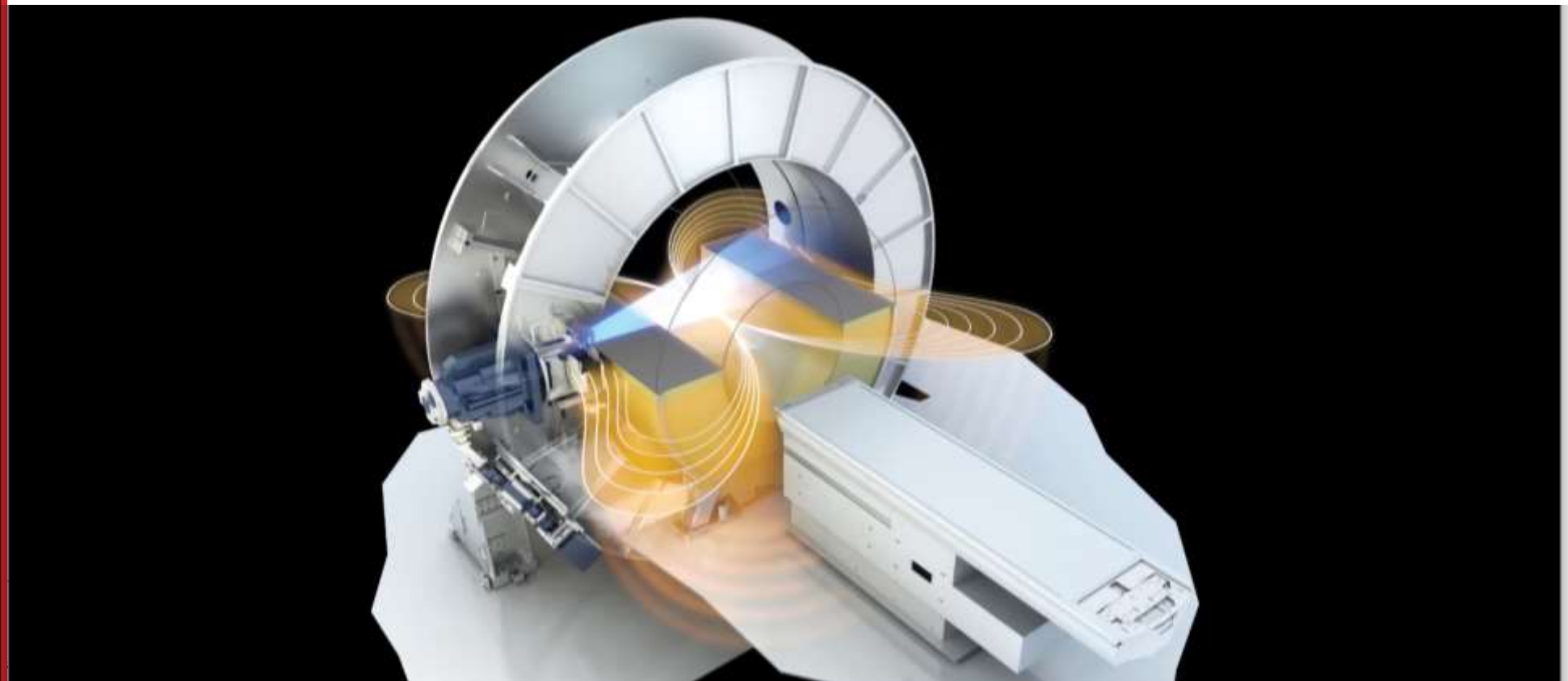
The Need for, and Implementation of, Image-Guidance in Radiation Therapy

Geoffrey S. Ibbott, Ph.D.

ICRP, October 10, 2017



THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

Disclosures

My institution holds Research Agreements with Varian, Elekta, and Philips

I will be discussing devices that are not currently available for sale, and that do not have FDA clearance.

Objectives

- Review the history of IGRT
- Discuss the clinical benefits of IGRT
- Introduce several major advances in IGRT
- Review developments leading to MR-based simulation and planning, and MR-guided radiation therapy
- Describe patient imaging and treatment procedures possible with an MR-guided linac
- Describe recent developments in biology-guided RT

Towards the elimination of invasion

Universitair Medisch Centrum Utrecht

REVIEW ARTICLE

200TH ANNIVERSARY ARTICLE

The NEW ENGLAND JOURNAL of MEDICINE

Two Hundred Years of Surgery

Atul Gawande, M.D., M.P.H.

N Engl J Med 2012; 366:1716-1723 | May 3, 2012 | DOI: 10.1056/NEJMra1202392

Meanwhile, the practice of surgery itself will continue to change. Prognostication is a hazardous enterprise. But if the past quarter century has brought minimally invasive procedures, the next may bring the elimination of invasion. One feels foolish using terms like nanotechnology — I haven't the slightest idea what it really means or can do — but scientists are already experimenting with techniques for combining noninvasive ways of seeing into the body through the manipulation of small-scale devices that can be injected or swallowed. Surgical work will probably even become fully automated.

Slide courtesy of Marco van Vulpen

Techniques versus approach

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Technical radiation delivery techniques:

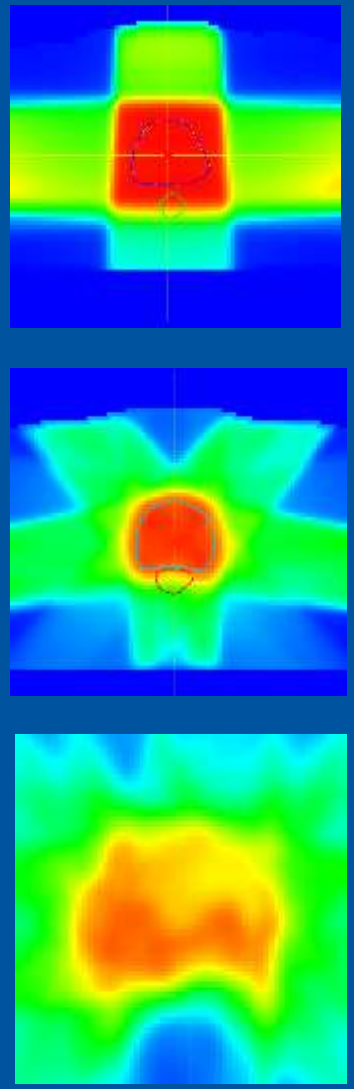
- Conventional / Conformal radiotherapy / …
- IMRT / VMAT / Tomotherapy / …
- Cyberknife / Radiosurgery /…
- Protons / Carbon Ions /
- Brachytherapy / …
- etc …

What do we want:

100% cure, 0% toxicity, 100% Quality of Life

Treatment approach: Image Guided RadioTherapy (IGRT)

- spatial control of the dose distribution
- Inhomogeneous dose distribution
- based on the 3D tumor-characteristics
- Individualized treatment

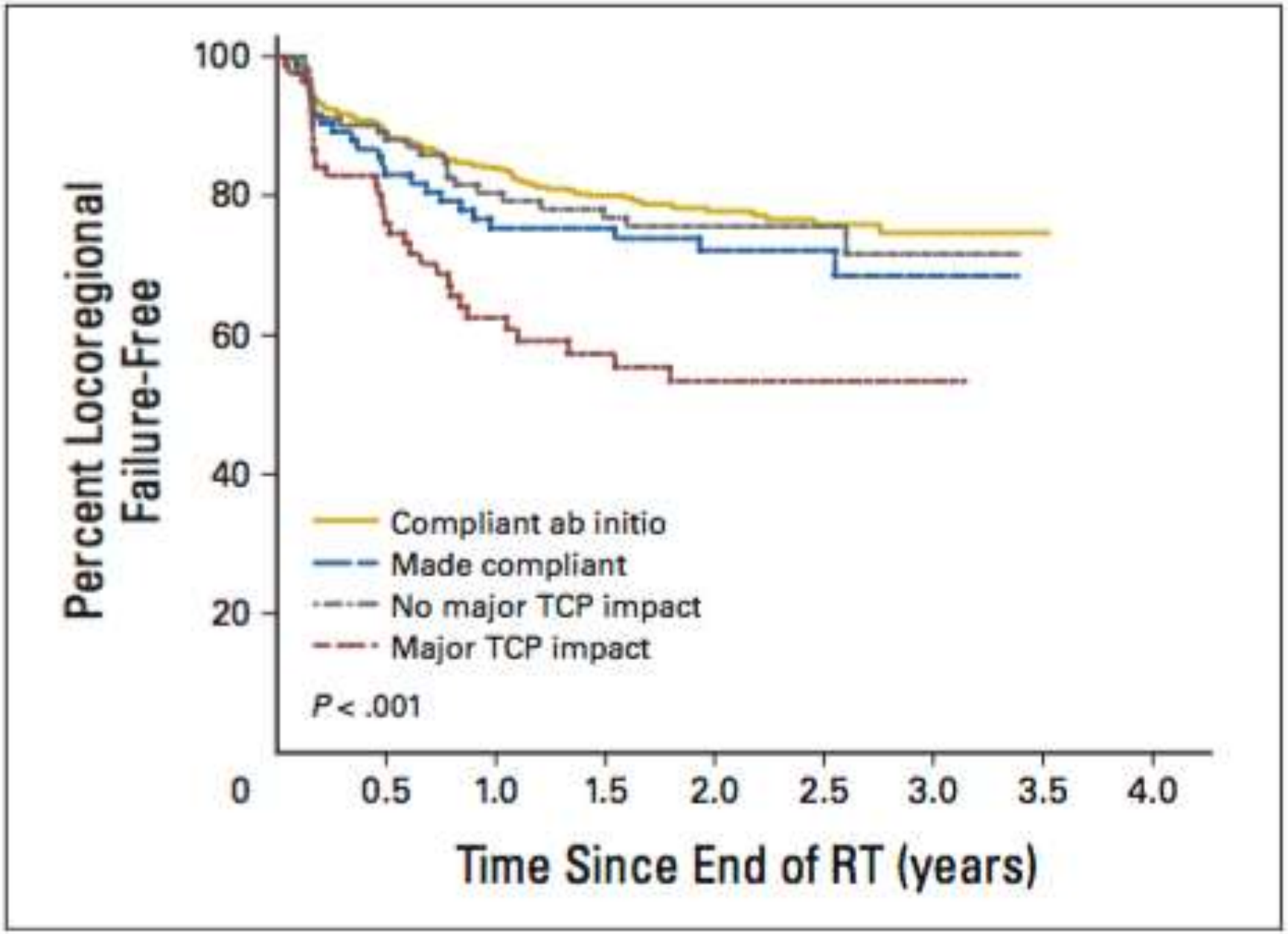


Critical Impact of Radiotherapy Protocol Compliance and Quality in the Treatment of Advanced Head and Neck Cancer: Results From TROG 02.02

Lester J. Peters, Brian O'Sullivan, Jordi Giralt, Thomas J. Fitzgerald, Andy Trotti, Jacques Bernier, Jean Bourhis, Kally Yuen, Richard Fisher, and Danny Rischin

Results

At TMC review, 25.4% of the patients had noncompliant plans but none in which QARC-recommended changes had been made. At secondary review, 47% of noncompliant plans (12% overall) had deficiencies with a predicted major adverse impact on tumor control. Major deficiencies were unrelated to tumor subsite or to T or N stage (if N+), but were highly correlated with number of patients enrolled at the treatment center (< five patients, 29.8%; ≥ 20 patients, 5.4%; $P < .001$). In patients who received at least 60 Gy, those with major deficiencies in their treatment plans (n = 87) had a markedly inferior outcome compared with those whose treatment was initially protocol compliant (n = 502): −2 years overall survival, 50% *v* 70%; hazard ratio (HR), 1.99; $P < .001$; and 2 years freedom from locoregional failure, 54% *v* 78%; HR, 2.37; $P < .001$, respectively.

