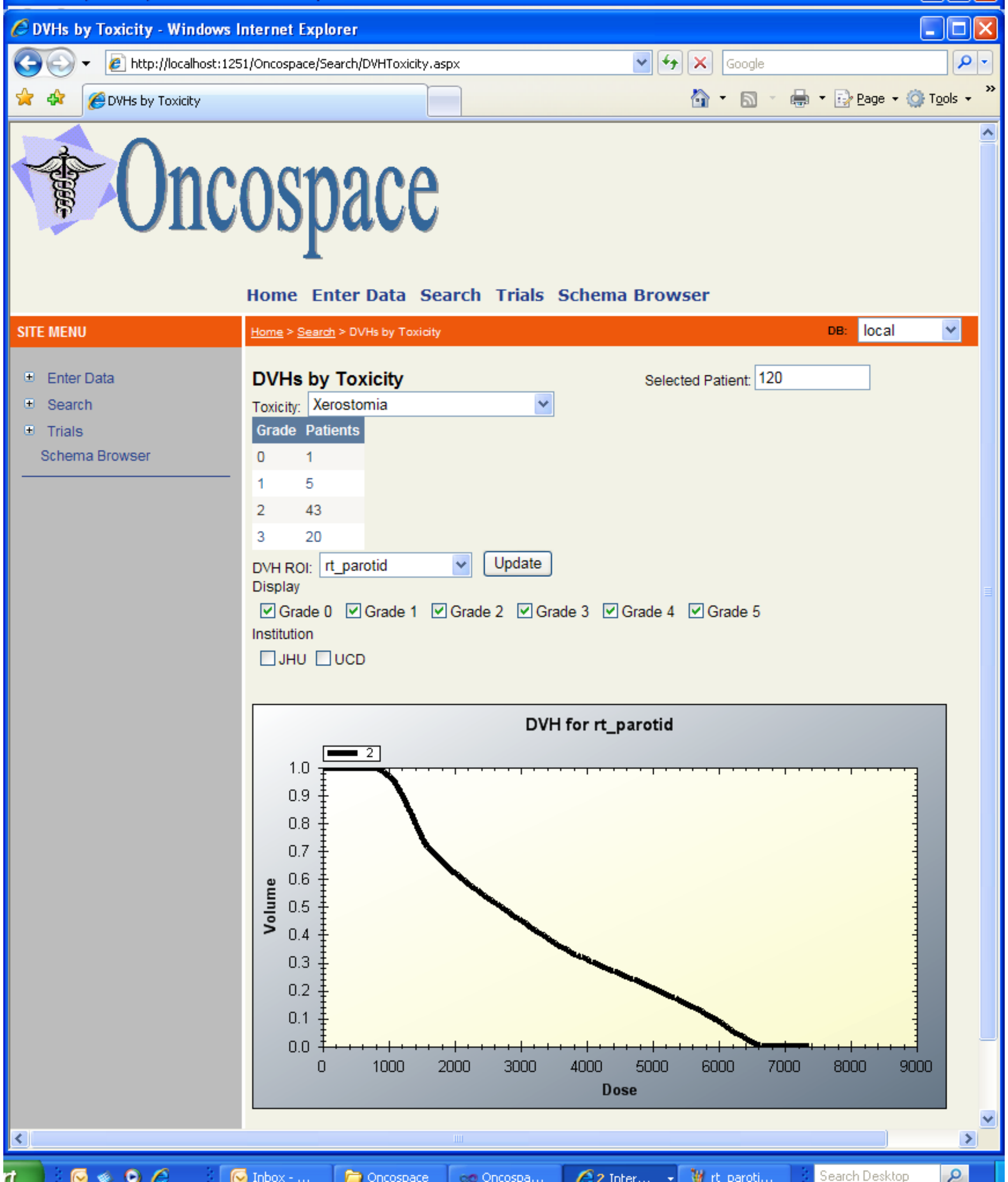
- How to ask questions of the data?
  - Given this DVH, what is the risk of toxicity?



