The ViewRay, Inc. Renaissance™

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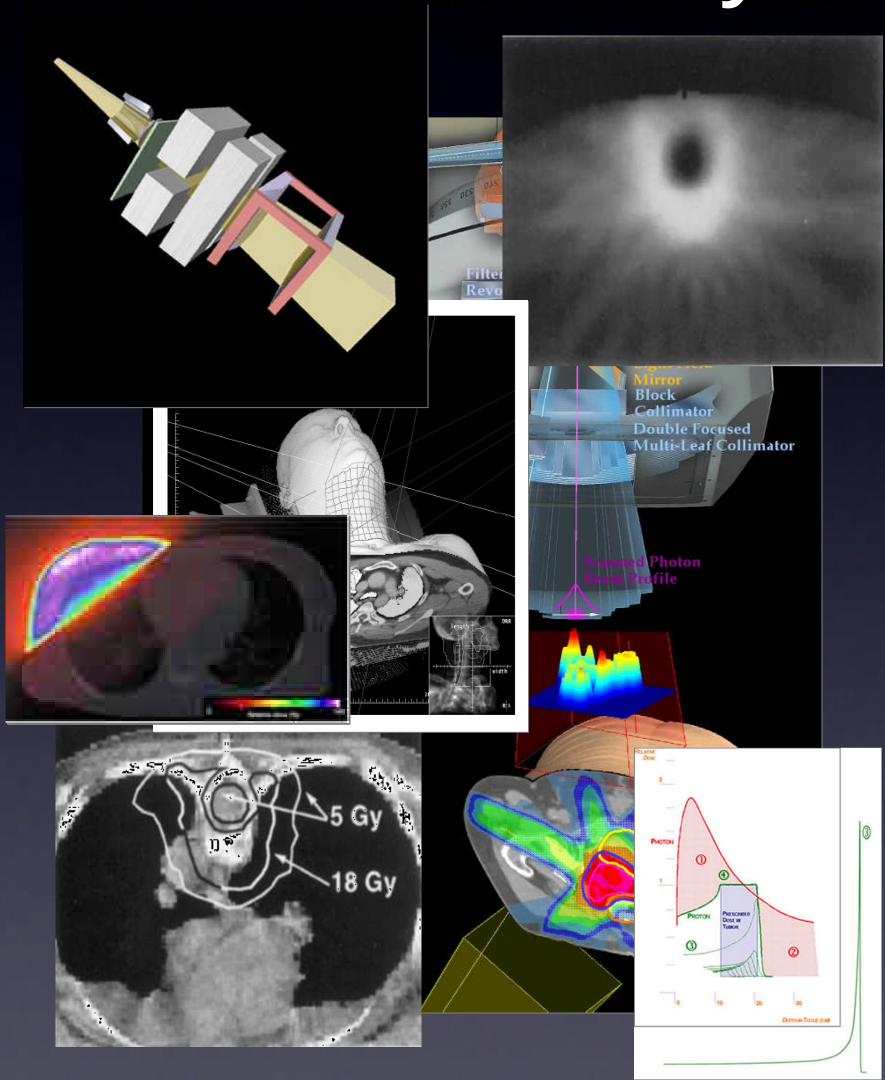
Outline

- The clinical problem
- Technical rationale
- The Renaissance™
- Feasibility Data
- Summary

Great progress in optimizing dose delivery to static objects



Technology Evolution

CT Sim

Convolution

IMRT Optimization

Monte Carlo

IMPT

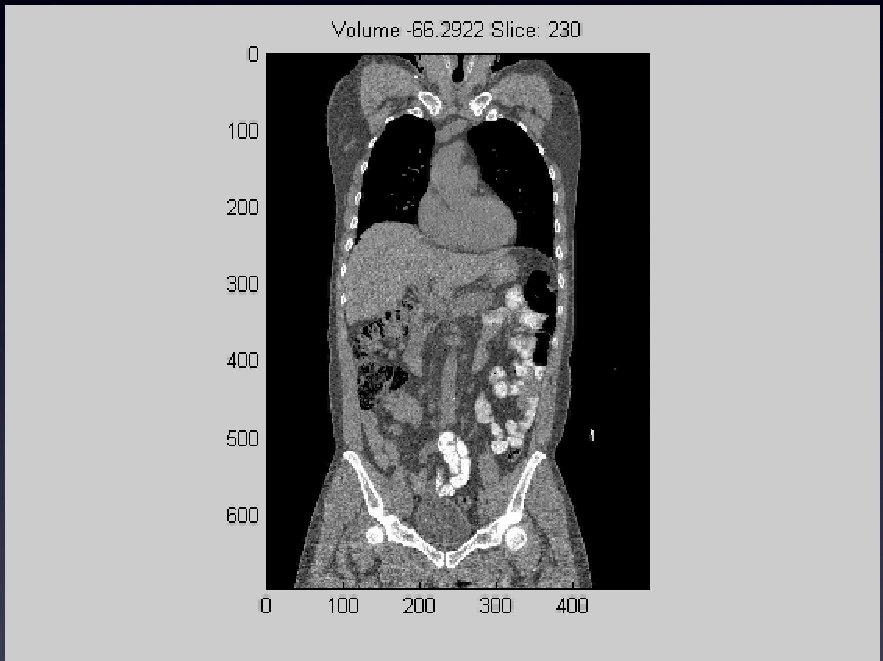
etc.