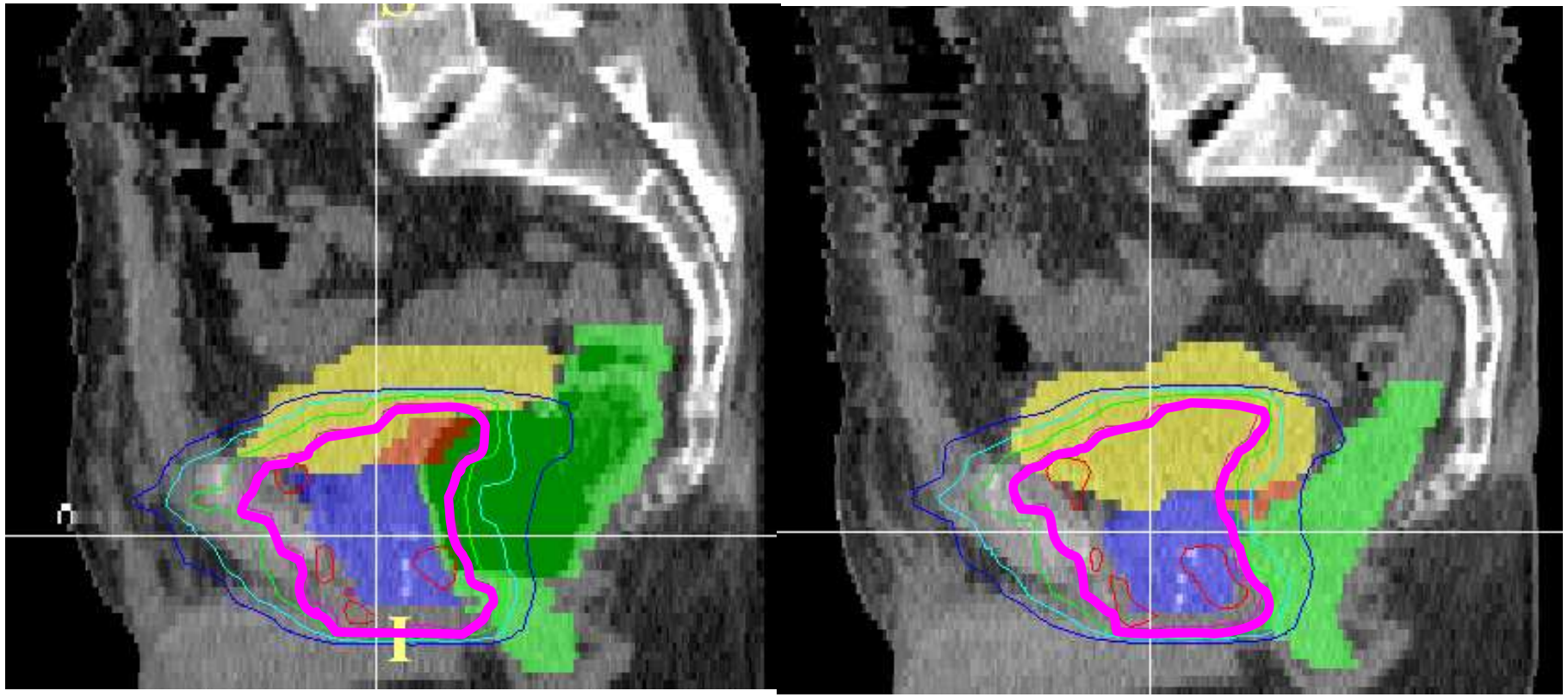

Percent Locoregional Failure-Free
100
80
60
40
20
0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
Compliant ab initio
Made compliant
No major TCP impact
Major TCP impact
P < .001
Time Since End of RT (years)

Why do we need image-guided RT?

Dosimetric Effect of Organ Variability

Original Plan

Original Plan on New CT

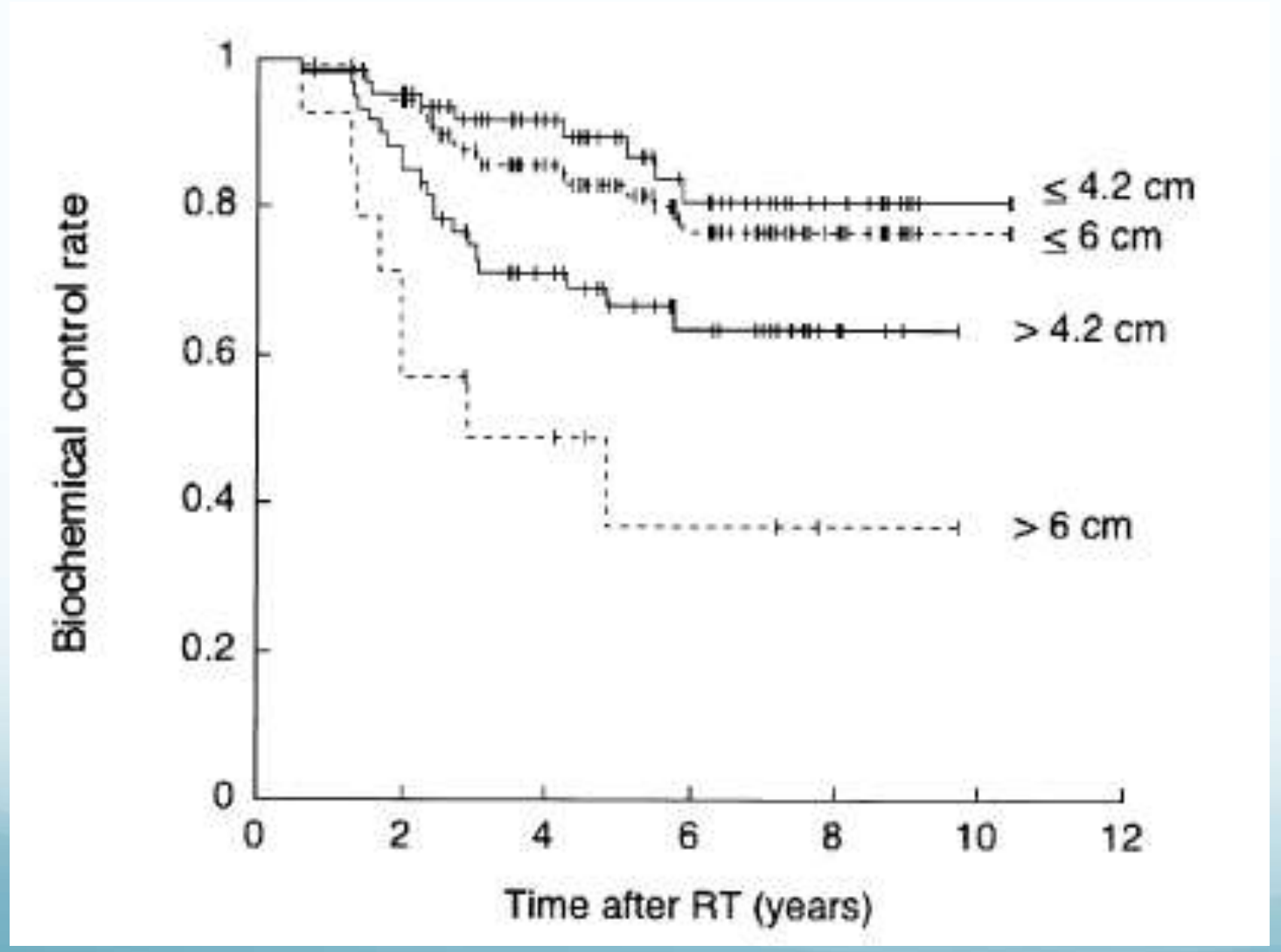


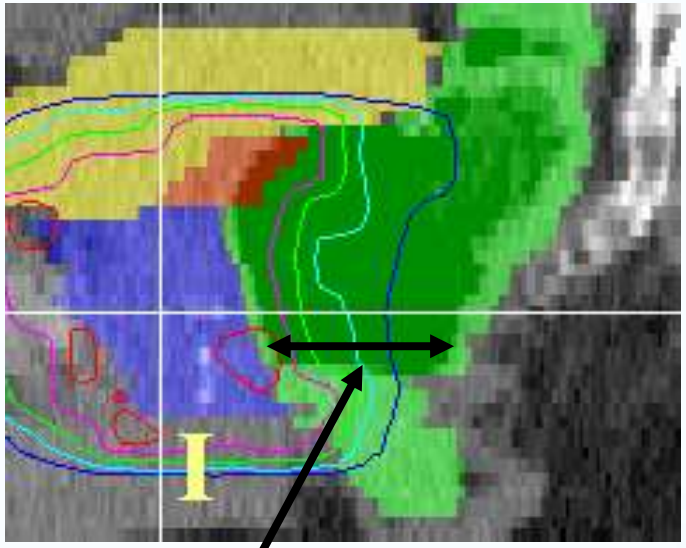
CT scan a week later

G. Ibbott, ASTRO, San Diego, 2017

Slide courtesy L. Court

Why do we need image-guided RT?