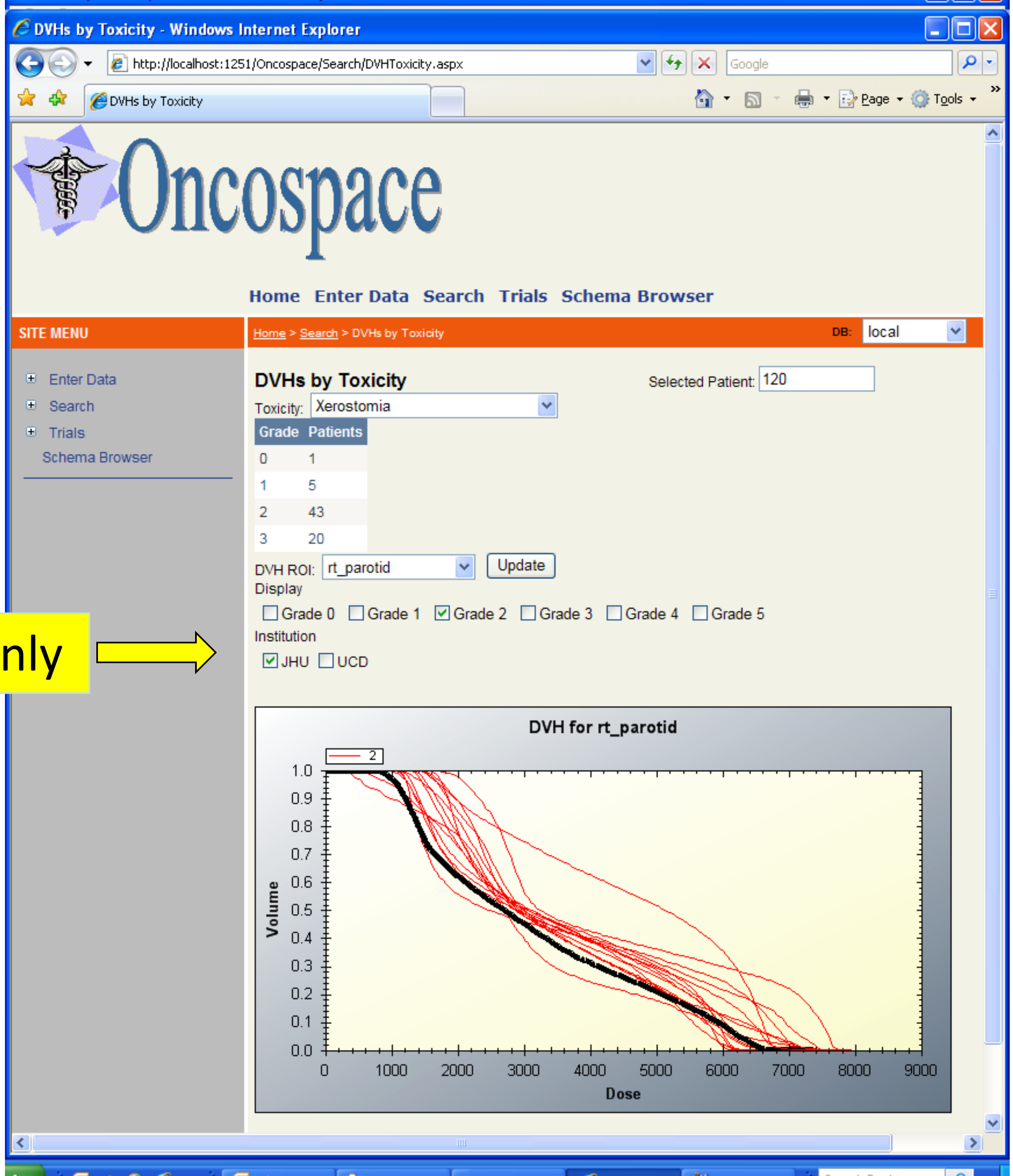



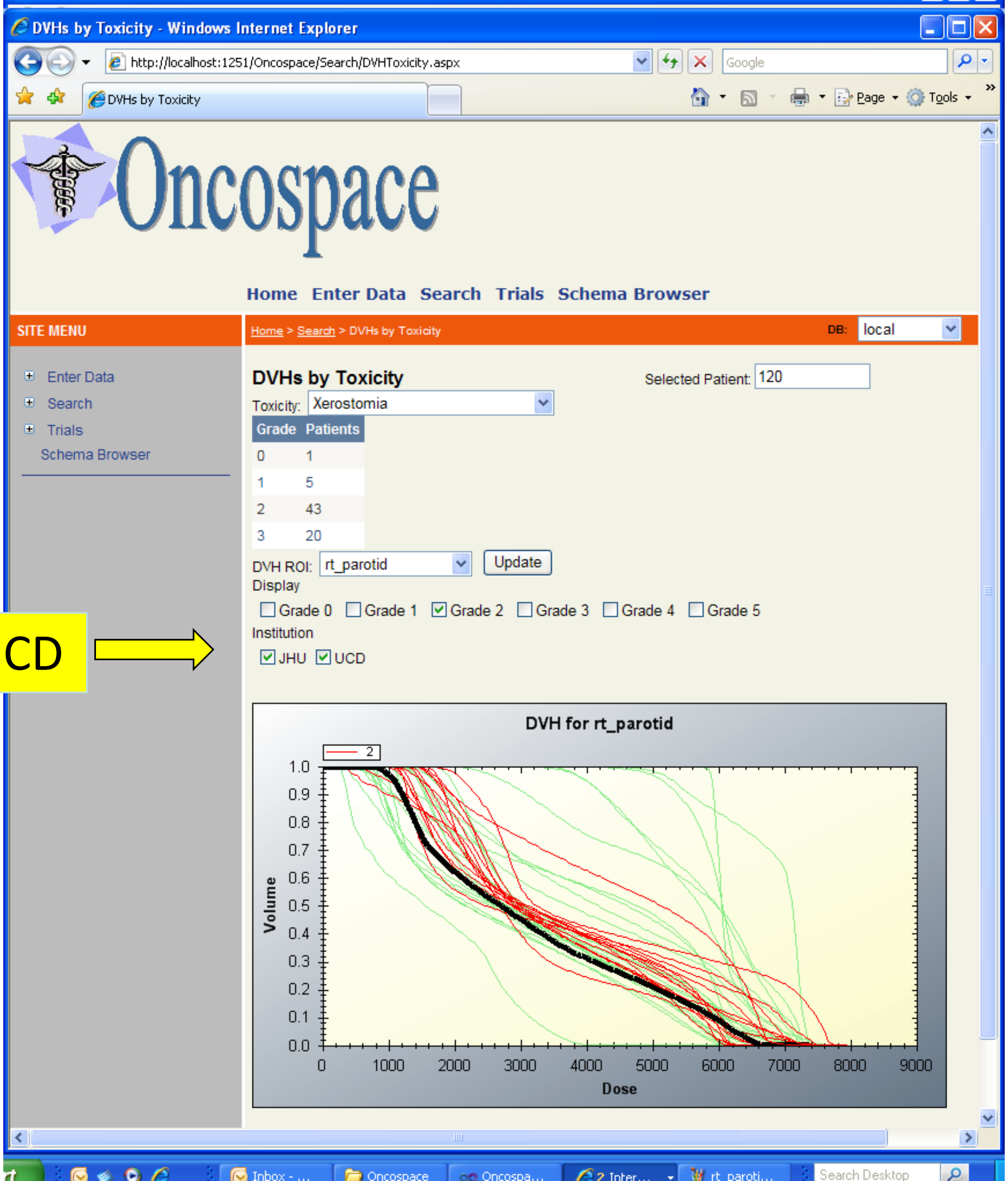


Hopkins
Institution 1,…n (6)
Clinicians
Researchers
Bio-
Statisticians
View/
Analyze
Data
Project 3
Tools
MS Web
Services
Security
Project 2
Active Data base
Project 1
PACs
MIS
IMPAC/
RTP
Labs
Clinicians
Researchers
Bio-
Statisticians
View/
Analyze
Data
Project 3
Tools
MS Web
Services
Security
Project 2
Active Data base
Project 1
PACs
MIS
IMPAC/
RTP
Labs


DVHs by Toxicity - Windows Internet Explorer
http://localhost:1251/Oncospace/Search/DVHToxicity.aspx
Google
DVHs by Toxicity
Page
Tools
Oncospace
Home
Enter Data
Search
Trials
Schema Browser
SITE MENU
Home > Search > DVHs by Toxicity
DB:
local
Enter Data
Search
Trials
Schema Browser
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
DVH for rt_parotid
2
Volume
Dose
0.0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
0
1000
2000
3000
4000
5000
6000
7000
8000
9000
Inbox - ...
Oncospace
Oncospa...
2 Inter...
rt_paroti...
Search Desktop

JHU Only


DVHs by Toxicity - Windows Internet Explorer
http://localhost:1251/Oncospace/Search/DVHToxicity.aspx
Oncospace
Home Enter Data Search Trials Schema Browser
SITE MENU
Home > Search > DVHs by Toxicity
DB: local
Enter Data
Search
Trials
Schema Browser
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
DVH for rt_parotid
2
Volume
Dose
0.0 0.1 0.2 0.3 0.4 0.5 0.6 0.7 0.8 0.9 1.0
0 1000 2000 3000 4000 5000 6000 7000 8000 9000


DVHs by Toxicity - Windows Internet Explorer
http://localhost:1251/Oncospace/Search/DVHToxicity.aspx
Oncospace
Home Enter Data Search Trials Schema Browser
SITE MENU
Home > Search > DVHs by Toxicity
DB: local
Enter Data
Search
Trials
Schema Browser
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
DVH for rt_parotid
Volume
Dose

JHU & UCD

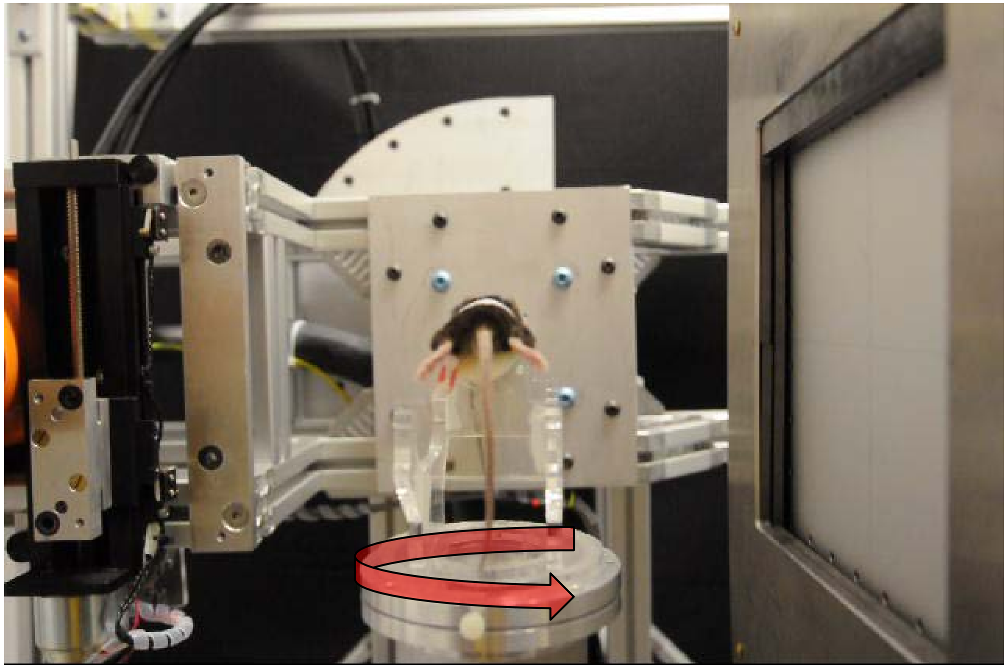
# Physics to engage Biology in Radiation Therapy

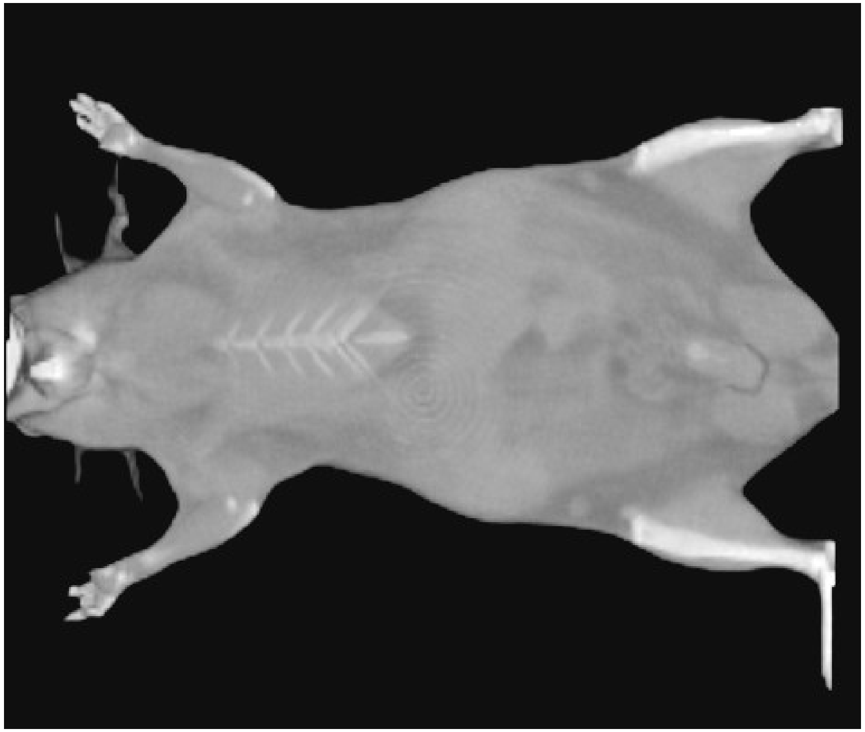
- Questions and Challenges:
  - The validity of EUD, NTCP, ……………
  - Validation and optimization of biological image guided or molecular targeted radiation therapy
  - Others questions:  biological target volume???
- Present small animal radiation research methods bear little resemblance to human treatment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

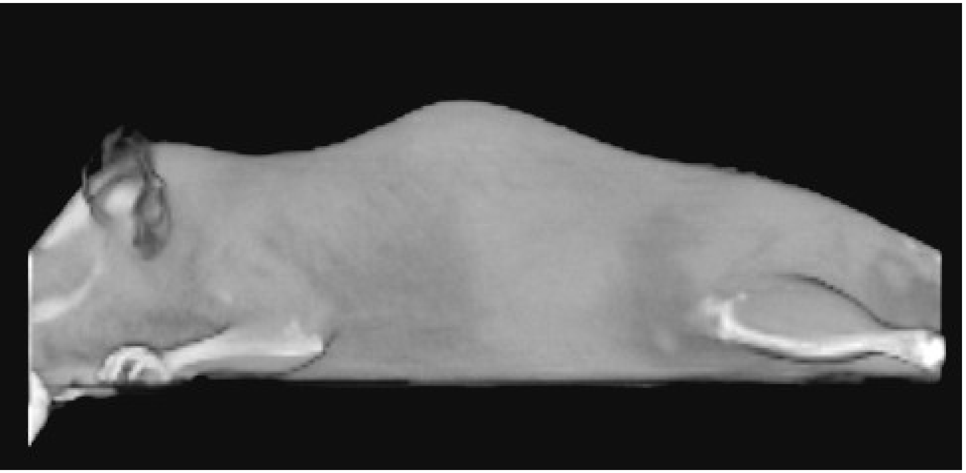
# Small Animal Radiation Research Platform

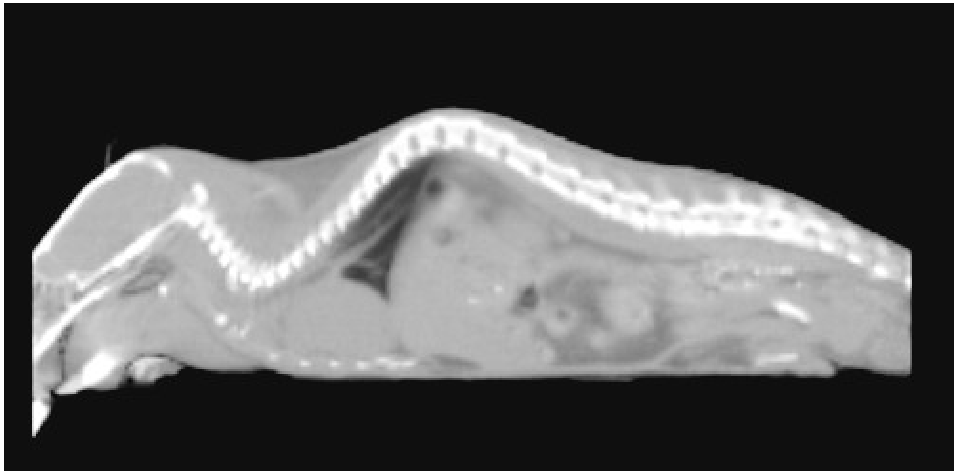

- Hopkins-Xstrahl partnership
- Integrated 3D-Slicer-GPU based treatment planning system
- Computer controlled
  - 360$^{o}$ gantry rotation
  - Non-coplanar delivery