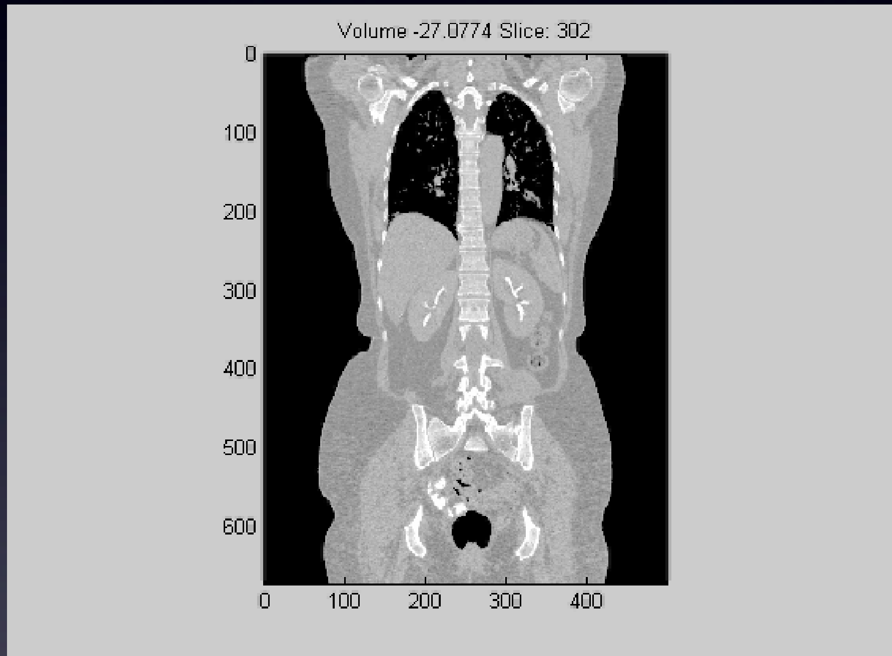
We have perfected the optimization of dose to static objects

However…

The Clinical Challenge

- Accurately delivery ionizing radiation to the real dynamic patient





4D CT Data from Low *et al. Med. Phys.* 30(6) (2003) 1254-1263.

Inter-fraction motion studies –few patients, large motions

Organ/Tumor	# of Studies	# of Patients	Motion Range [mm]
		Inter-fraction Motion	
Bladder	7	11-30	27 A.P. 4% vol. loss per week 40-80% vol. change
Gynecological Tumors	1	29	<7 Sup. <4 Pos.
Prostate	18	6-55	5.3-20.0 A.P. 1.7-9.9 S.I. 2.0-8.8 Lat.
Rectum	5	11-30	17-76 Dia. Change 6%/week vol. decrease
Seminal Vesicles	5	6-50	1.5-22.0 A.P. 0.35-14.0 S.I. 0.3-5.5 Lat.

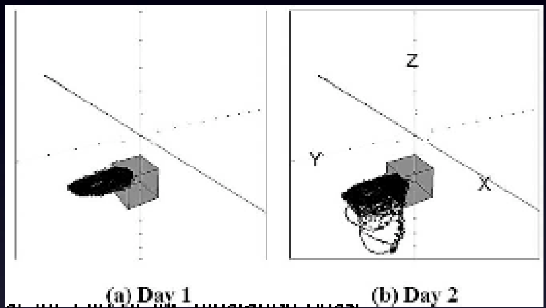
Jones and Langen Int. J. Rad. Oncol. Biol. Phys., Vol. 50, No. 1, pp. 265-278, 2001

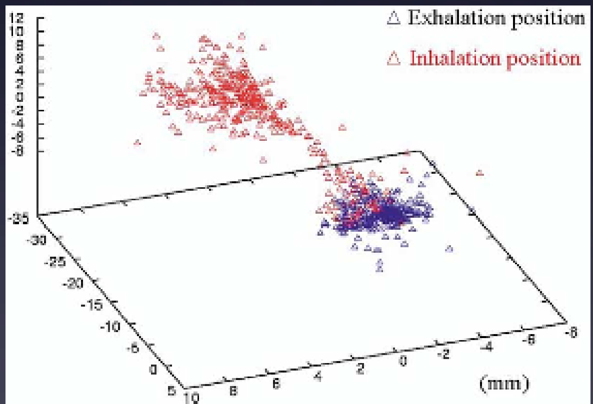
Intra-fraction motion studies –few patients large motions