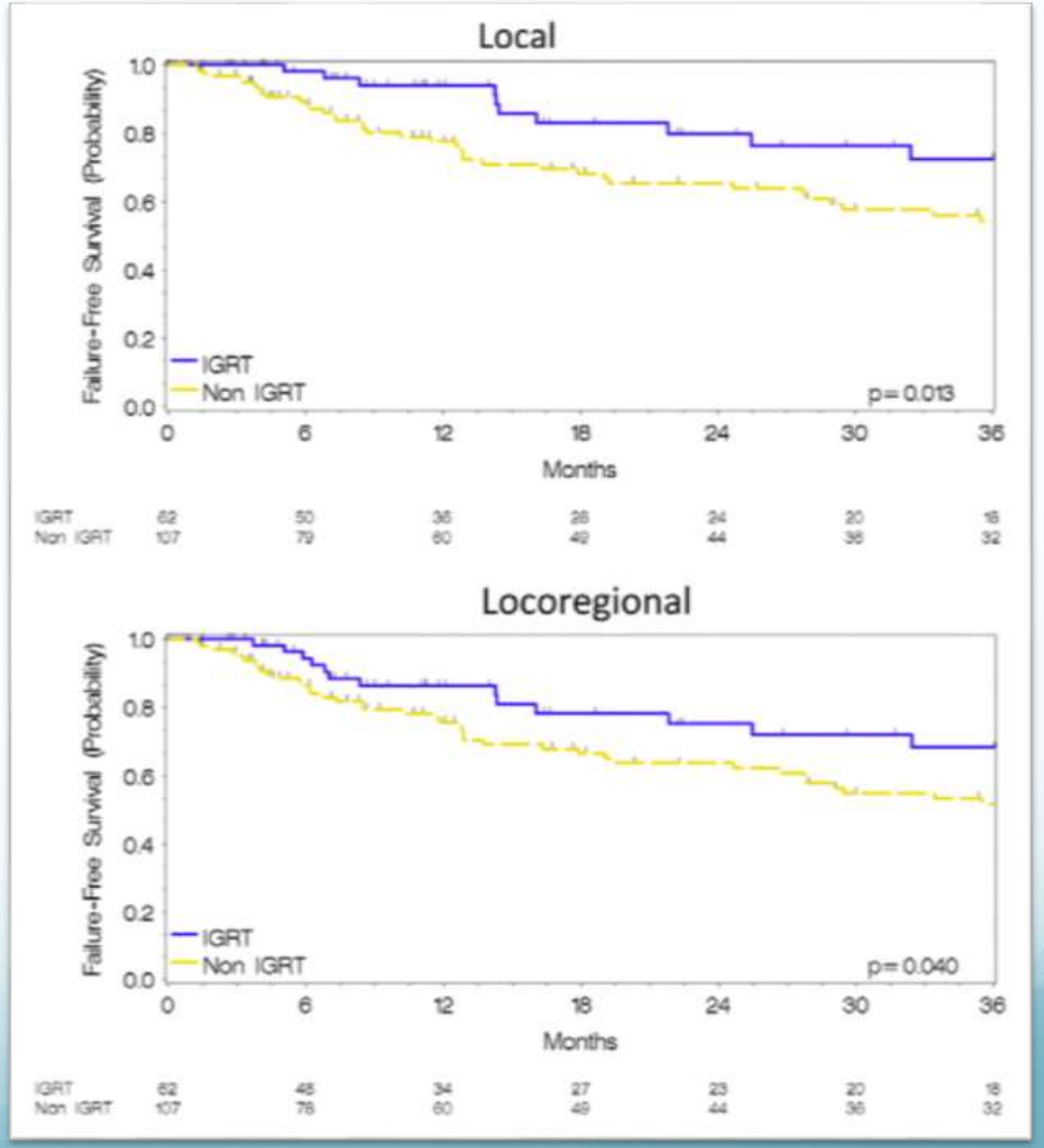


Rectal diameter at simulation

de Crevoisier et al, IJROBP 62 (4): 965-973, 2005

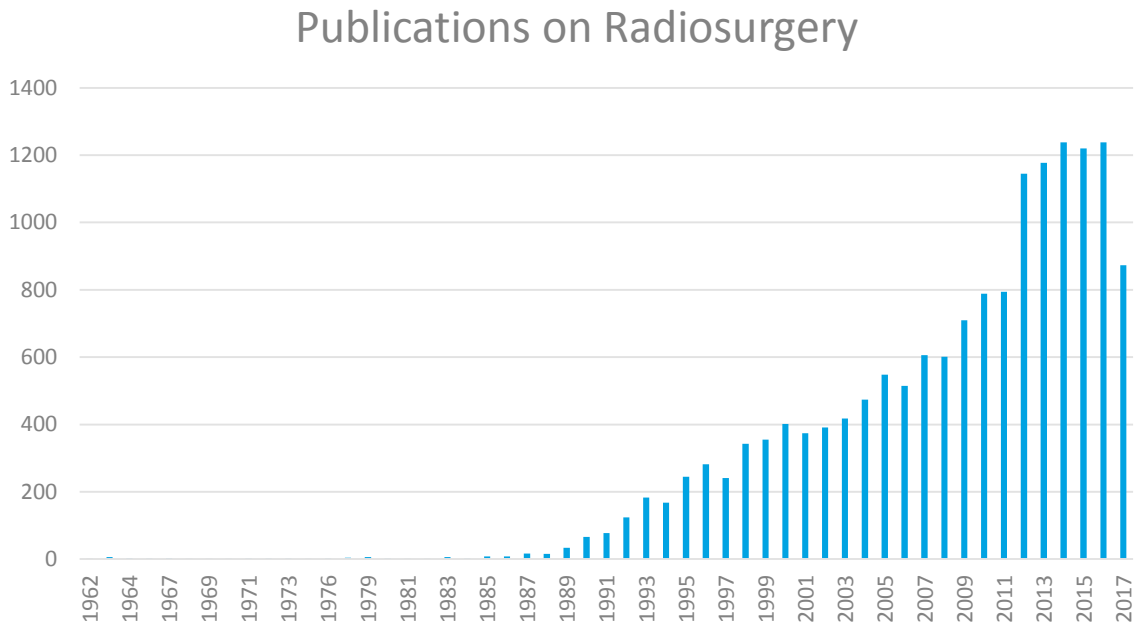
Why do we need image-guided RT?

Local and locoregional failure-free survival rates
Patients receiving IGRT were more likely to receive a higher tumor dose.

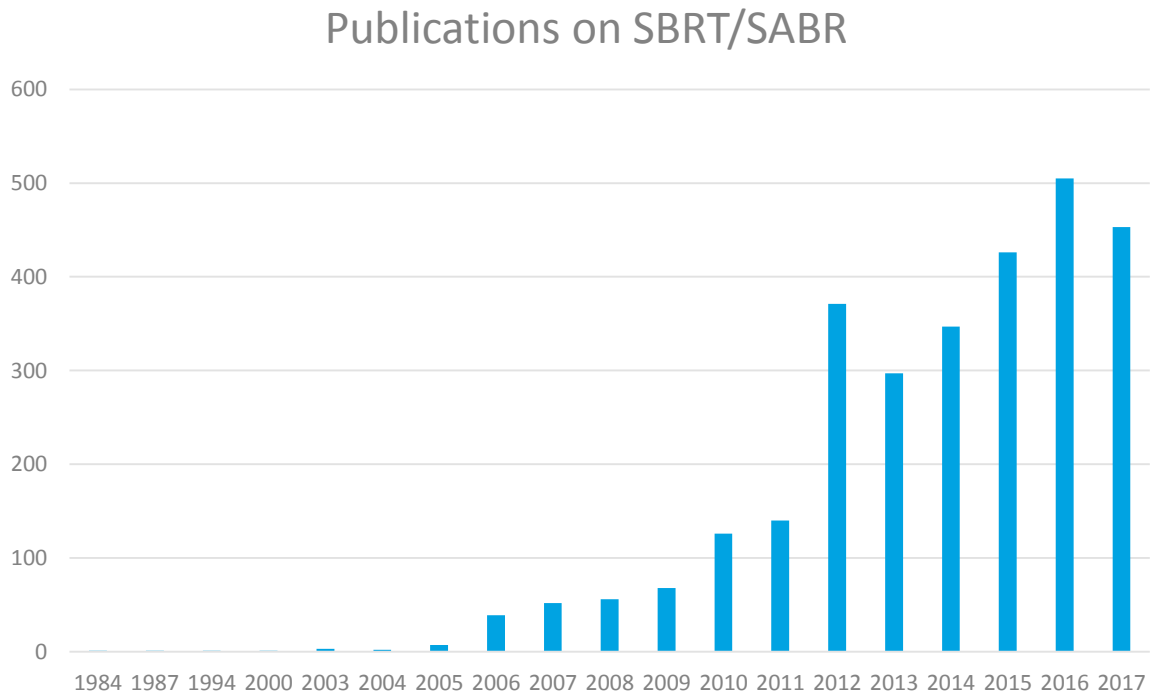


Kilburn, J.M., et al, 2016. Image guided radiation therapy may result in improved local control in locally advanced lung cancer patients. Pract Radiat Oncol 6, e73-80.

Increasing Treatments with Higher Conformality Requires Better Targeting



Improved image guidance allows for more conformal treatment delivery



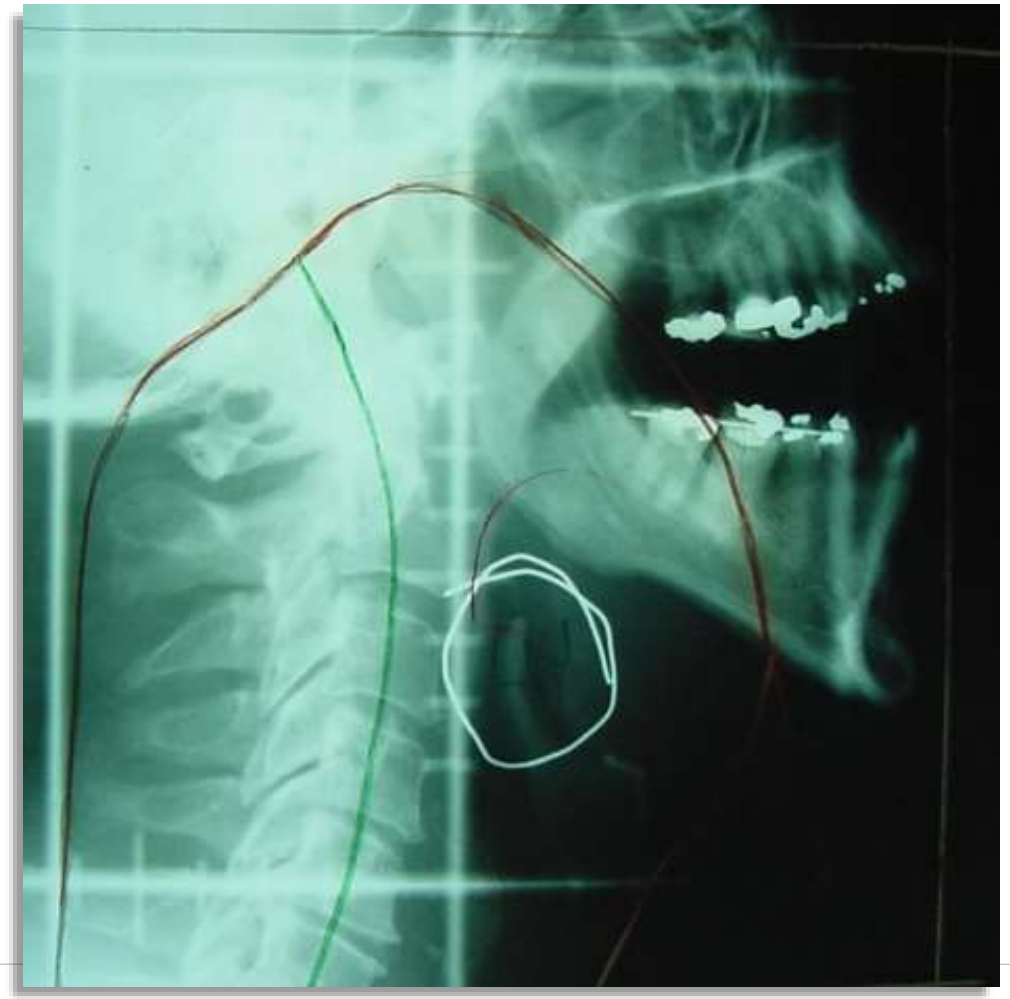
Improved imaging allows for better tumor delineation for RT planning

Image-Guided RT

- Not a new idea
- Benefits of imaging patient in treatment position
- Position can be assessed at time of beam-on
- Real-time corrections can be made
- Margins can be reduced

IGRT c. 1970

From 2D to 3D, 4D, IMRT and IGRT



Courtesy P. Balter

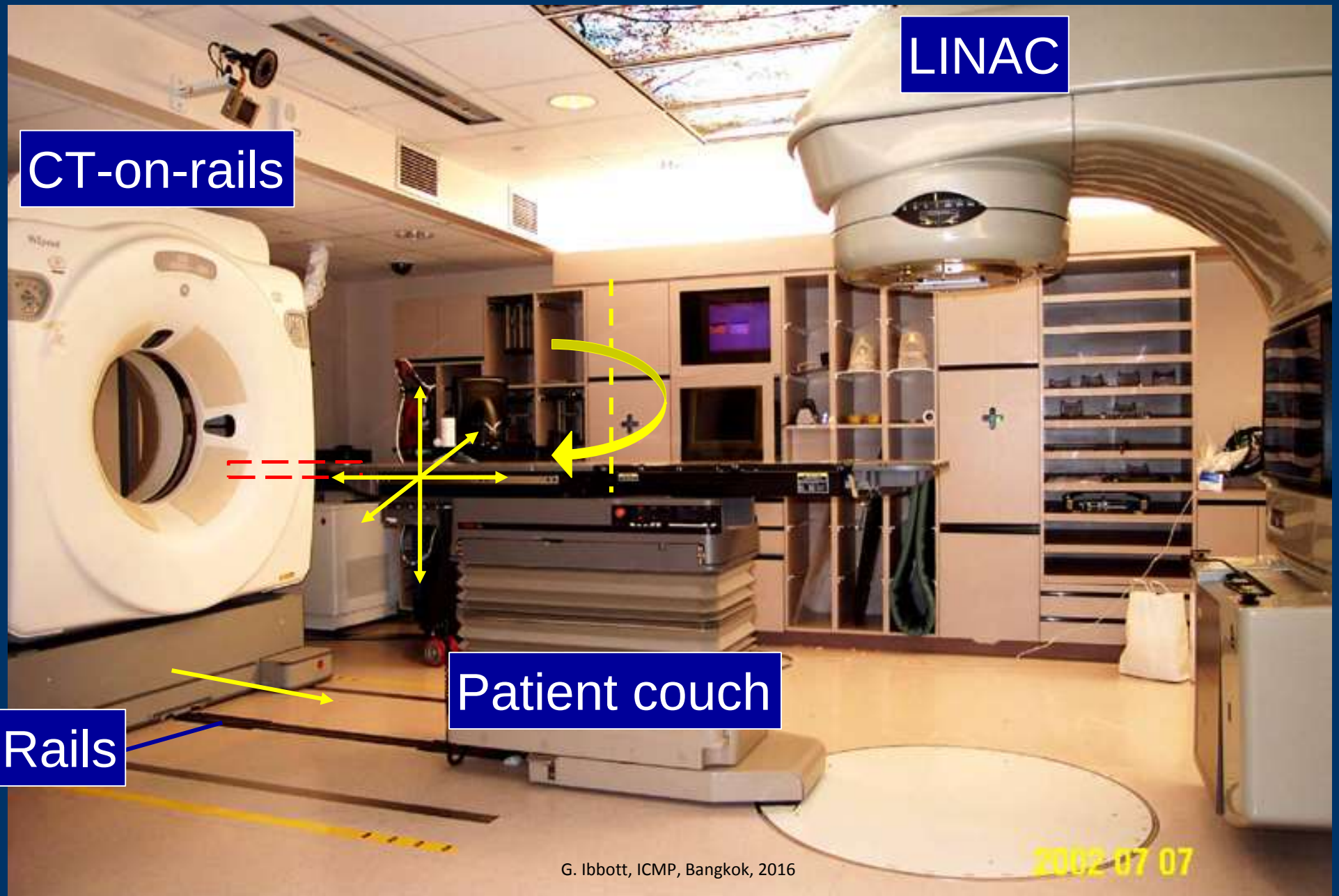
Common IGRT technologies

- 2D projection x-rays (kV or MV)
- CT (cone-beam) (kV or MV)
- Ultrasound
- Surface imaging
- Implanted marker