# SARRP CBCT: "Pancake" geometry

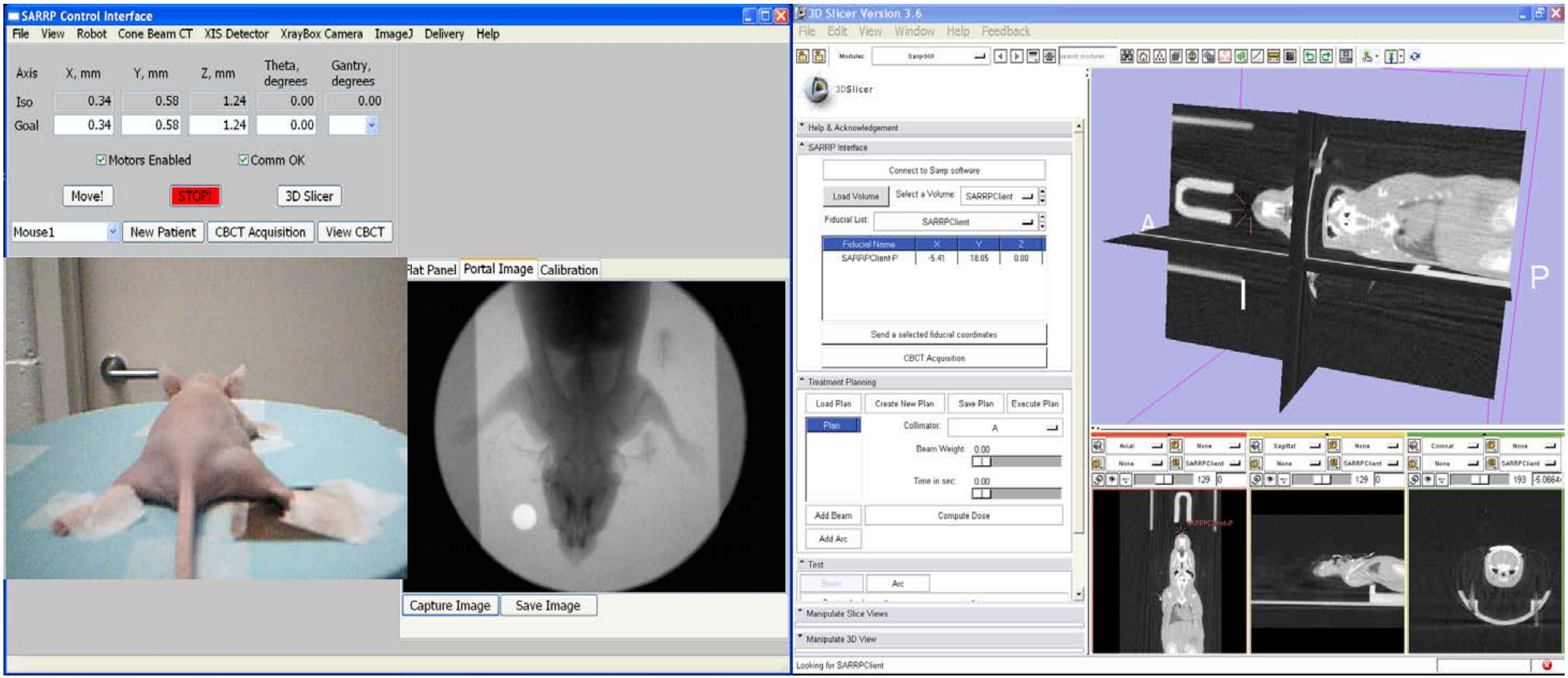




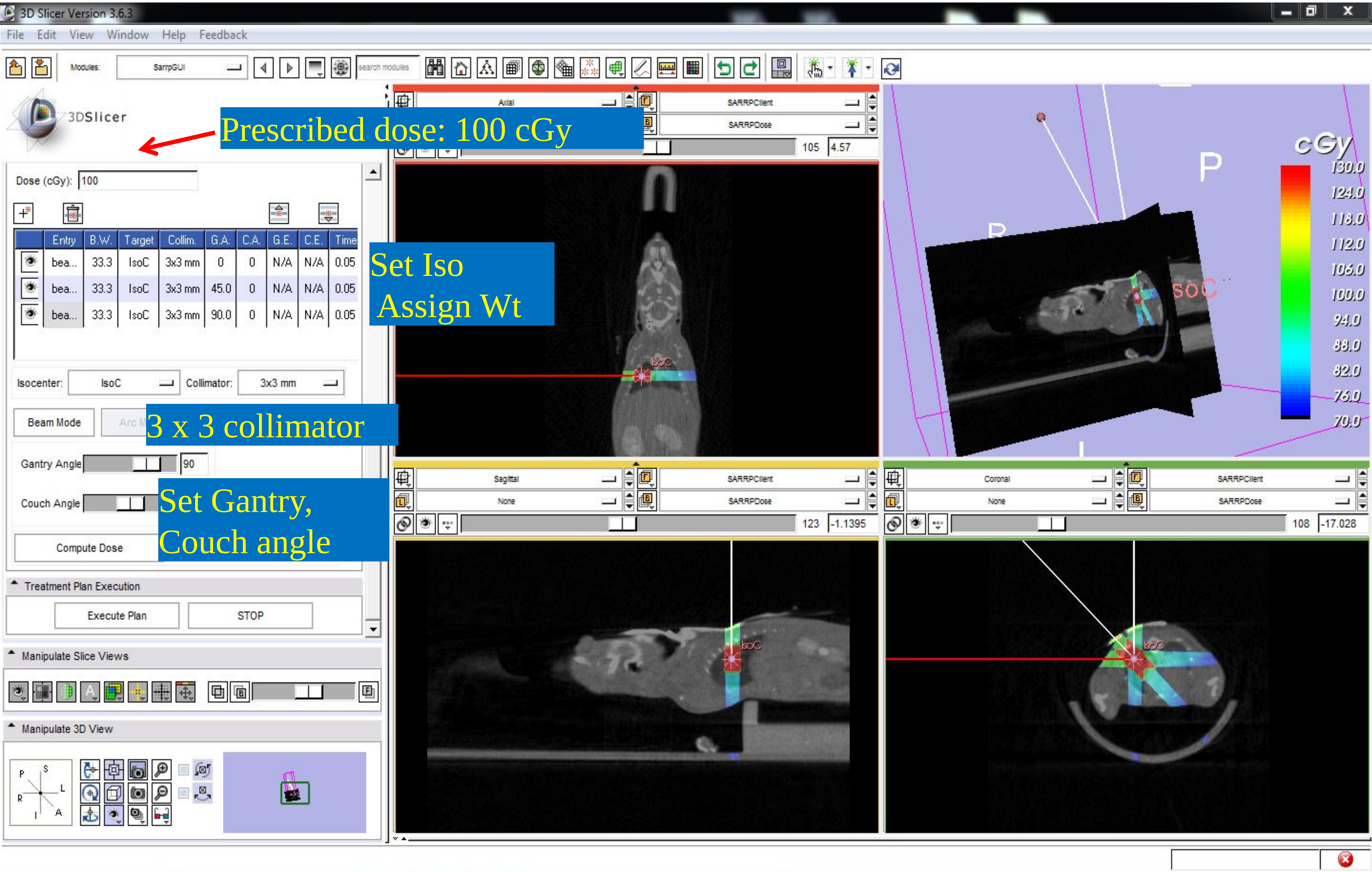




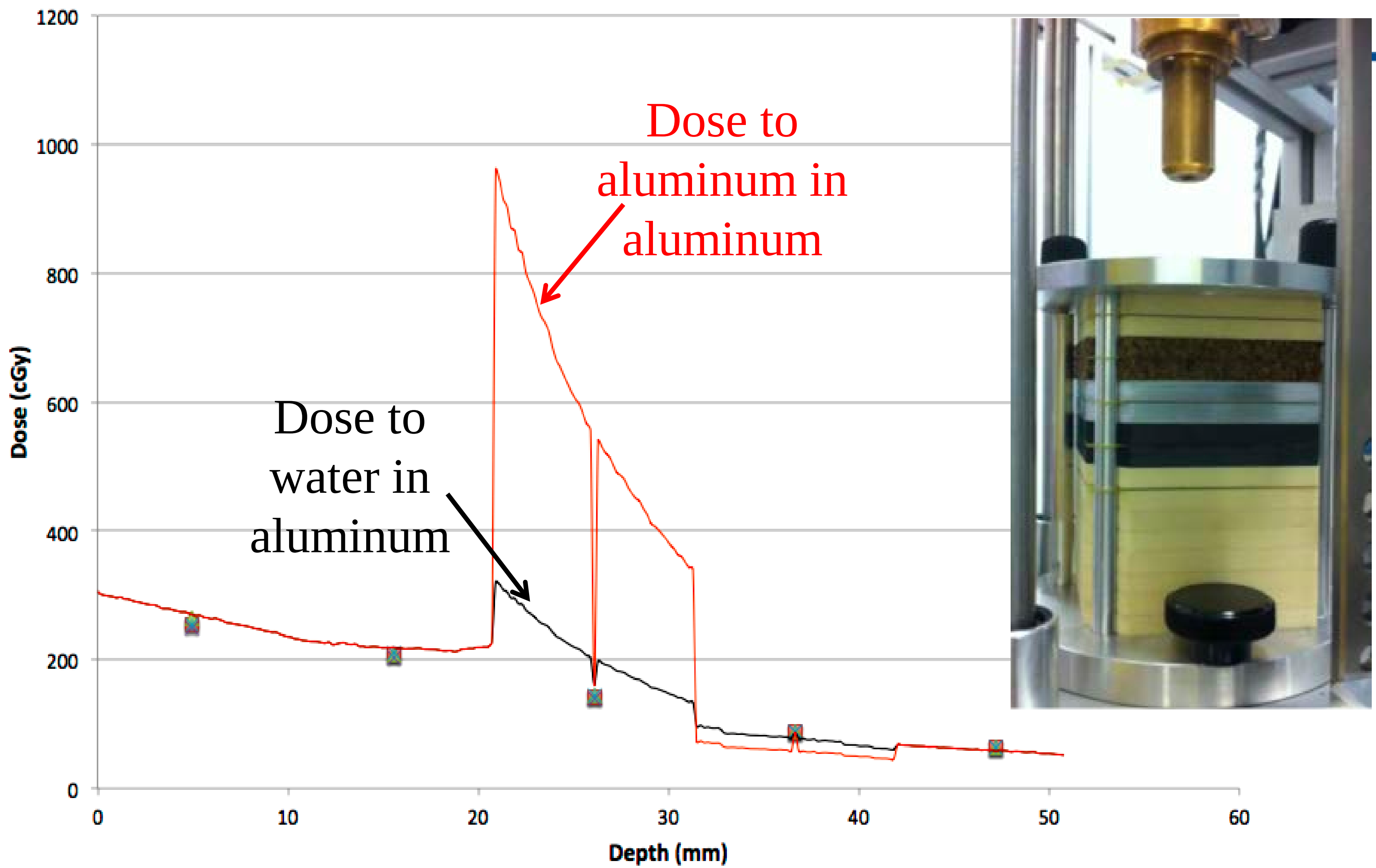