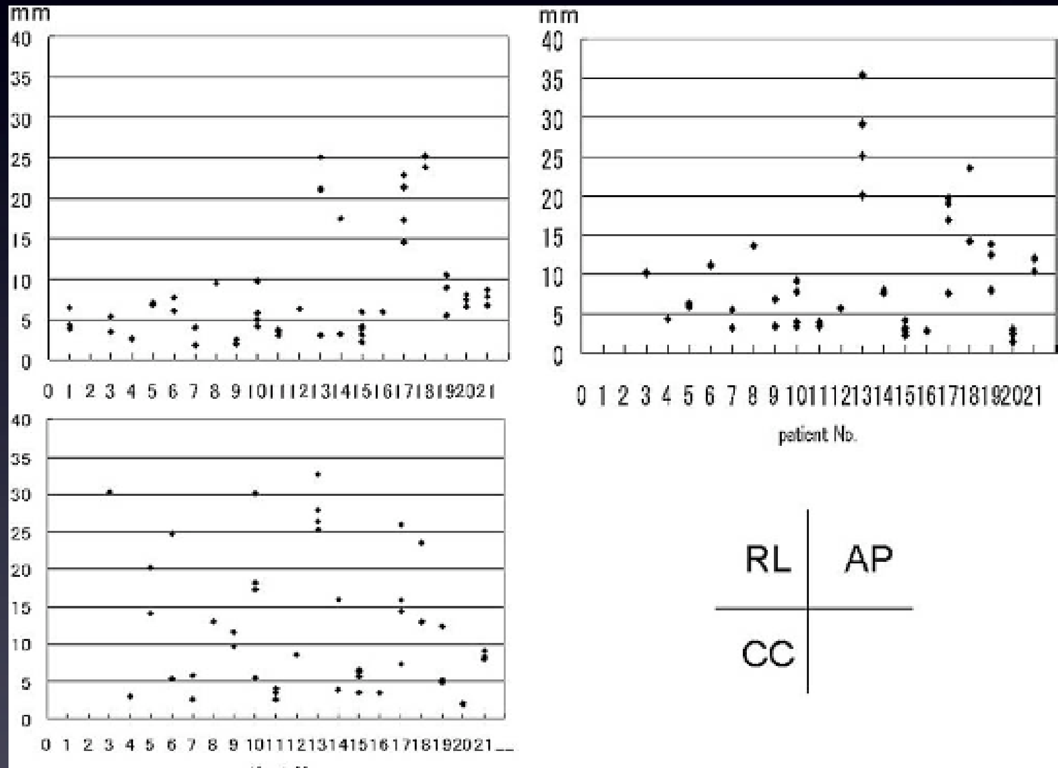
Organ/Tumor	# of Studies	# of Patients	Motion Range [mm]
		Intra-fraction Motion	
Diaphragm	6	5-30	5-40 Normal Breathing 25-80 Deep Breathing
Kidneys	6	8-100	2-40 Normal Breathing 4-86 Deep Breathing
Liver	5	9-50	7-38 Normal Breathing 10-103 Deep Breathing
Lung Tumors	2	20	5-22 A.P. 0-16 Lat. 1.3-6.5 S.I.
Pancreas	2	36-50	10-30 Normal Breathing 20-80 Deep Breathing
Prostate	3	55	No Motion in EPID 0-15 Transient motion with Ciné MRI

Jones and Langen Int. J. Rad. Oncol. Biol. Phys., Vol. 50, No. 1, pp. 265-278, 2001

Lung Tumor Inter- and Intra-Fraction Motion Changes All the Time

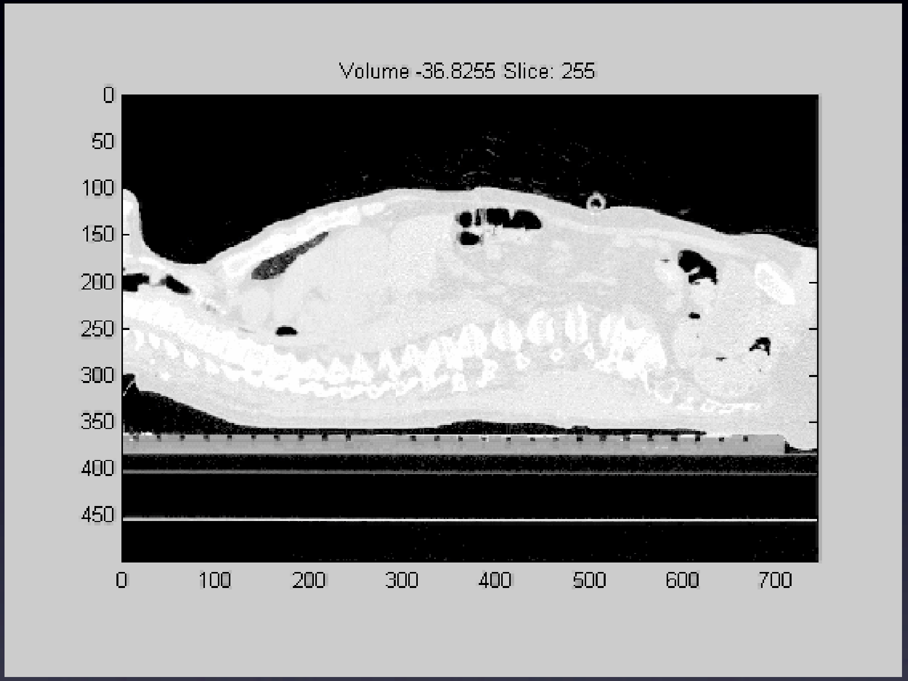






Hiroki Shirato, Keishiro Suzuki, Gregory C. Sharp, Katsuhisa Fujita, Rikiya Onimaru, Masaharu Fujino, Norio Kato, Yasuhiro Osaka, Rumiko Kinoshita, Hiroshi Taguchi et al. Int J Radiat Oncol Biol Phys. 2006 Mar 15;64(4):1229-36.

Real-Time 3D Image-Guidance



Intra-fraction motion occurs continuously -from the base of the tongue to bottom of the pelvis-