Kamino et al, IJROBP, 66, 271, 2006

Novalis Exactrac: 2D/3D

CT-guided Radiation Therapy



Breakthrough: CT-linac

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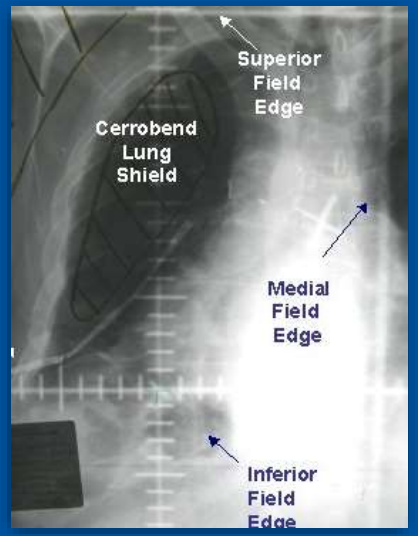
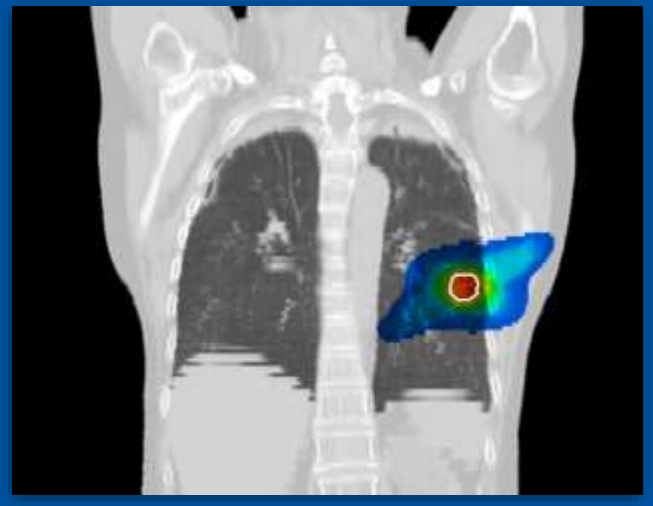
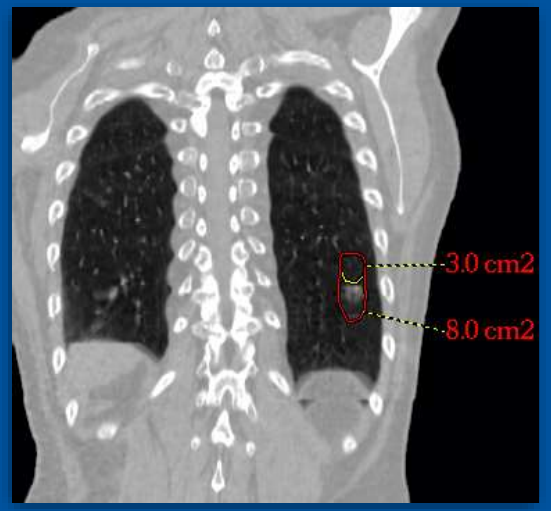




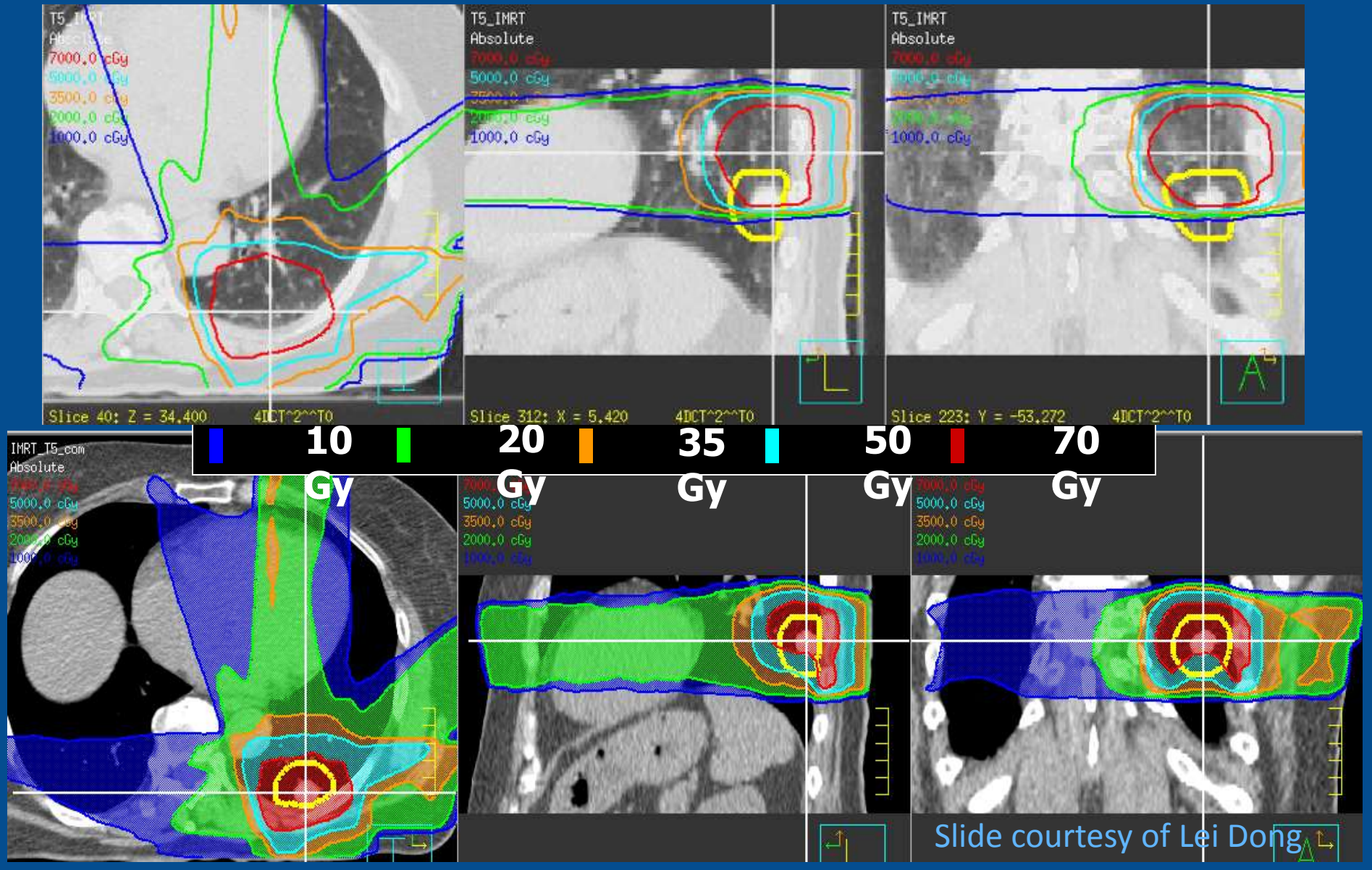


Changing concepts:

History	Tendency
• Fractionated	Hypofractionated
• Homogeneous dose	Inhomogeneous dose / stereotaxy
• Dose prescription ICRU	Maximum dose less important, if safe
• Radioresistant tumors	Probably do not exist (e.g. kidney)
• Etc	

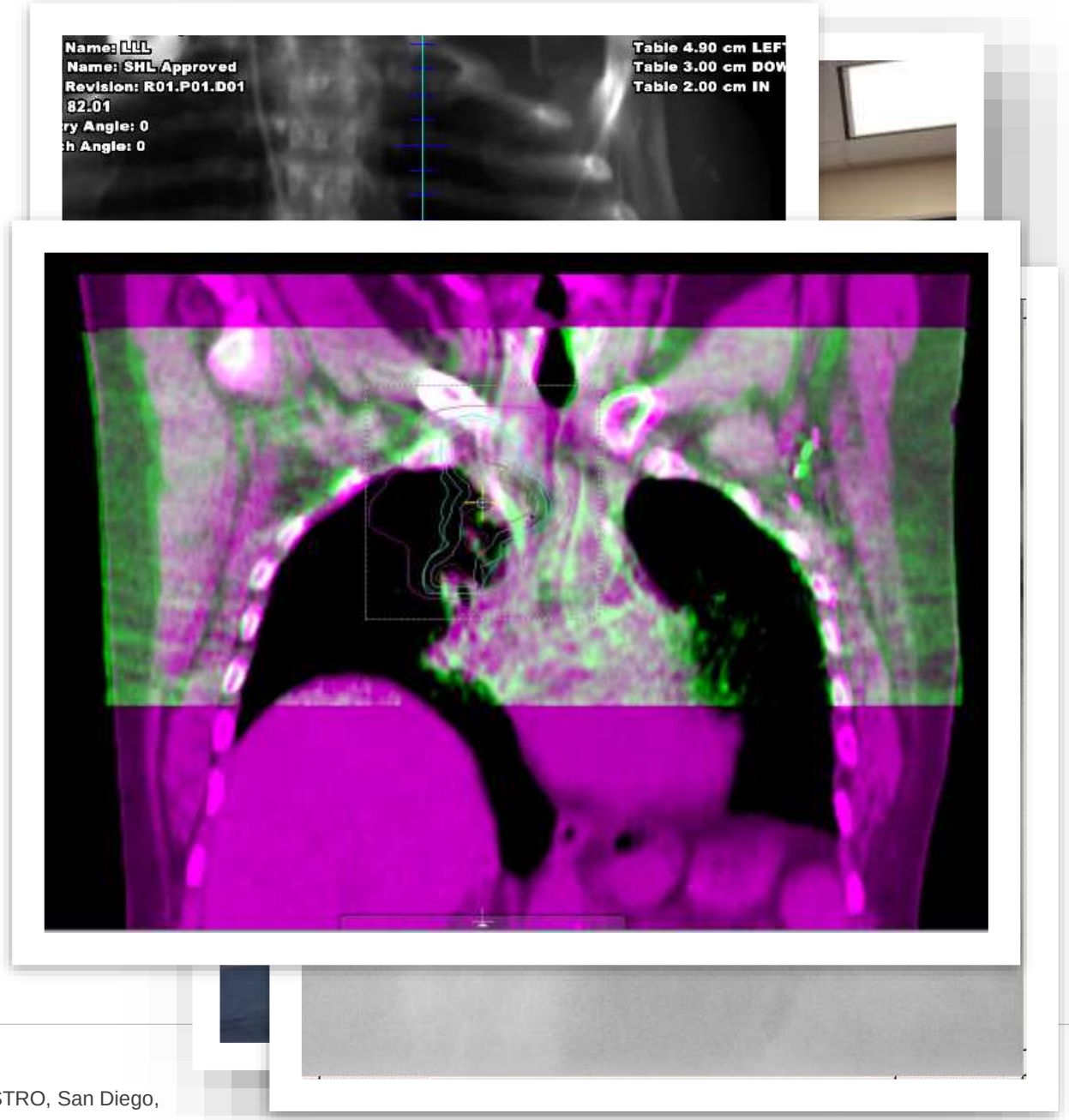
This makes Image Guided Radiotherapy a real alternative for surgery

Respiratory Motion and its effect on dose – example planned on 3DCT evaluated on 4DCT