# Small Animal Treatment Console



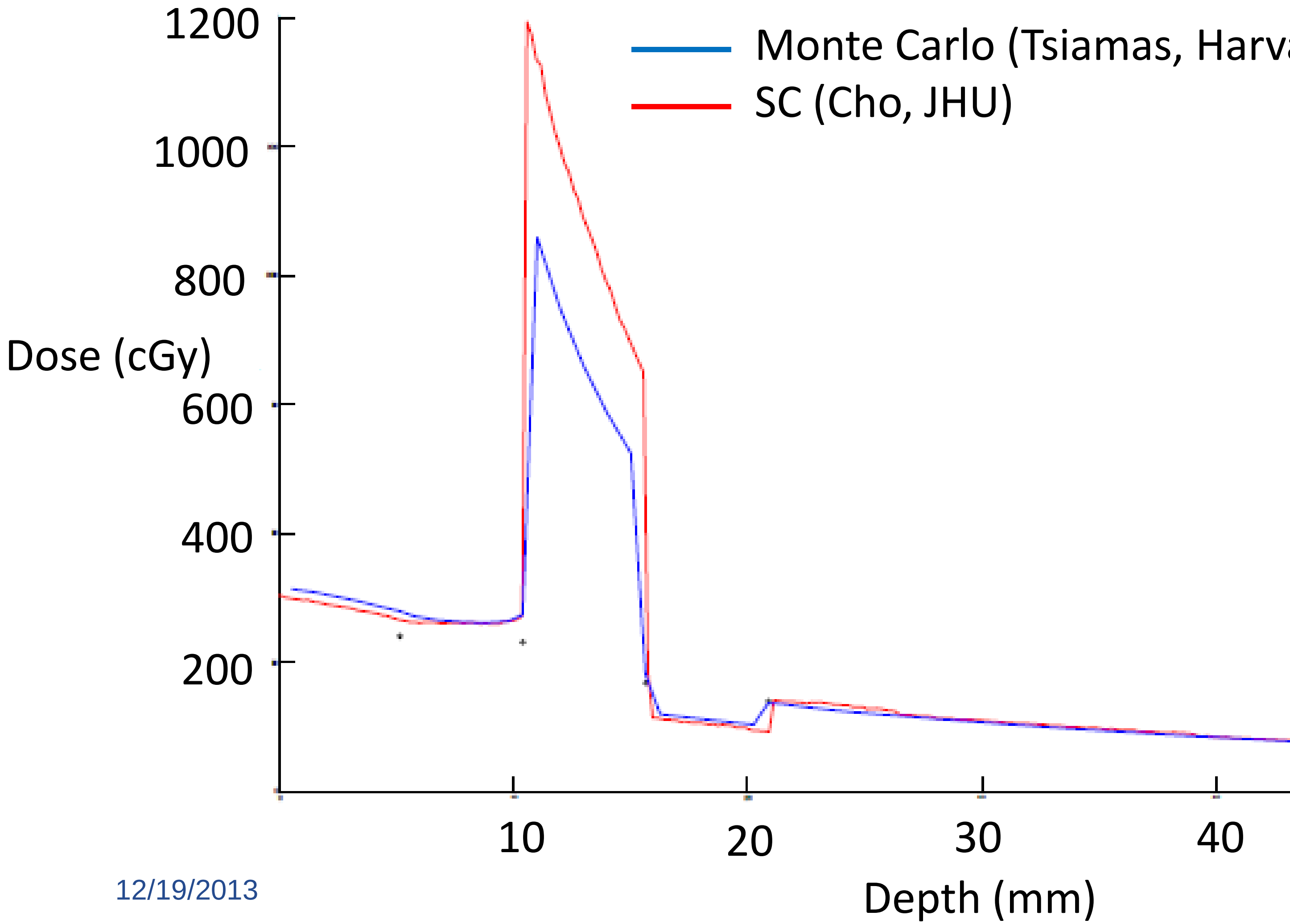
# SARRP Slicer- 3D RTP: GPU Dose – CBCT Engine



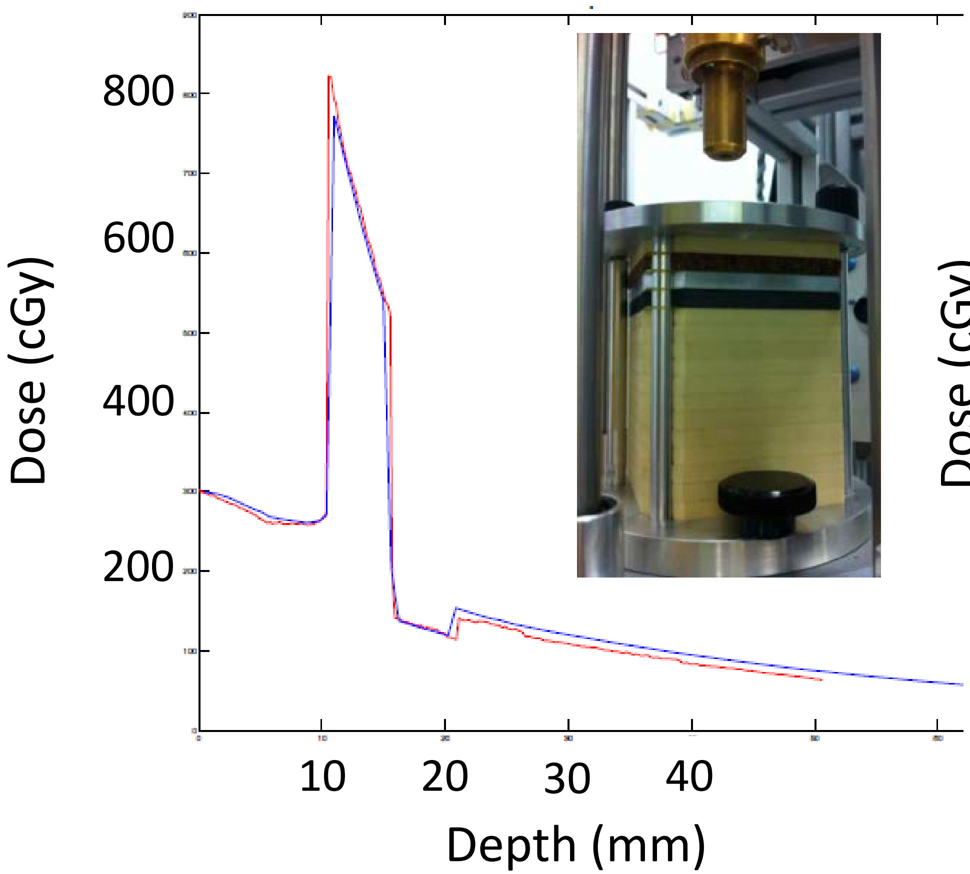
# Depth dose (SET2, double)