real-time imaging is the only comprehensive answer

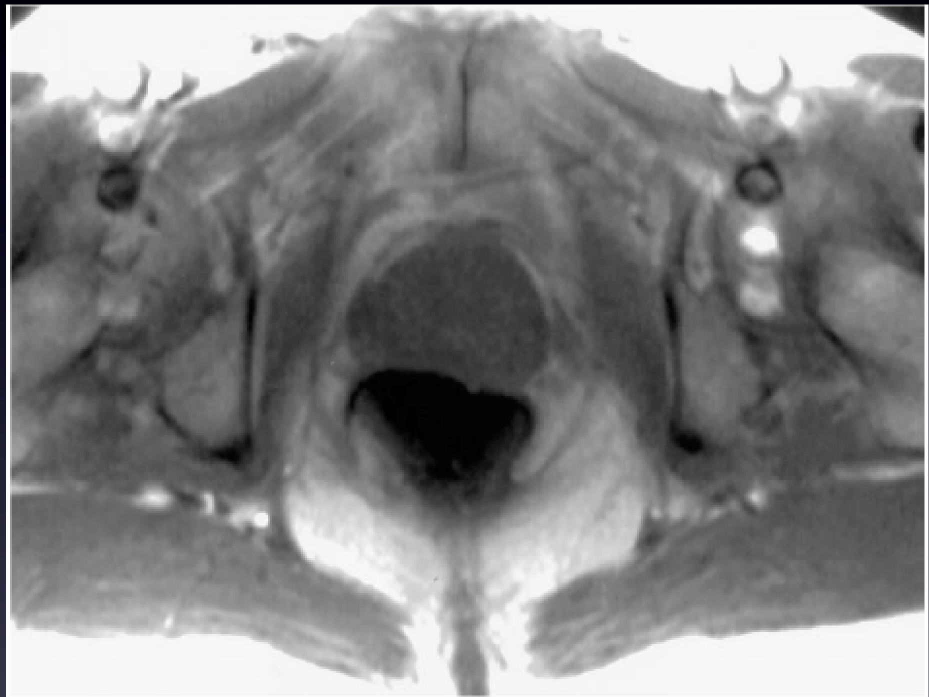
Intra-fraction Organ Motion Example Rectal: Gas Distention

In 1999 Padhani *et al.* scanned 54 prostate cancer patients in axial plane every 10 second for 7 minutes

Padhani *et al.* Int. J. Rad. Oncol. Biol. Phys., Vol. 44(3) pp. 525–533, 1999
Ghilezan *et al.* Int J Radiat Oncol Biol Phys. 2005 Jun 1;62(2):406-17.

Intra-fraction Organ Motion Example Rectal: Gas Distention

> 0.5 cm Prostate Motion for 20-80 seconds observed in 16% of patients



No considerable motion in 1/2

16.7% (9/54) had prostate move > 5mm

median prostate AP displacement was anterior by 4.2

Lasting 10-80s w/ mean of 20s

What would the impact on TCP be?

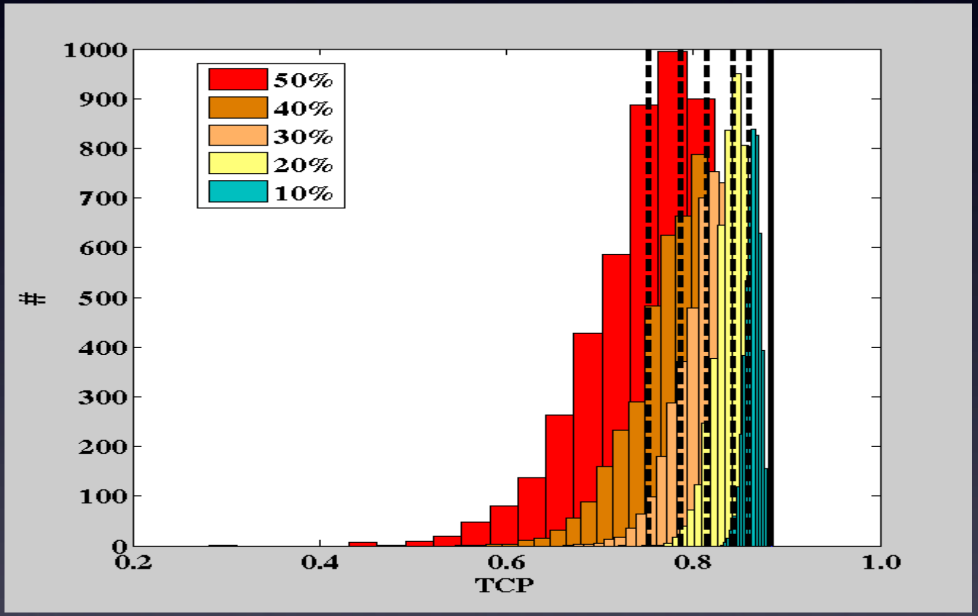
Back-of-the-envelope: Loss of TCP from Prostate Motion

TCP Model of Stavrev et al. (Phys. Med. Biol. **50** (2005) 3053–3061)

- α =0.14 [Gy^{-1}]
- β =0.04 [Gy^{-2}]
- λ =0.12 [$days^{-1}$] cell repopulation
- τ =0.576 [days] sub-lethal damage repair time

Valid for different dose/time
Monte Carlo 5K cases
16.4% chance of X% dose error in f_x
X = 10,20,30,40,50%

TCP @ 5yrs



Adaptive Therapy?

Onboard volumetric imaging is here and it allows for

- Currently: Takes snapshots before or after therapy & shifting the patient position
- Preferably: Automated IMRT re-optimization