Current Status of IGRT

- kV imaging widely used but relies on bony landmarks or fiducials
- CBCT IGRT has transformed RT practice and perception. Its potential may not have been fully exploited
- However, several issues remain …
- Inadequate soft tissue visualization
  - particularly in abdomen and pelvic anatomy
- Lack of functional information
  - CT cannot reveal tissue characteristics
- Intrafraction motion
  - Long acquisition time of CBCT largely limits it to pre-treatment or periodic imaging



G. Ibbott, ASTRO, San Diego, 2017

Clinical benefits of MRI-based IGRT

Soft-tissue visualization

- Difficult-to-image targets and critical structures become ‘easy’
- Improved ability to adapt treatment
- Ability to see the tumor not just the organ - GTV boost

Real-time 2D and 3D imaging

- Imaging simultaneous with irradiation
- Gating and tracking without surrogates

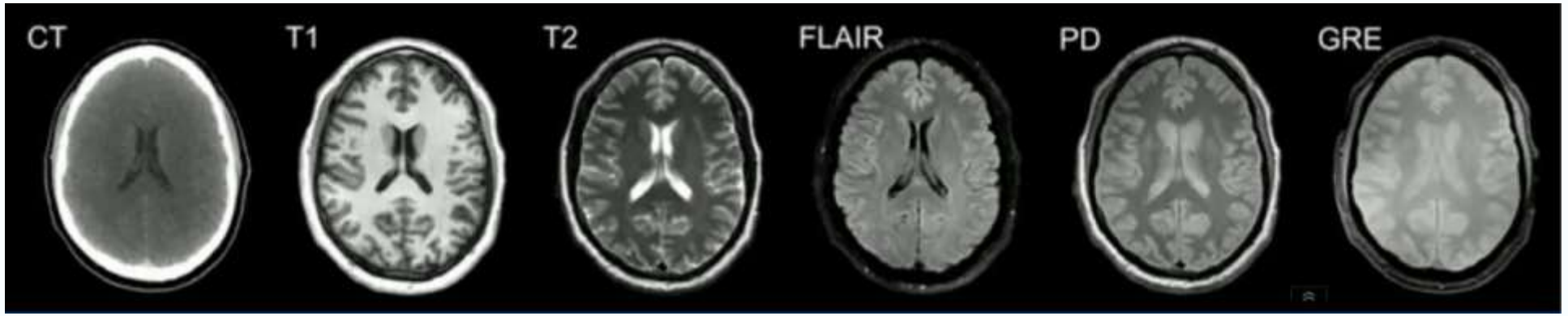
No imaging dose

- Freedom to image at any time

Quantitative imaging

- Tumor treatment response assessment (inter- and intra-fractions)

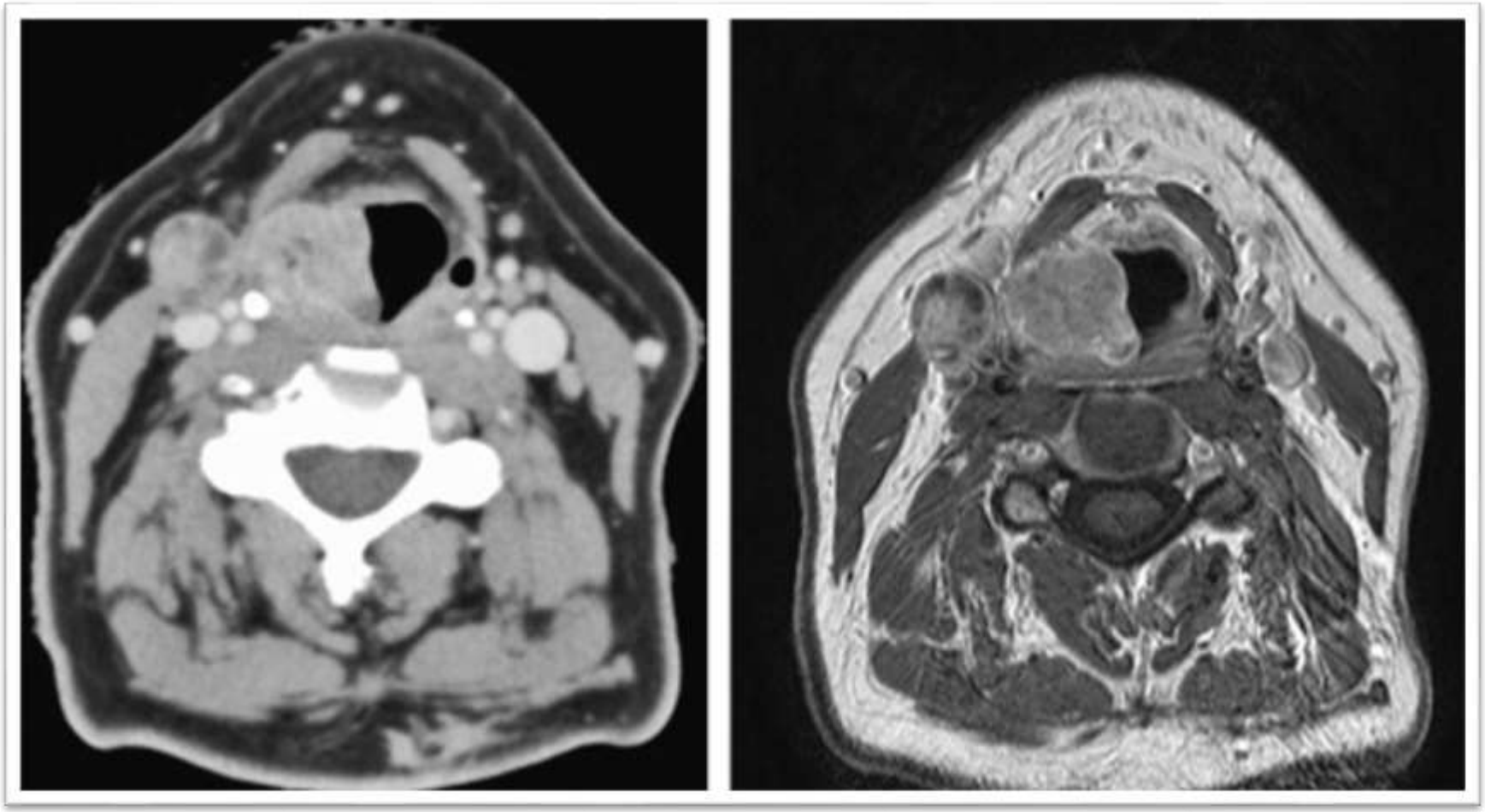
What does MR bring to IGRT?



- ‘Real time’ no radiation dose imaging
  - Simultaneous with irradiation
- Soft tissue visualization
  - Many targets and structures become easier to visualize
  - Improved ability to adapt treatment
- Ability to see the tumor not just the organ
  - Prostate, brain, liver, etc,
- Potential for functional and molecular imaging
- Therefore addressing the two remaining IGRT problems

Images courtesy of Jing Cai, PhD

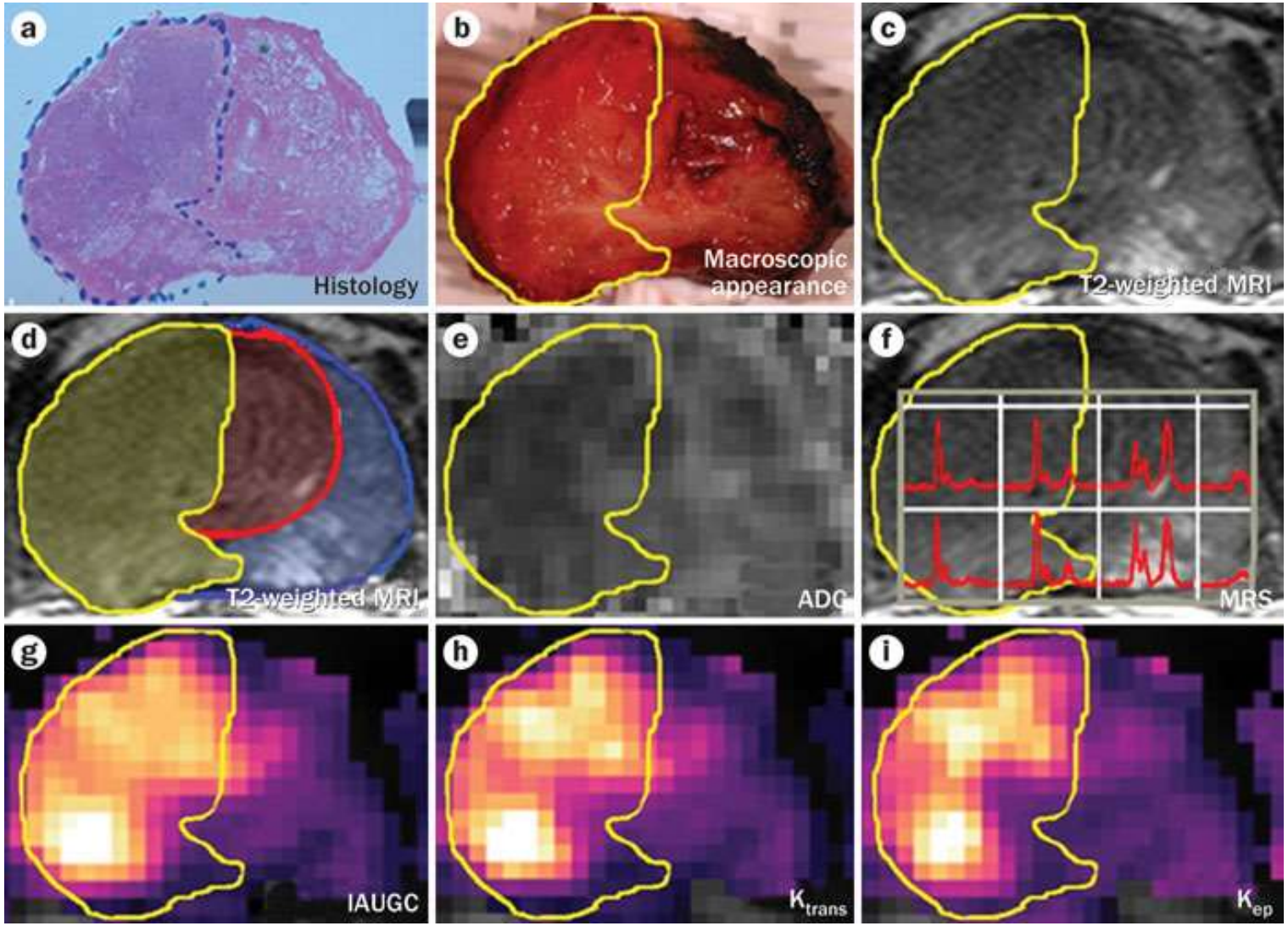
Improved Anatomical Imaging:
Better Soft Tissue Contrast for Target Delineation



Better soft tissue contrast helps us delineate tumor and lymph nodes and normal structures in H&N