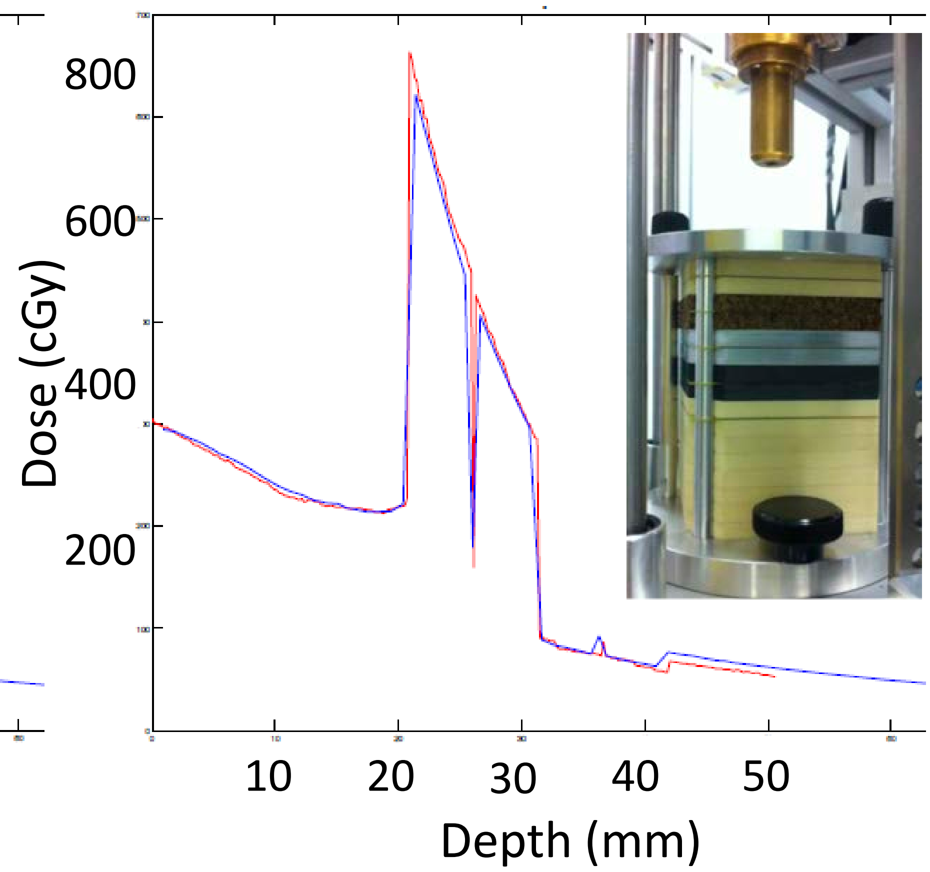


# Comparison of SC to Monte Carlo

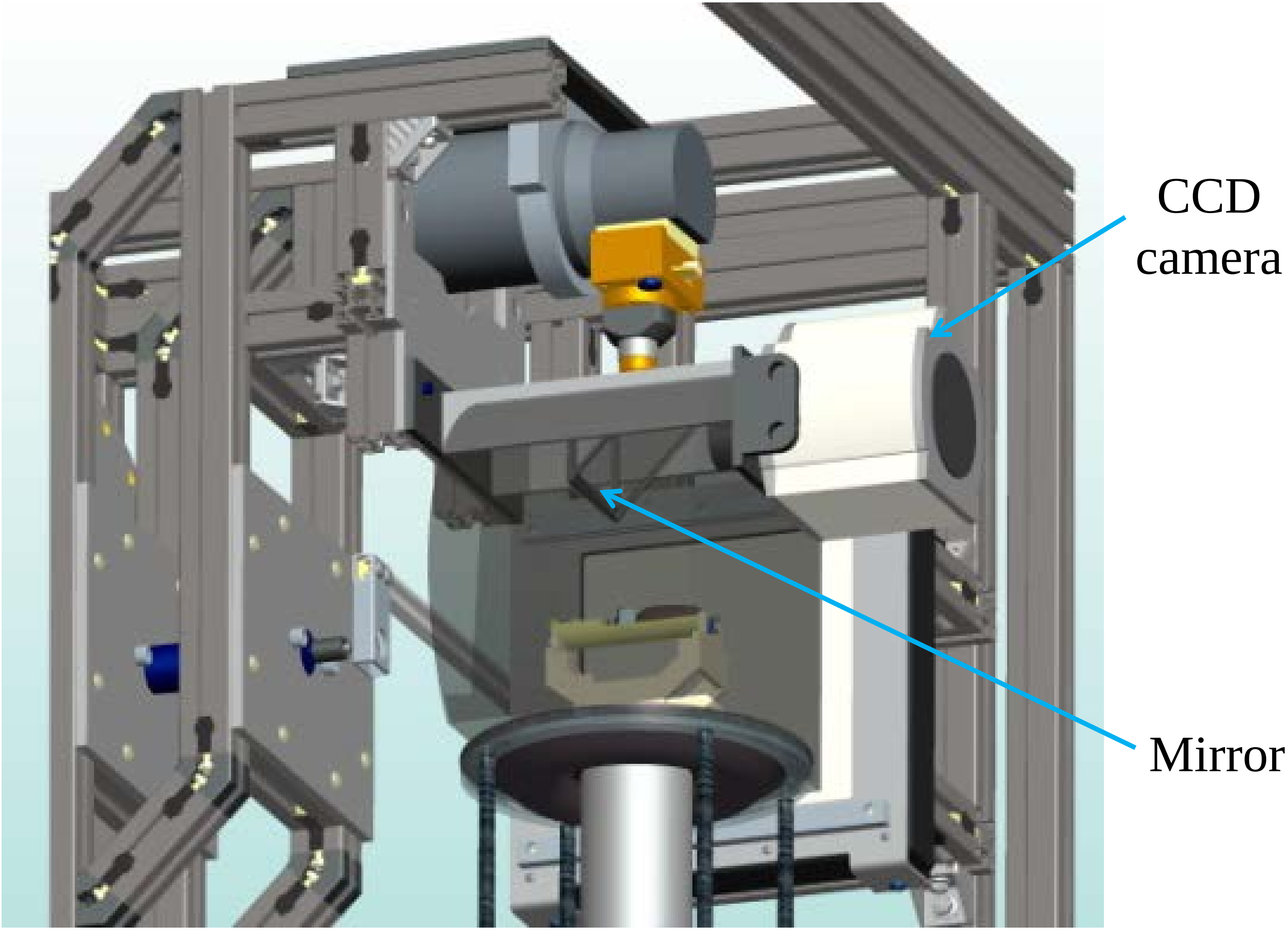


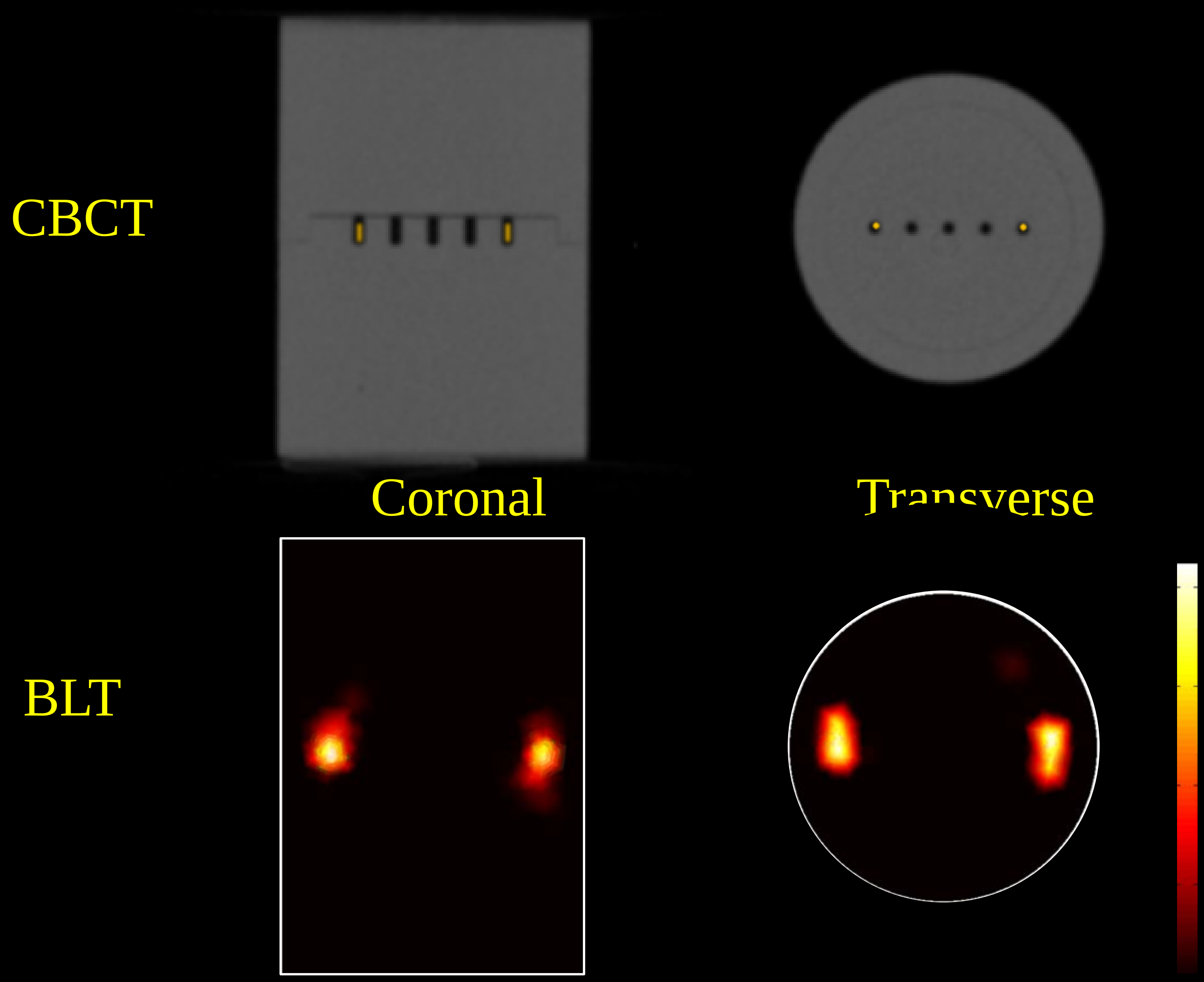

# Comparison of SC with MC
## Correcting for density scaling



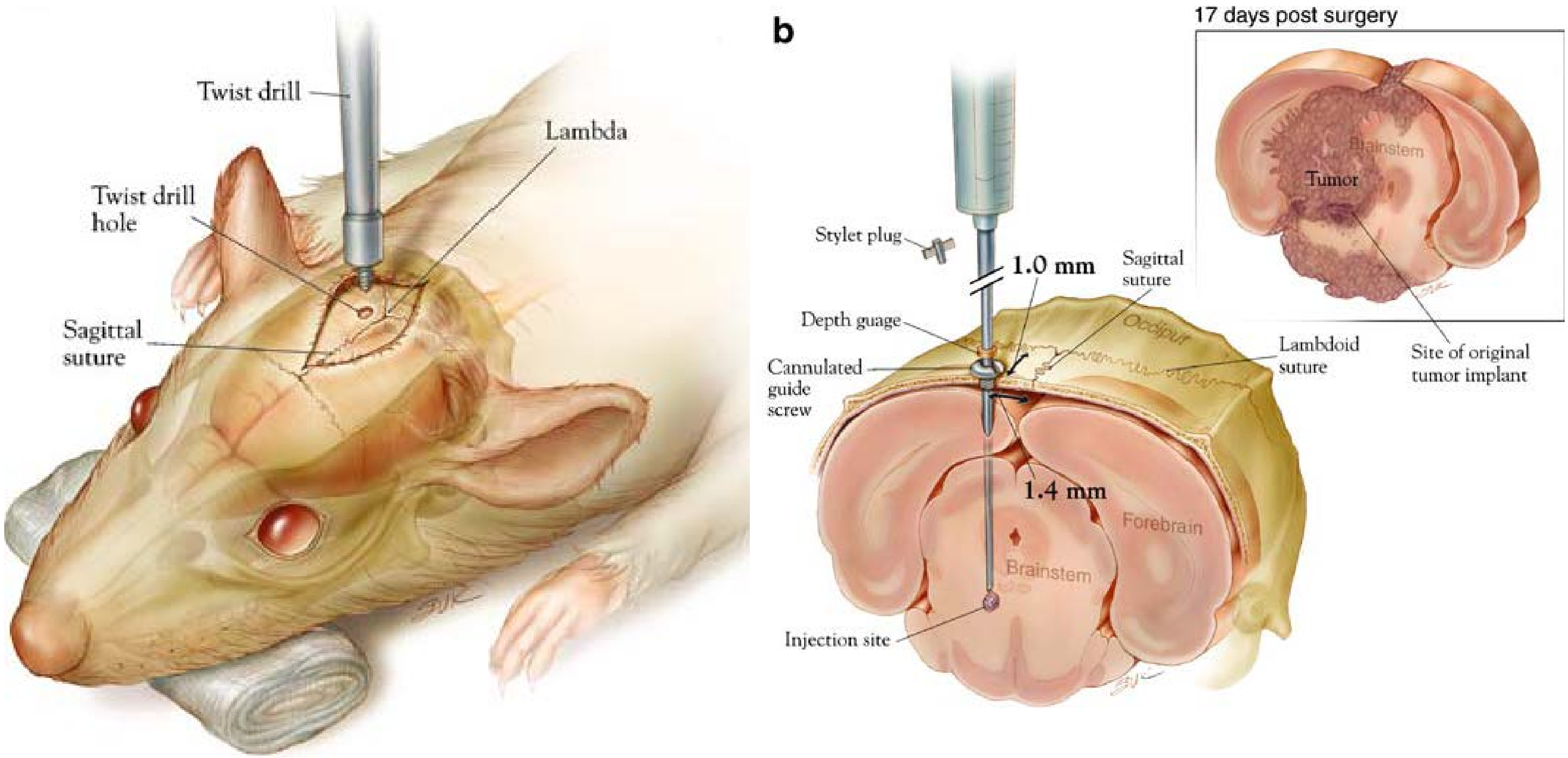
# On-board BLI/BLT for Beam's Eye View Irradiation with the SARRP (R01 CA158100)