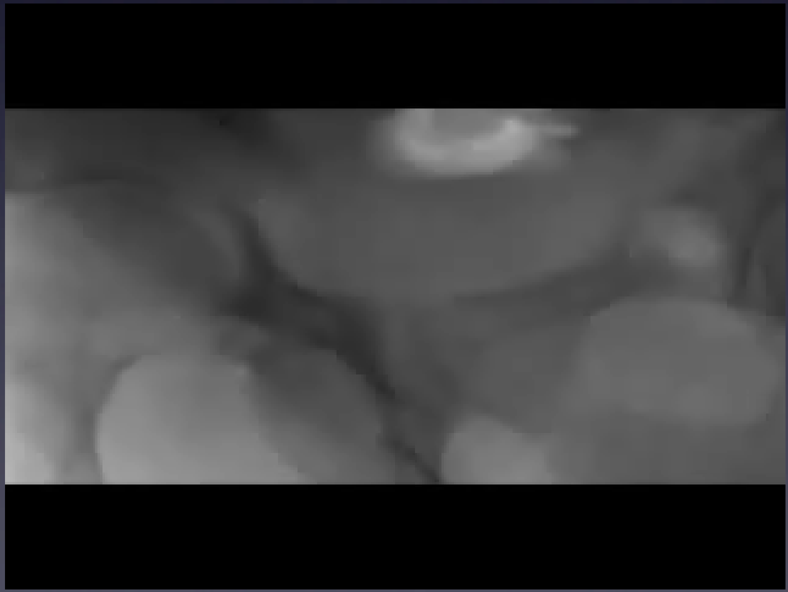

A great advance for radiotherapy, but

Current technology has no ability to account for intra-fraction motions!

Intra-fraction Motion is Observed in During Cone-Beam CT Acquisition

Lung breathing artifacts are clearly evident
Rectal gas artifacts seen in prostate for every 1 of 6 cases
See Smitsmans *et al.* Int J Rad Oncol Biol Phys 63(4):975-984

Looking down the CBCT



Real-Time X-Ray based IGRT?

CT imaging systems

Are currently slow ~1 min. per volume

Provide extra dose to the patient

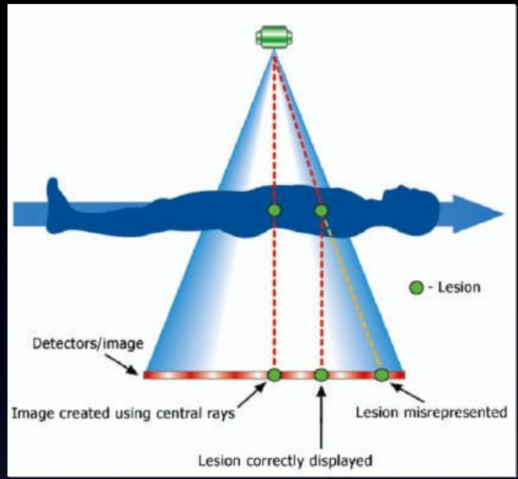
Real-time: 1 CT/sec over 5 min. w/ 0.5 cGy/CT = 150 cGy extra!