Tumor assessment: Biological Characterization

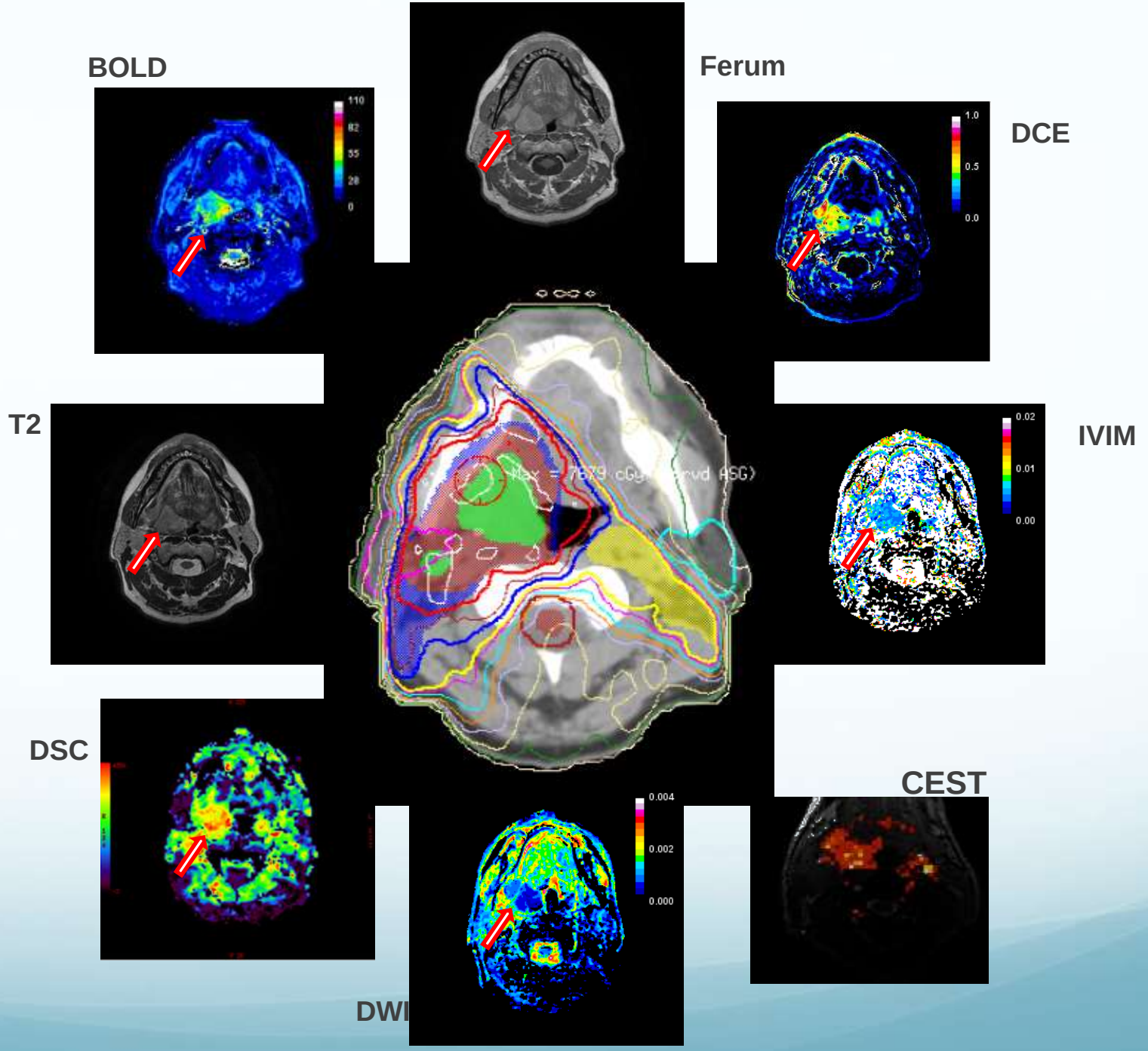
The heterogeneity of functional indices across pixels within a histologically defined, Gleason grade 4 + 3 tumor in the right lobe of the prostate



de Souza, N. M. Standardizing the use of functional MRI in prostate cancer *Nat. Rev. Urol.* (2011)

ELEKTA

For radiation oncologists, *spatial* dose/response data is what separates us from other cancer paradigms



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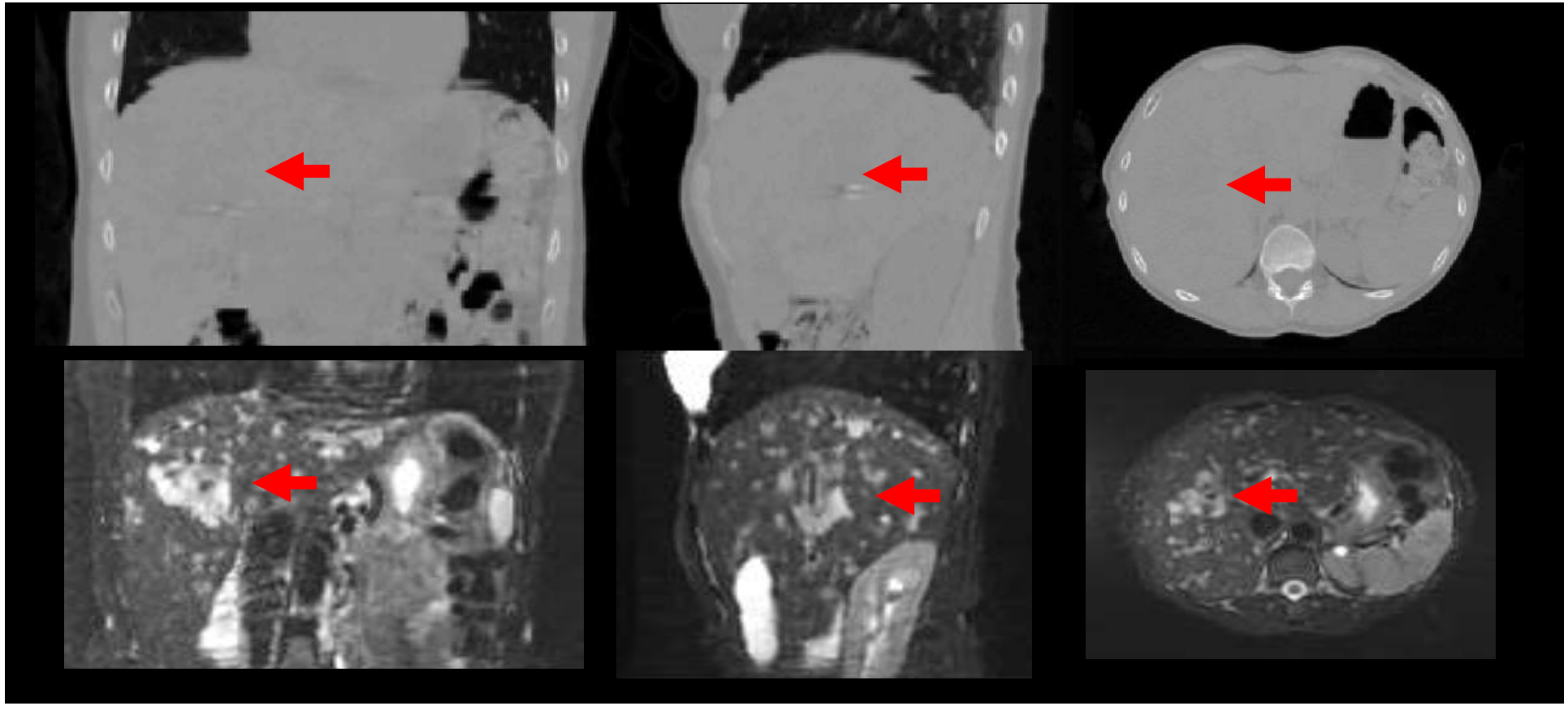
4D-MRI: Volume Delineation of Moving Target in Abdomen



Courtesy of Jing Cai, PhD

Special Precautions Required

- Radiation Oncology staff are generally not familiar with safety precautions required for working with 1.5 T magnet
- Develop safety zones
- Staff must have appropriate training to enter successive zones
- Must consider both MR safety and radiation safety concerns

PMH - MR on Rails

ViewRay MR-Cobalt Unit

Images courtesy of ViewRay
http://www.viewray.com/

Philips/Elekta Solution for MR-IGRT

Purpose

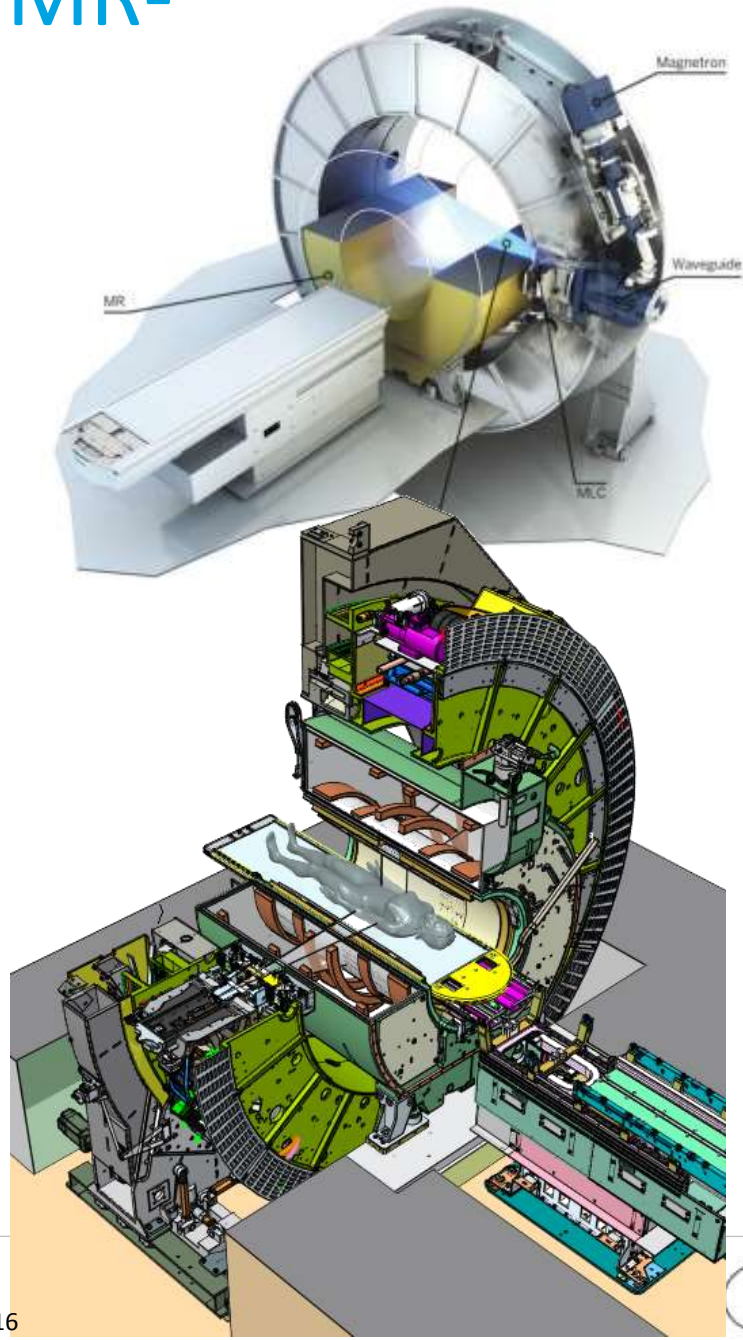
Treat the patient while simultaneously imaging with a ‘conventional’ 1.5T diagnostic MRI

How

1. Mount the Linac on a rotatable gantry around the MRI magnet
   The radiation isocenter is at the centre of the MRI imaging volume
2. Modify the Linac to make it compatible with the MR environment
3. Modify the MRI system

   Minimize material in the beam path

   Minimize magnetic field at the Linac



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Atlantic delivers high quality volumetric images

Example volunteer images

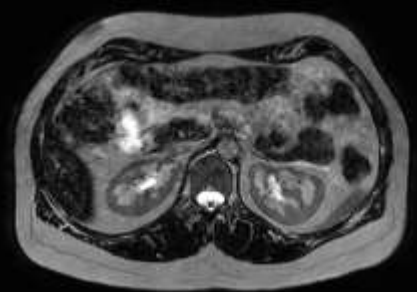
T2w 3D TSE
0.7 x 0.7 x 1 mm^3
Imaging time 2 min 12s