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

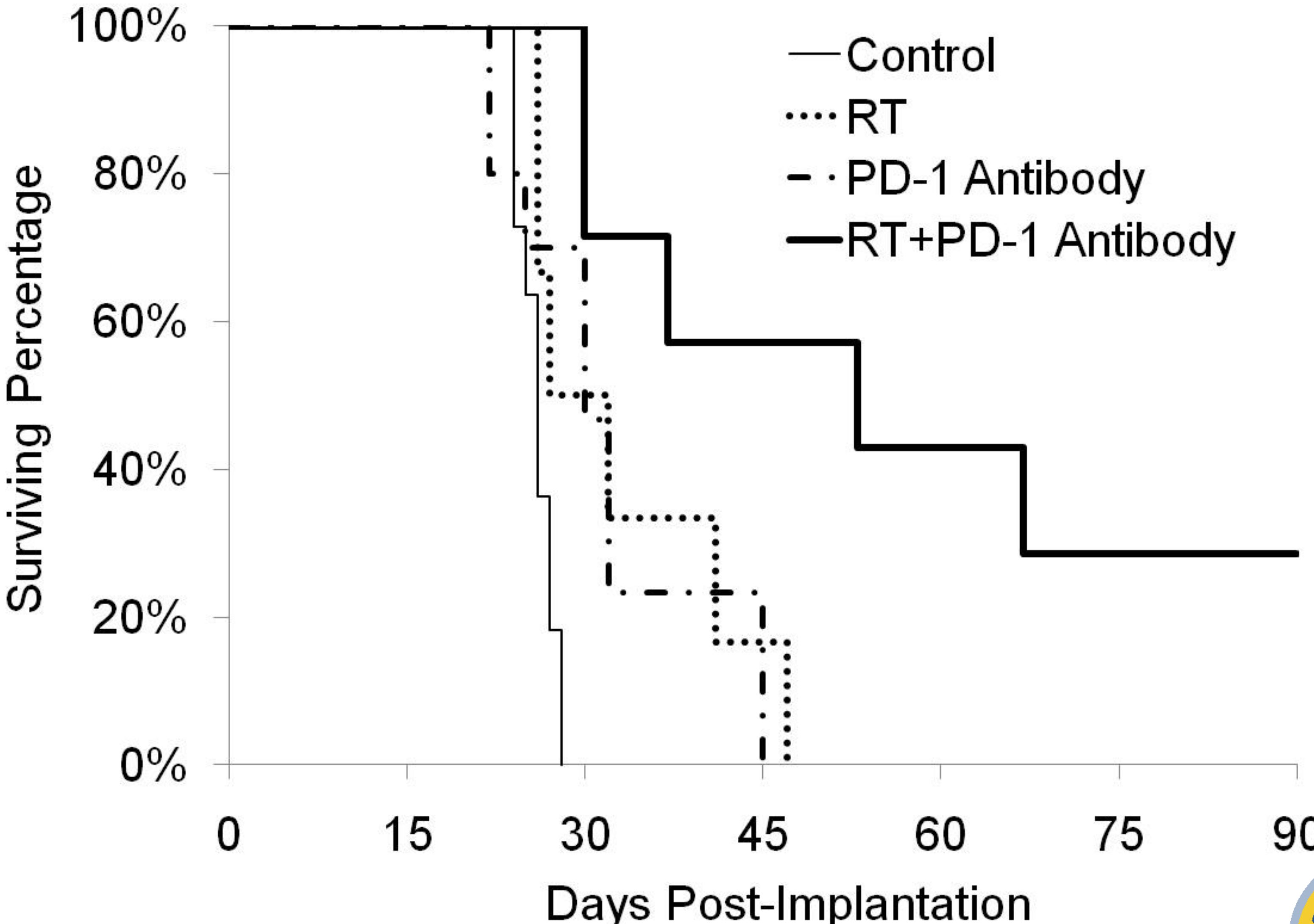
| Day | No Tx | RT only | PD-1 only | RT+PD-1 |
|---|---|---|---|---|
| 0 | Tumor Implantation | | | |
| 7 | Bioluminescent Imaging | | | |
| 10 | | Radiation | 1st antibody dose | Radiation; 1st antibody dose |
| 11 | | | | |
| 12 | | | 2nd antibody dose | 2nd antibody dose |
| 13 | | | | |
| 14 | |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