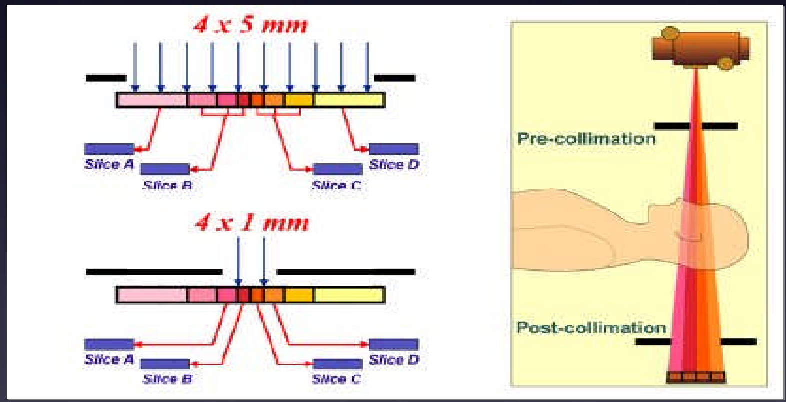
Requires fast moving parts

Cone-beam at 1 RPM

Multi-Slice CT systems

Fast ~0.5 seconds/ image, but small field of view



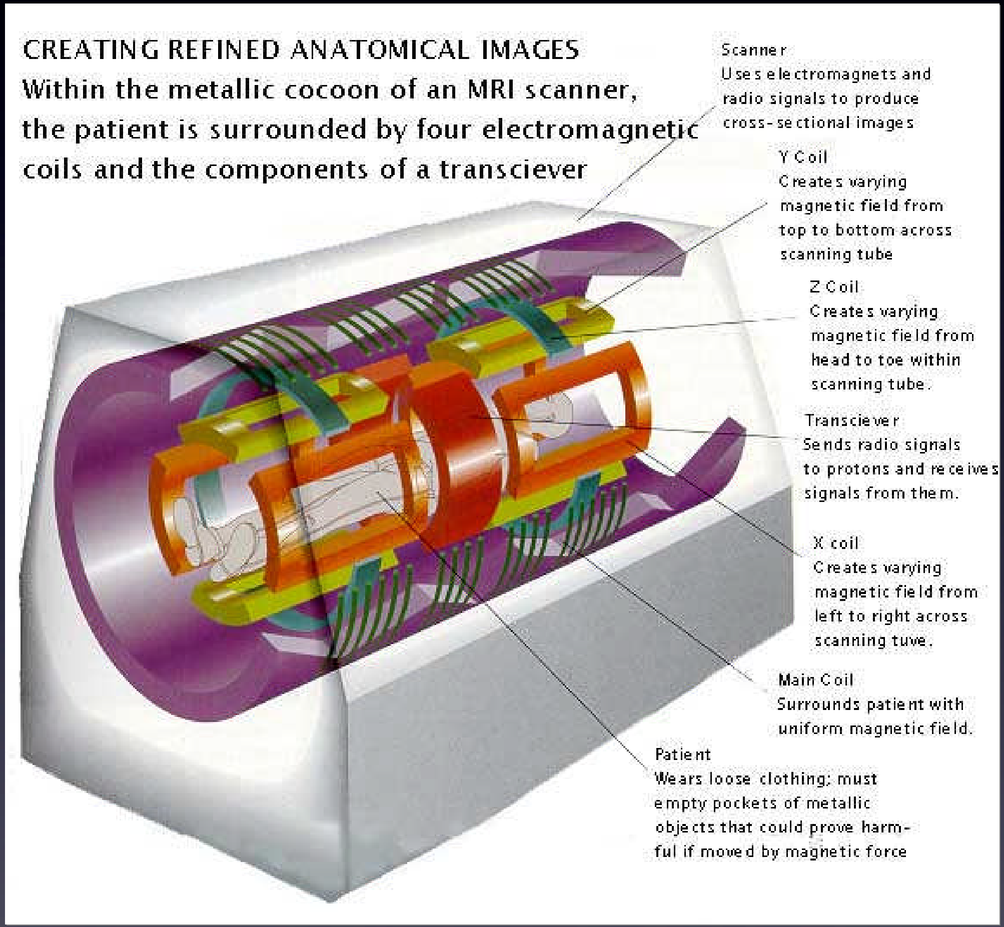


Why Not MRI?

No moving parts!
Used for Simulation
Very, very fast volume acquisition!
Parallel or dynamic MRI

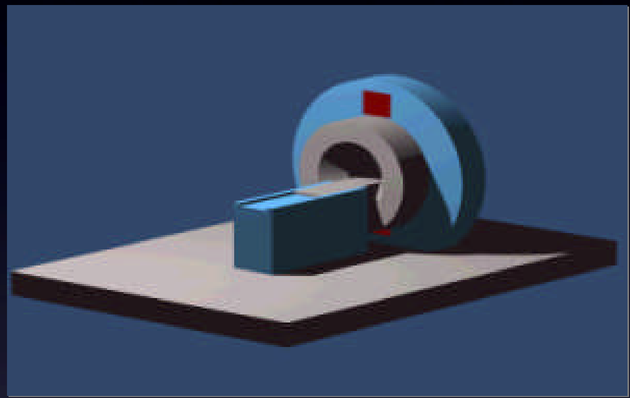
No ionizing radiation dose to the patient!

MRI can image metabolic & physiologic information



MRI + Linac System = Conflict

Mr. Green from Varian Med. Sys. filed patent in 1997
Extensive combinations of linac and MRI
Conceptual System Announced in 2001 by Utrecht University in the Netherlands
6MV Linac +1.5 Tesla MR
Simultaneous imaging and radiotherapy will NOT be possible with their device
Treating through the device ~20 cm of Al
Technically Feasible?
Economically Feasible?