T2w 3D TSE
Voxel size 1.5 x 1.5 x 2 mm^3
Imaging time 4 min 10 s

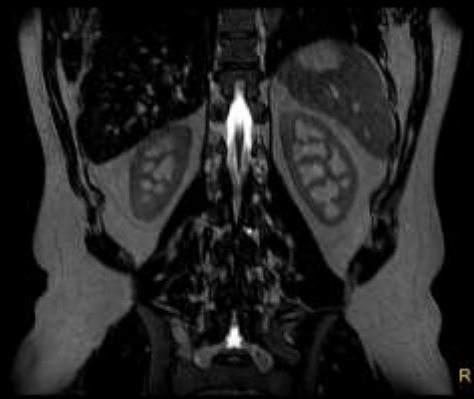
MR-Linac

Diagnostic MRI

Original axial



Reformatted coronal



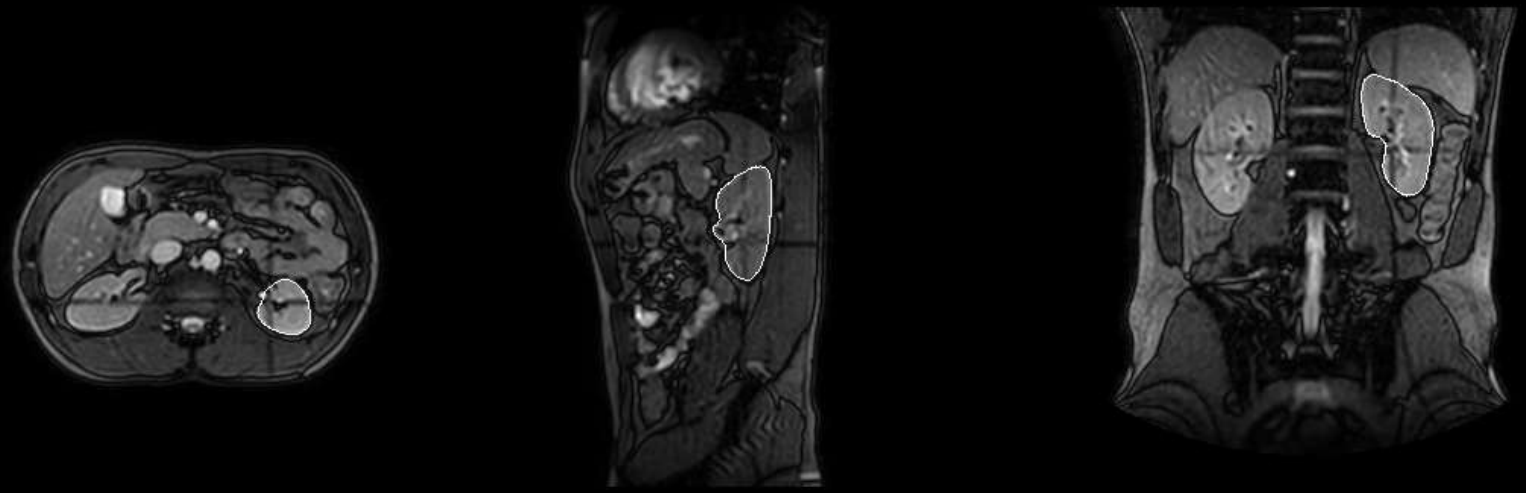
Images courtesy of Philips

MR-Linac is a research programme. It is r

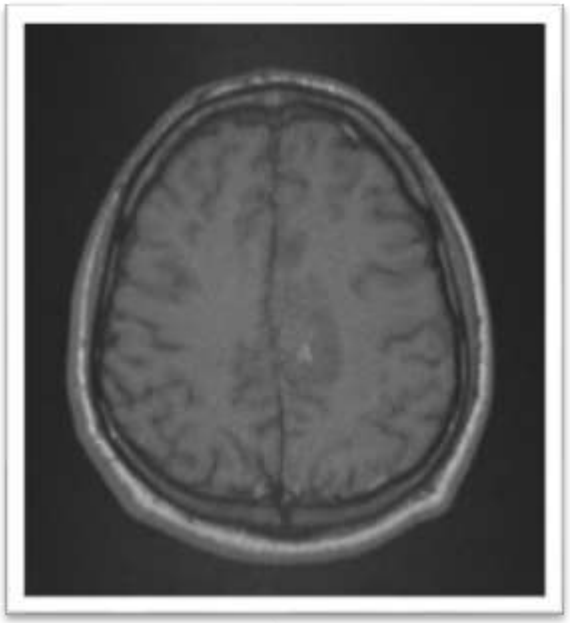
ELEKTA

Atlantic can image and detect the target in real time simultaneous with irradiation

- Localization results for Kidney
- Alternating axial, coronal and sagittal slices
- Acquired and processed in 200 ms



MR-Simulation and Treatment Planning

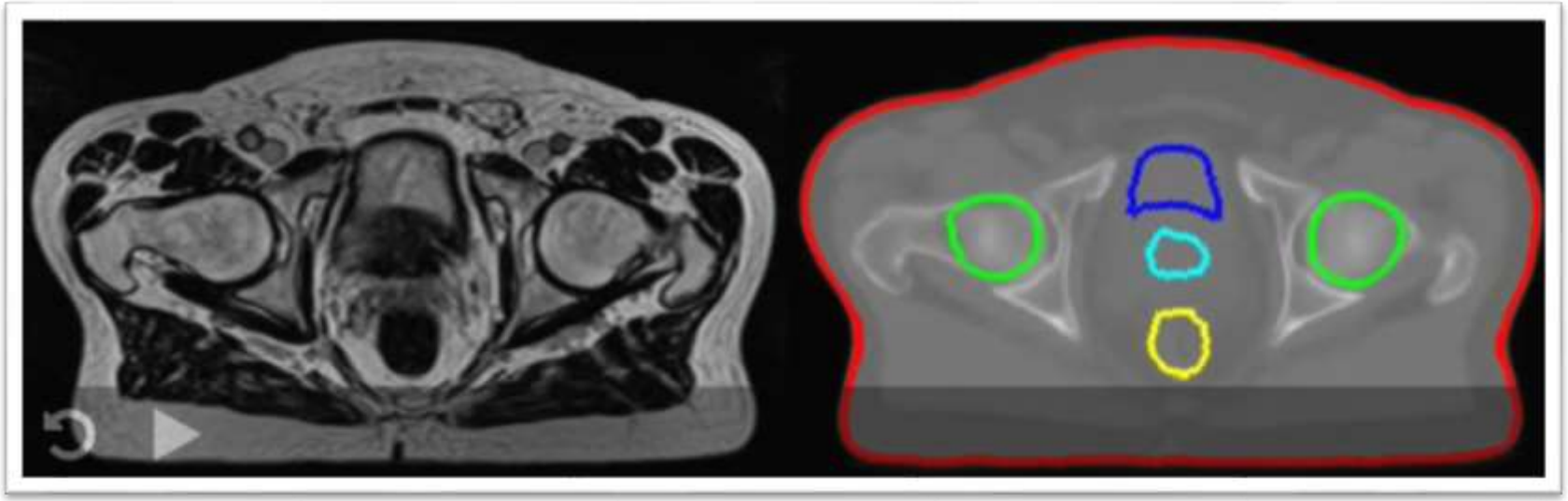


MR segmentation - Lund Univ has developed automatic tools

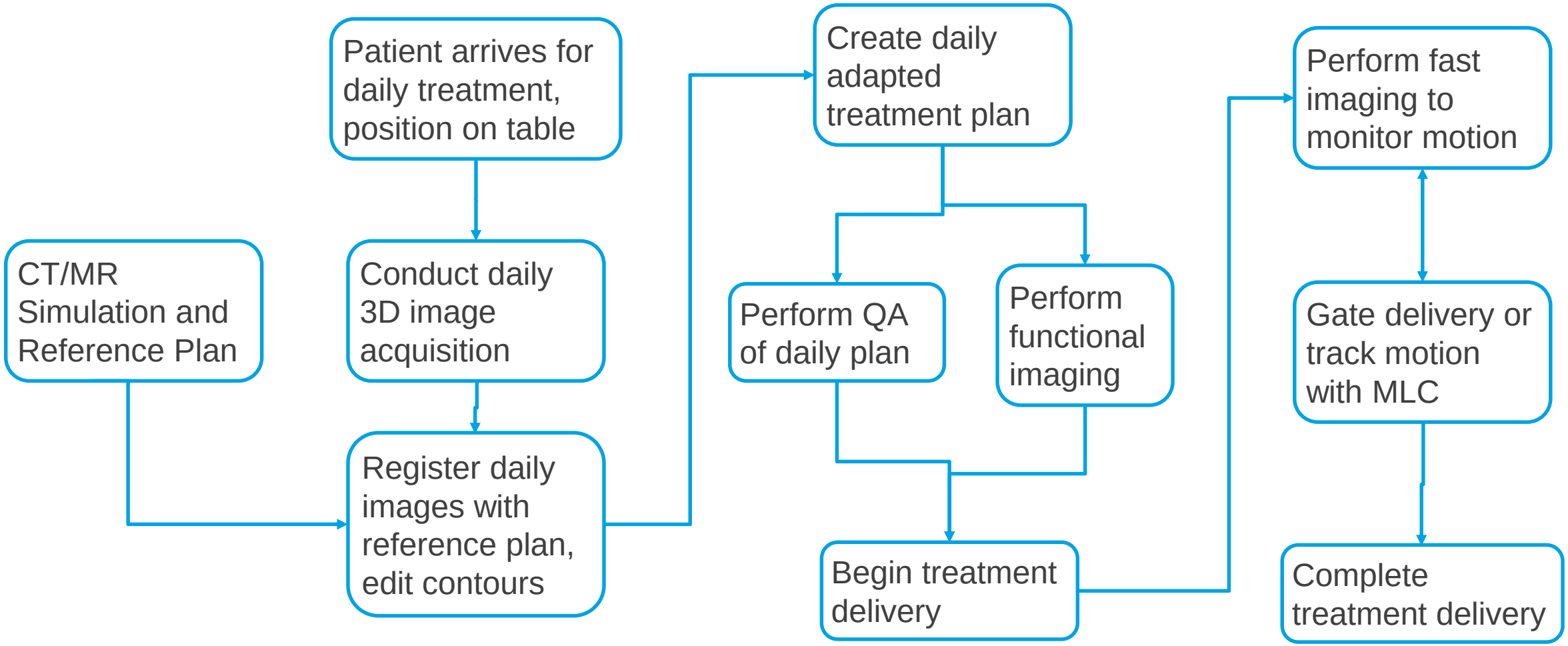
Synthetic CT from MR images

Use for treatment planning

Generate sDRR for image guidance



Clinical Workflow for Daily Adaptive Treatment



Preclinical study of the effect of a magnetic field on cell survival

- Objective: To study whether magnetic fields affect the dose response cells irradiated in culture
- Past work:
  - Cells plated and exposed to magnetic field or sham exposure - demonstrated no change in plating efficiency
  - Cells irradiated to identical dose/fractionation with prototype MR Linac and with conventional linac - demonstrated no change in survival
- Ongoing work:
  - Animals will be irradiated under identical conditions with and without magnetic field to confirm cell results

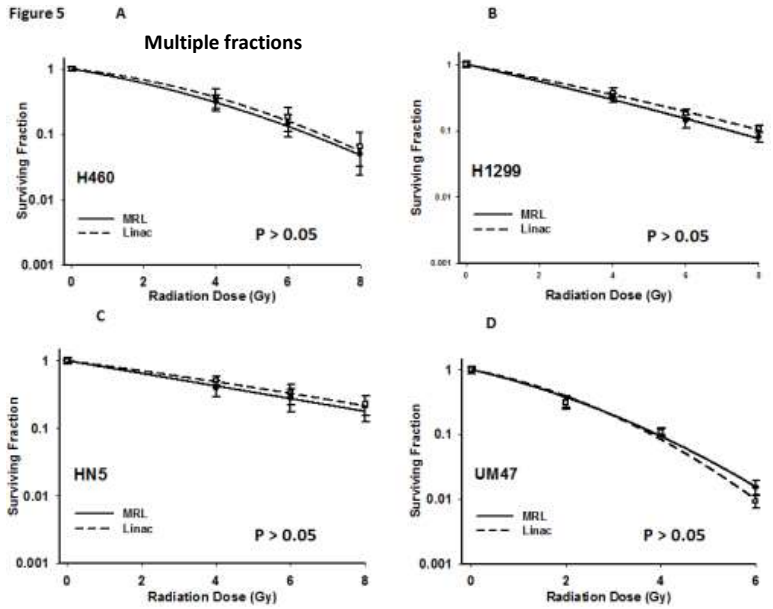
MRL Radiation Biology Study

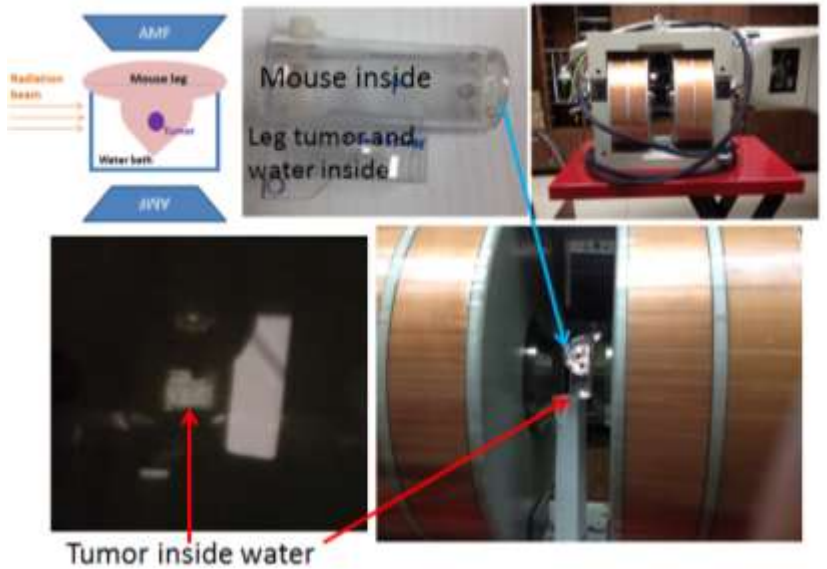
MRI-Linac radiation effect (MRL vs. Linac)