Radiation = 10 Gy in 3 mm beam

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

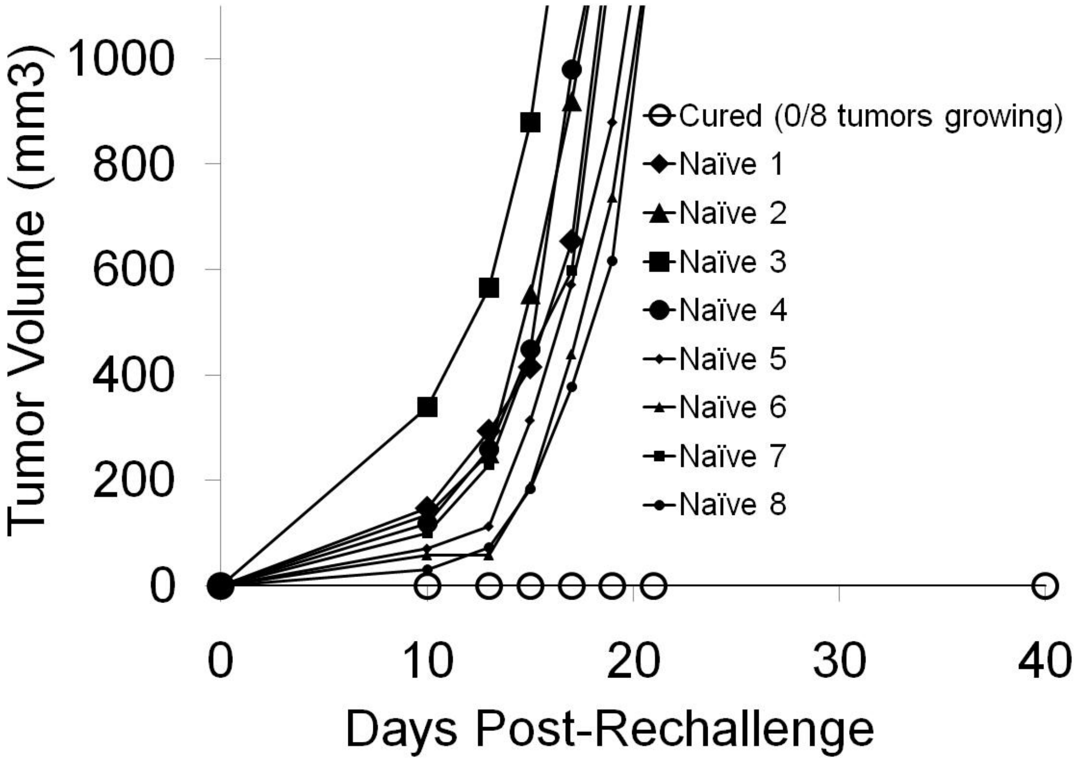
JOHNS HOPKINS MEDICINE

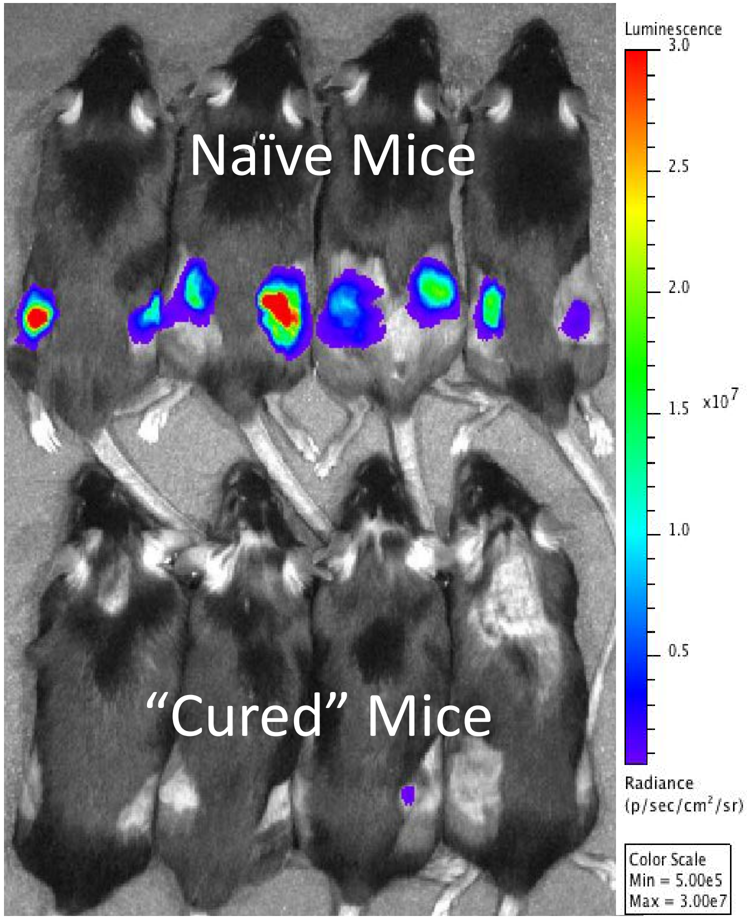
# Survival Outcome




JOHNS HOPKINS
MEDICINE

# Flank Re-challenge



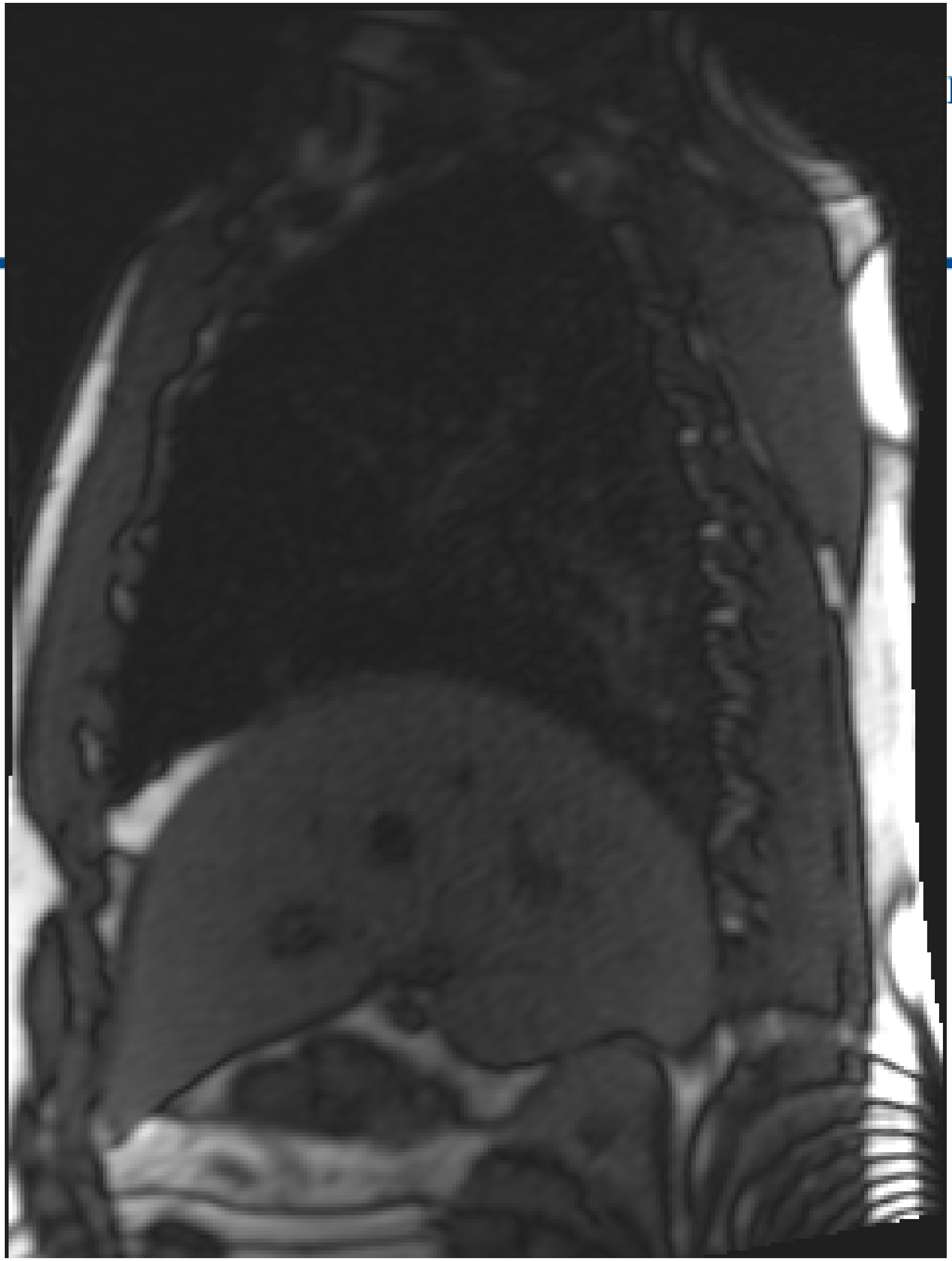
# What do we do for the next 5 years?

JOHNS HOPKINS MEDICINE

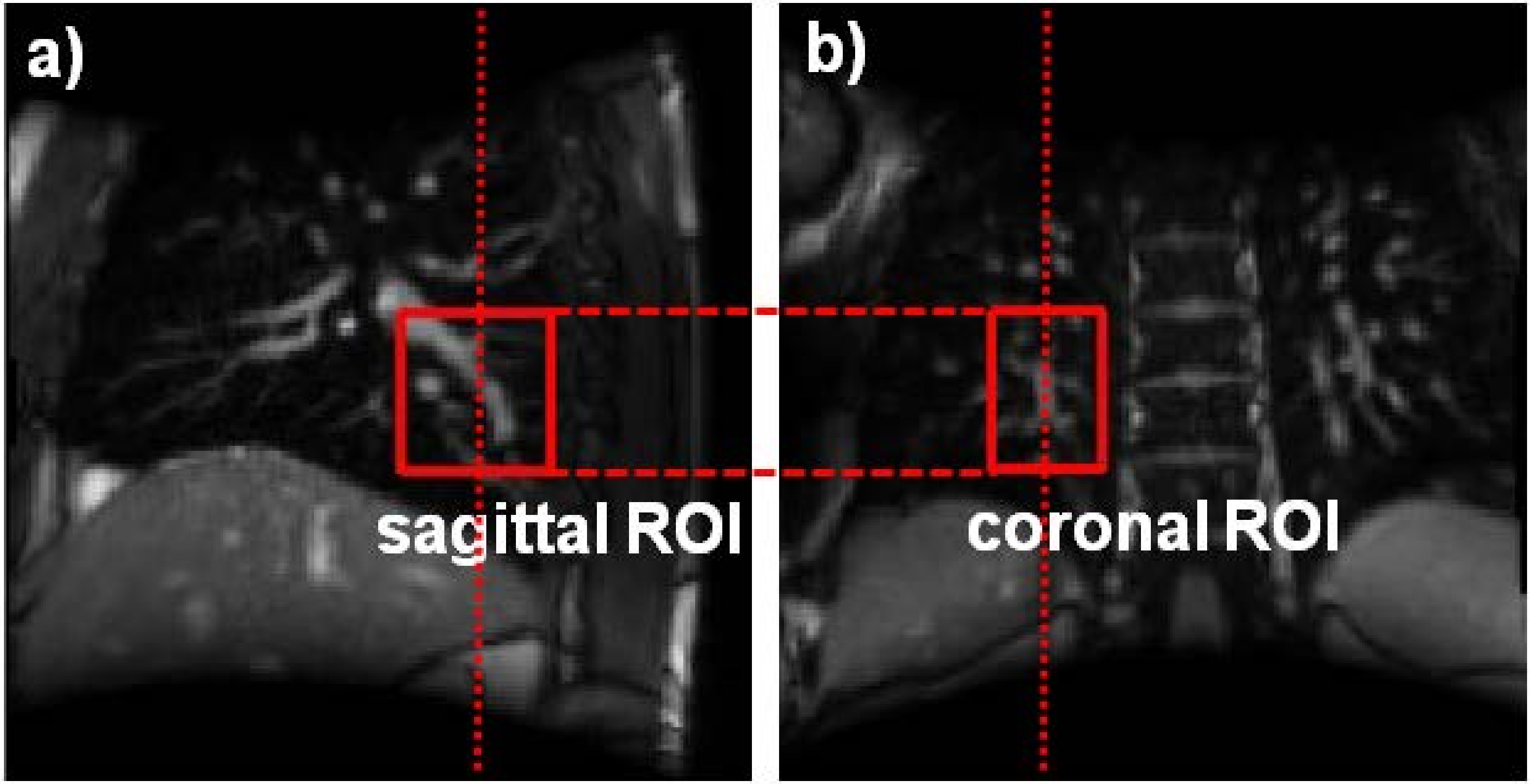
- Medicine (and radiation oncology) is undergoing tremendous changes driven by technologies and information
- Treatment strategies will employ multiple therapeutic agents with radiation
- Personalized medicine will be based on genetics, treatment response, functional/anatomic ….
- Physics need to expand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