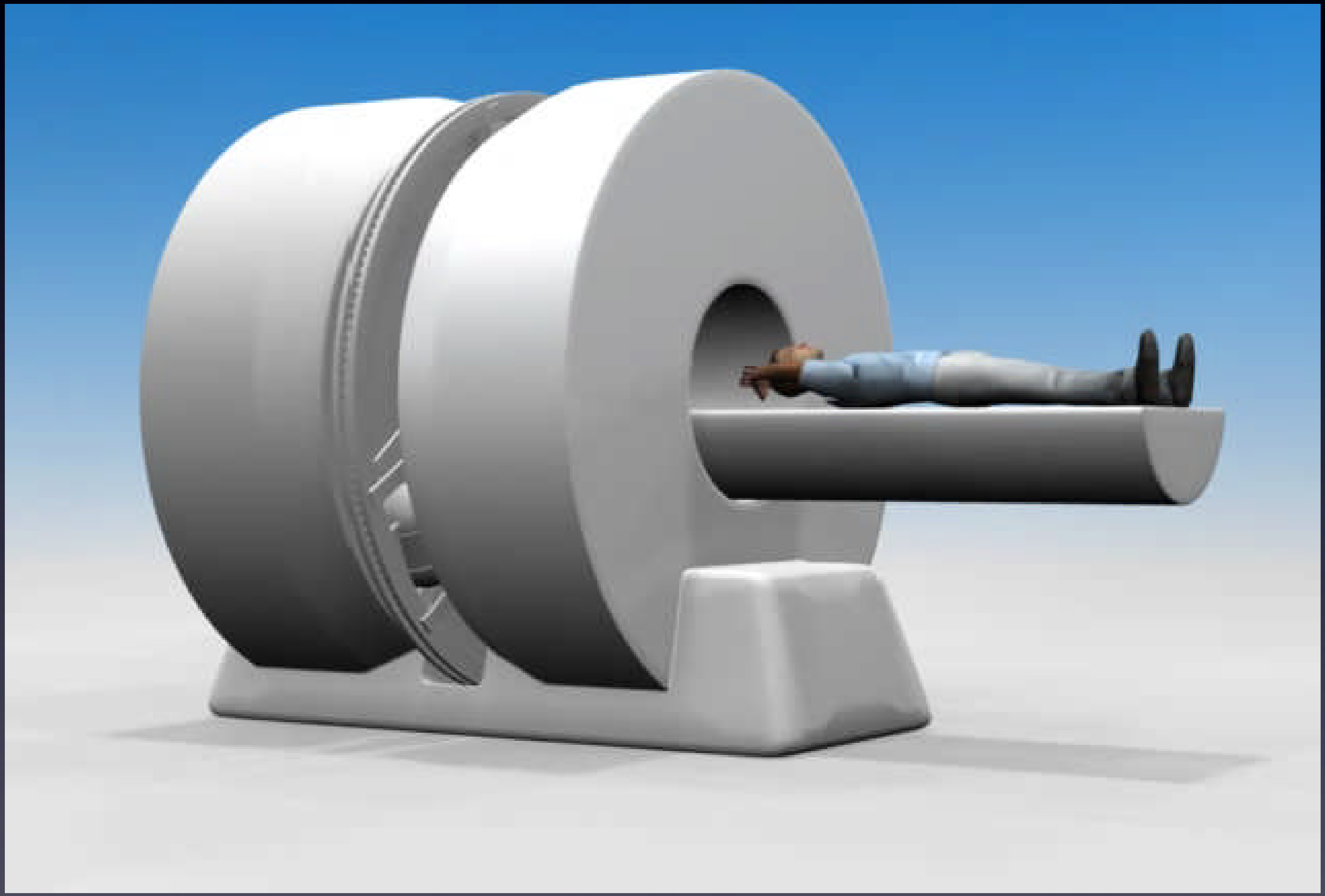


MRI vs. Linac

The magnetic field will shut off the Linac

The Linac RF can destroy delicate circuitry & ruin images

The Renaissance™ System *1000*



Preliminary Specifications

- Superconducting Open 0.3 Telsa MRI w/ 50 cm FOV & 80 cm bore
- 3 x 13 KCi sources with 750 cGy/min. @ 1 m and double focused MLC
  - IMRT or Conformal photon beam therapy
- Supercomputing grid for fast
  - Monte Carlo Simulation including magnetic field
  - Deformable Image Registration
  - IMRT Optimization
  - Parallel MRI Reconstruction

Why Low Field MRI?

Low field MRI is a must for radiation therapy because:

1) High field causes a loss of spatial integrity

Magnetic Susceptibility artifacts due to the patient scale with B_o field strength e.g. 1 cm distortion at 3T => 1 mm distortion at 0.3T

2) High field ruins the dose distribution
see next slide

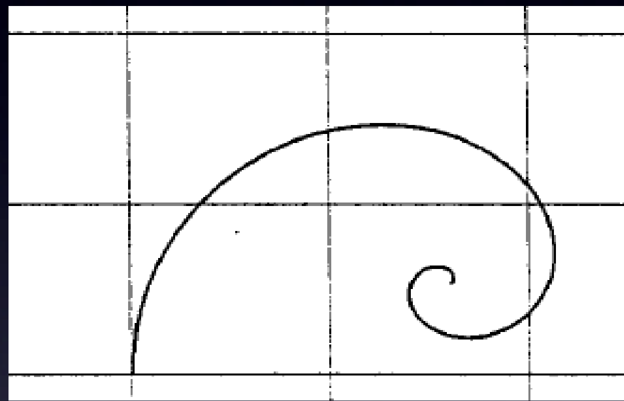
See Petersch et al. Radiotherapy and Oncology 71 (2004) 55–64

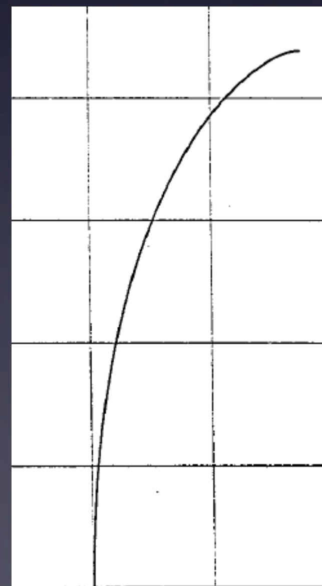
0.3 T -> 3.24 mm max distortion

1.5 T -> 16.2 mm max distortion

Physics of Electron Transport in MRI

CSDA electrons in B field





Lorentz Force causes a force perpendicular to the magnetic field direction

This causes the electrons to gyrate in a circle or spiral if loosing energy

Competition between large-angle electron scattering and the radius of gyration

In a 0.3 Tesla field the radius of gyration for a 1 Mev electron in vacuum is 1.3 cm

In a 1.5 Tesla field the radius of gyration for a 1 Mev electron in vacuum is 3.4 mm

In theory the electron will radiate synchrotron radiation but this is << eV/cm

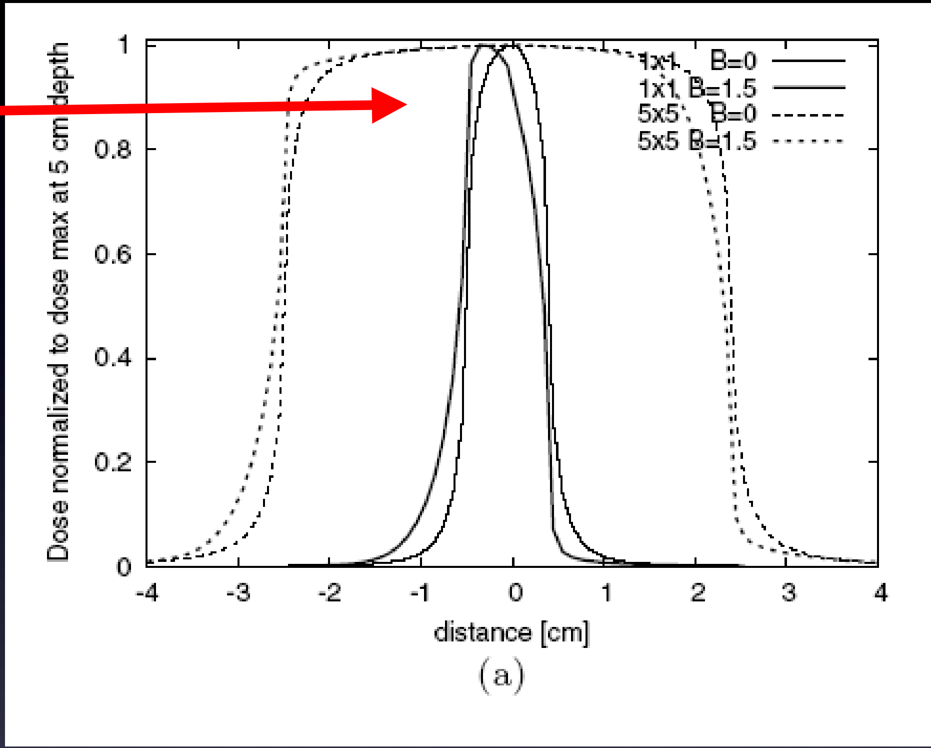
See Beliajew Med. Phys. 20(4) 1993 1171-1179