In vitro (Funded by Elekta)

Manuscript submitted

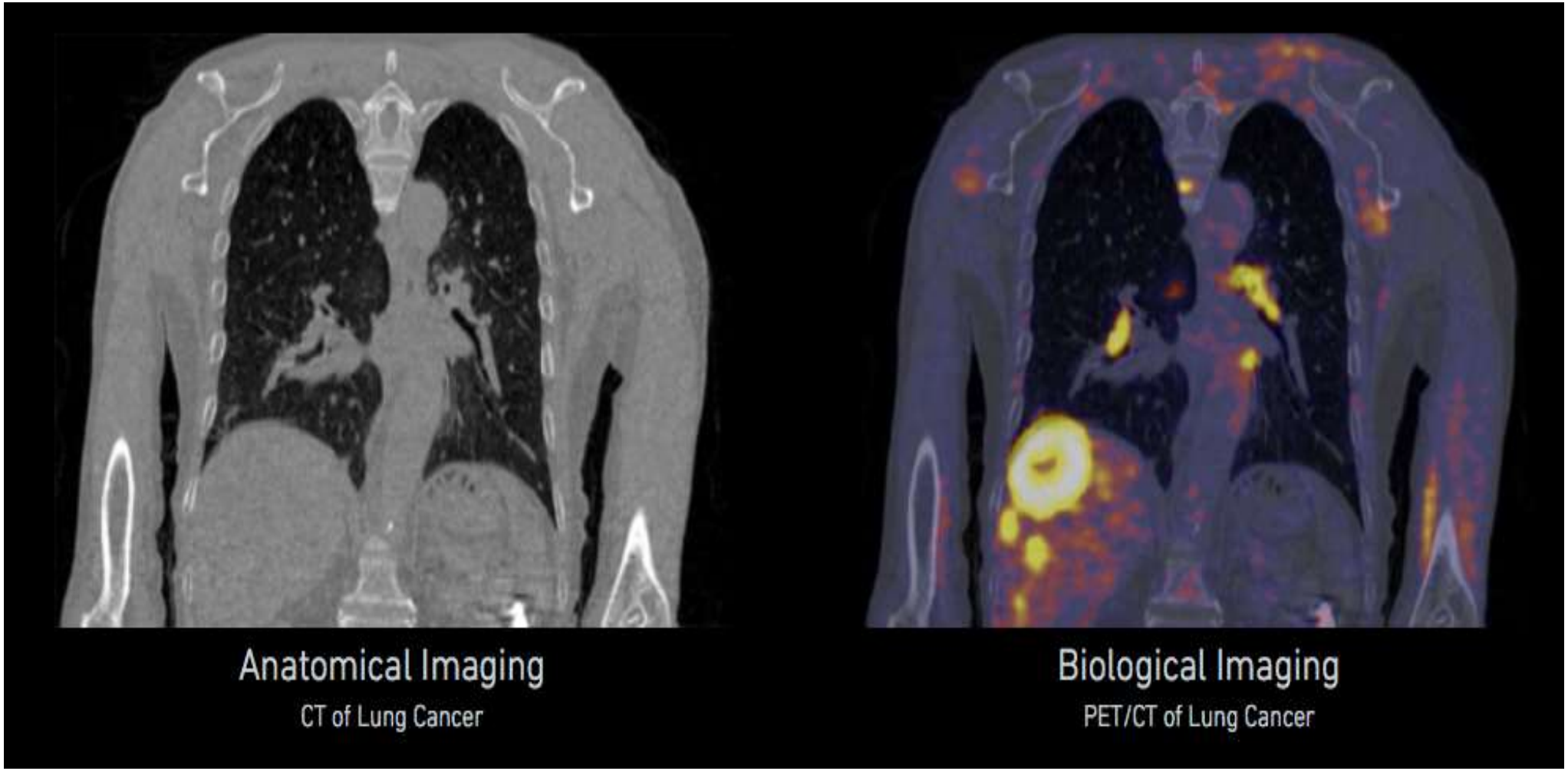
In vivo (Funded by Elekta)



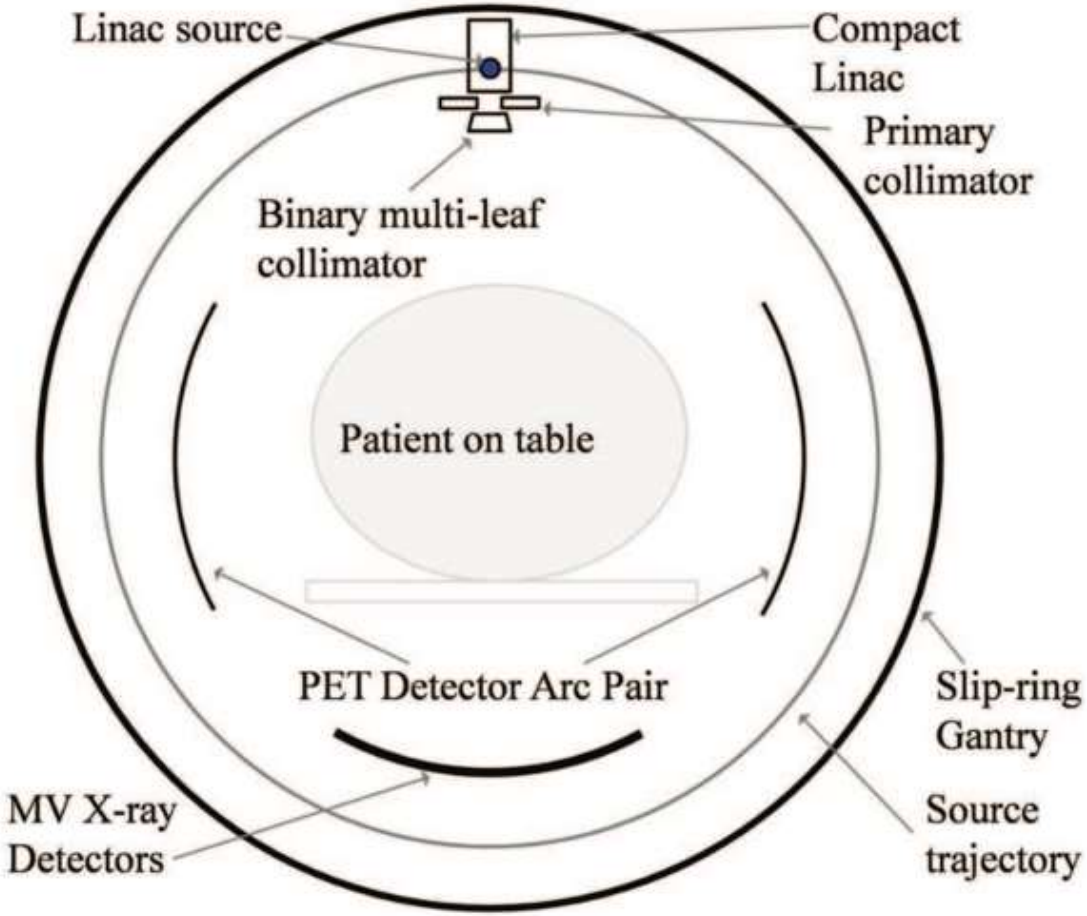


In vivo experiments set up and Xenograft models

Emission-Guided Radiation Therapy



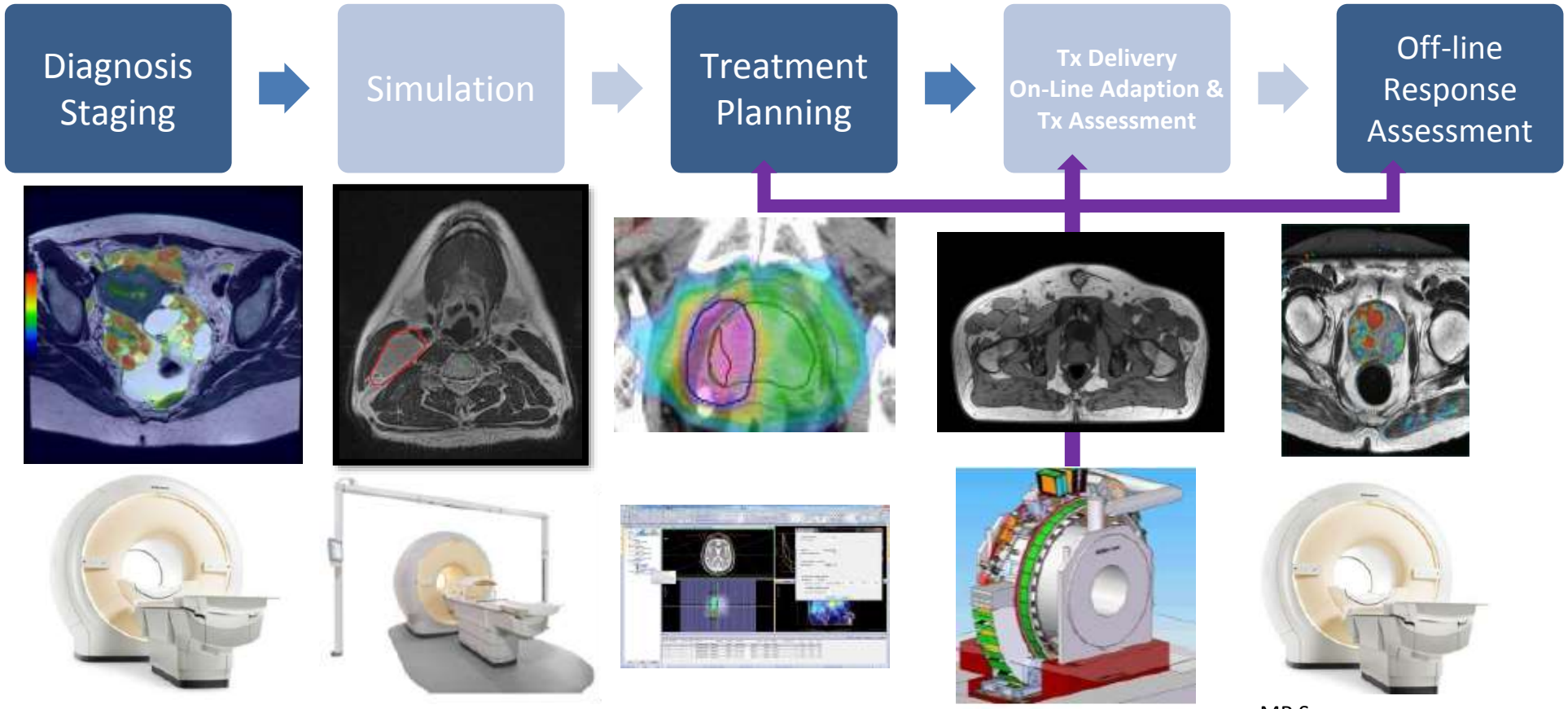
Emission-Guided Radiation Therapy



Courtesy RefleXion Medical

MRI's role is growing in Radiation Oncology

Expansion to Treatment Time imaging



MR Images courtesy of Philips

Thank you for your attention!

Thanks to:
Hannah Lee, Yvonne Roed, Diane Choi, Ryan Lafratta,
Mitchell Carroll, Mamdooh Alqathami, Jihong Wang