# 4D MRI (JHU/Siemens)

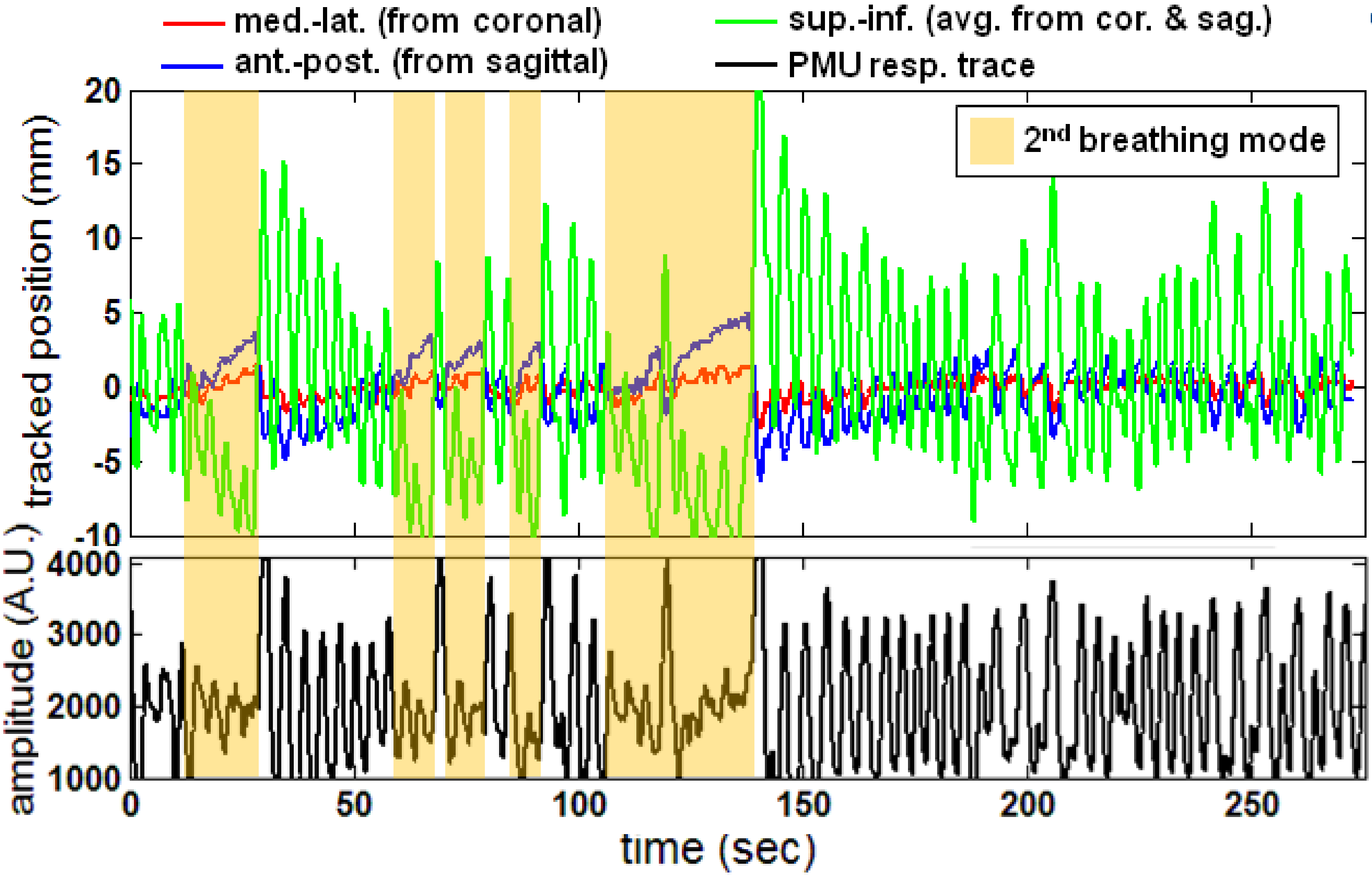
- 4D CT is a 2 min snapshot, not often re-evaluated
- Long duration (15 – 30 min) MRI to represent treatment



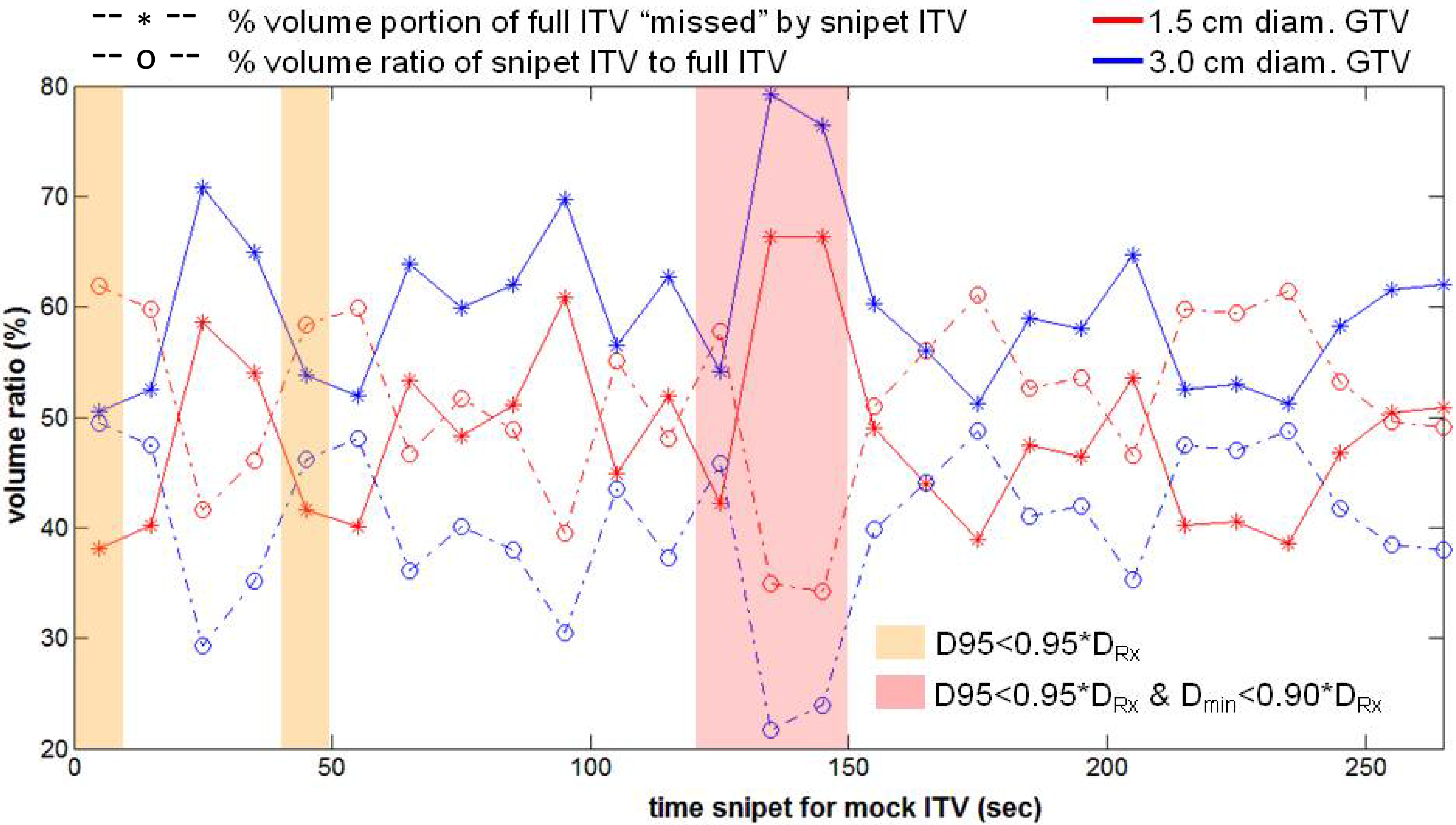
# 4D MRI – Tracked Motion



# 4D MRI – Characterization of Motion



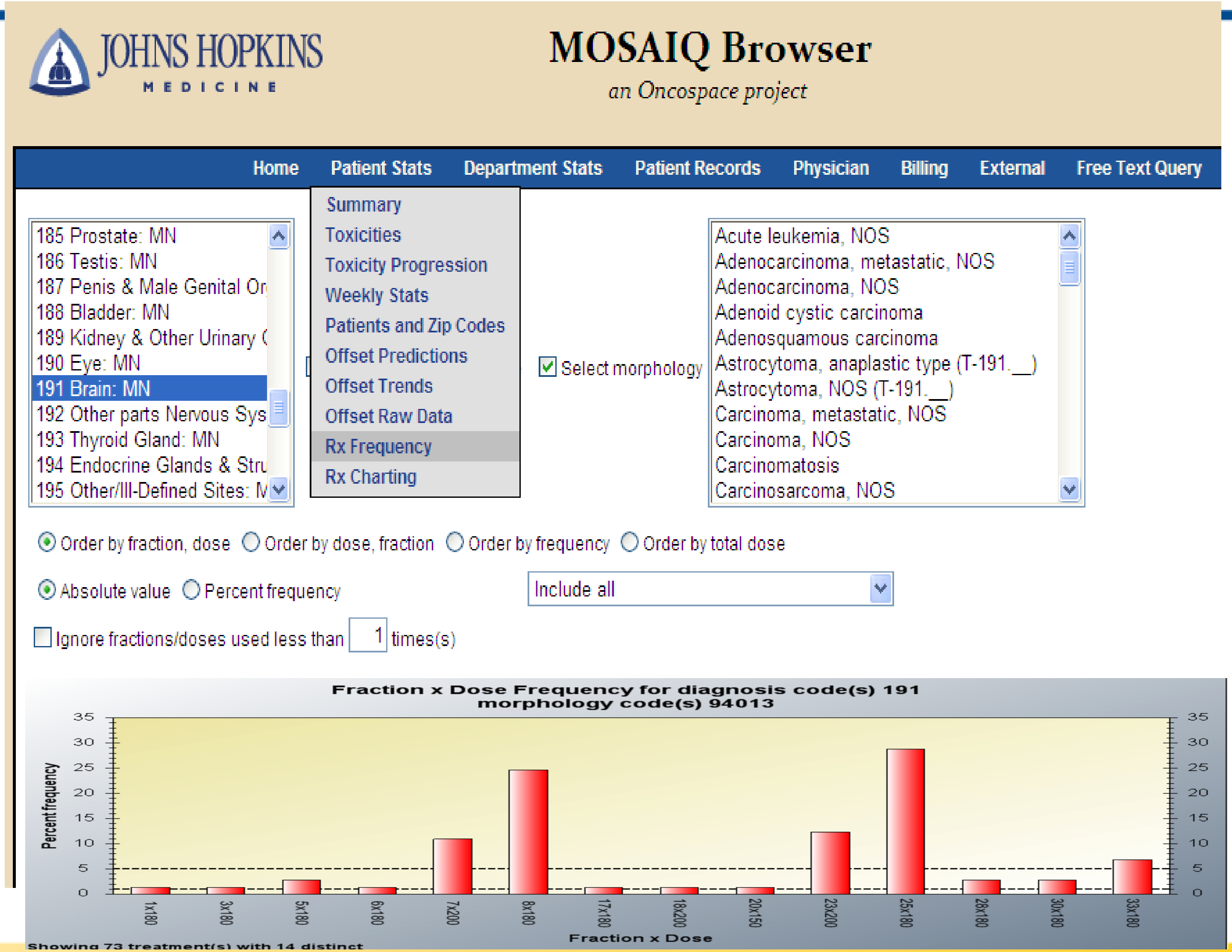
# 4D MRI – Characterization of Motion



# 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



# OncoSpace: Adapting the SkyServer Approach


- 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

***Alex Szalay PhD - JHU***
***Jim Gray PhD - Microsoft***