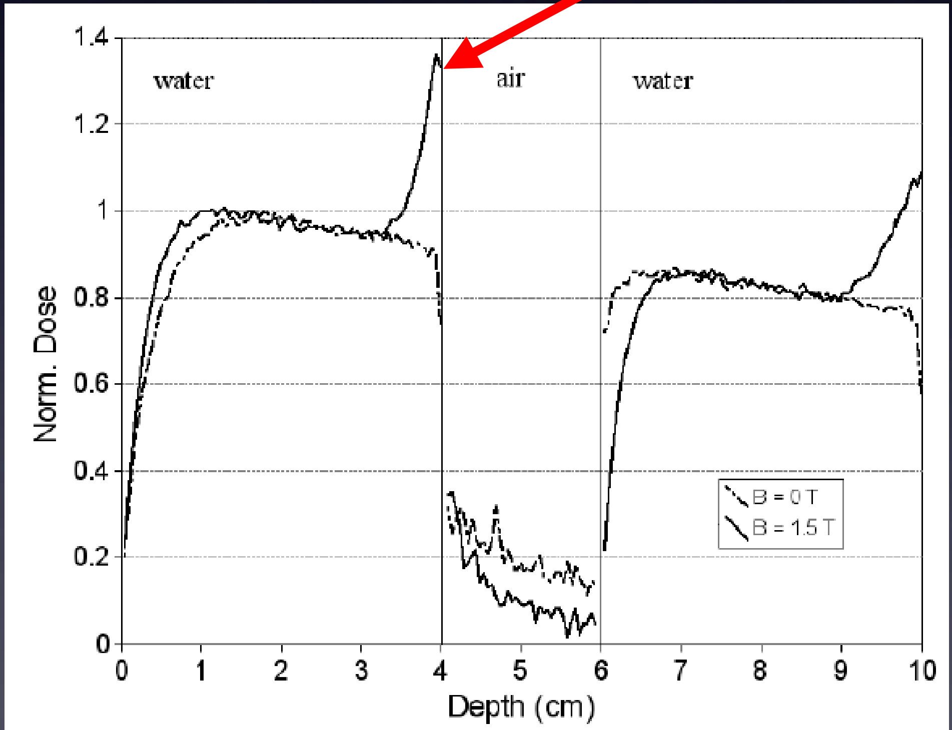
And Jette Med. Phys. 27(8) 2000 1705-1716

Photon Beam Dose Distortion @ 1.5 T

Significant distortion of the dose in water at 1.5 Tesla & 6MV

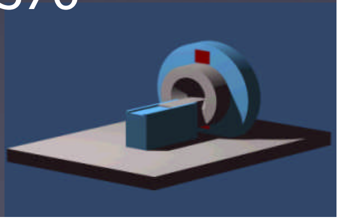
Electron Return Effect



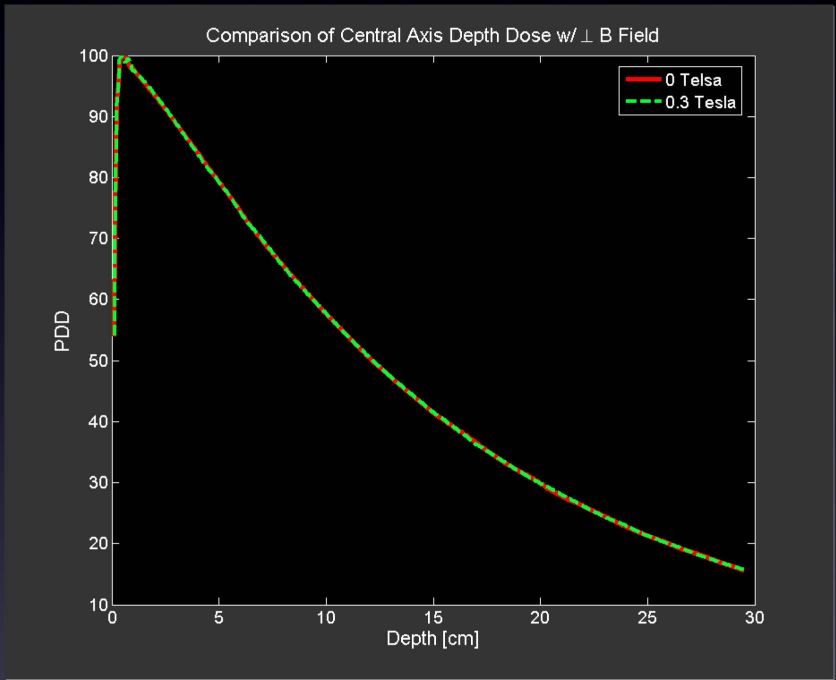


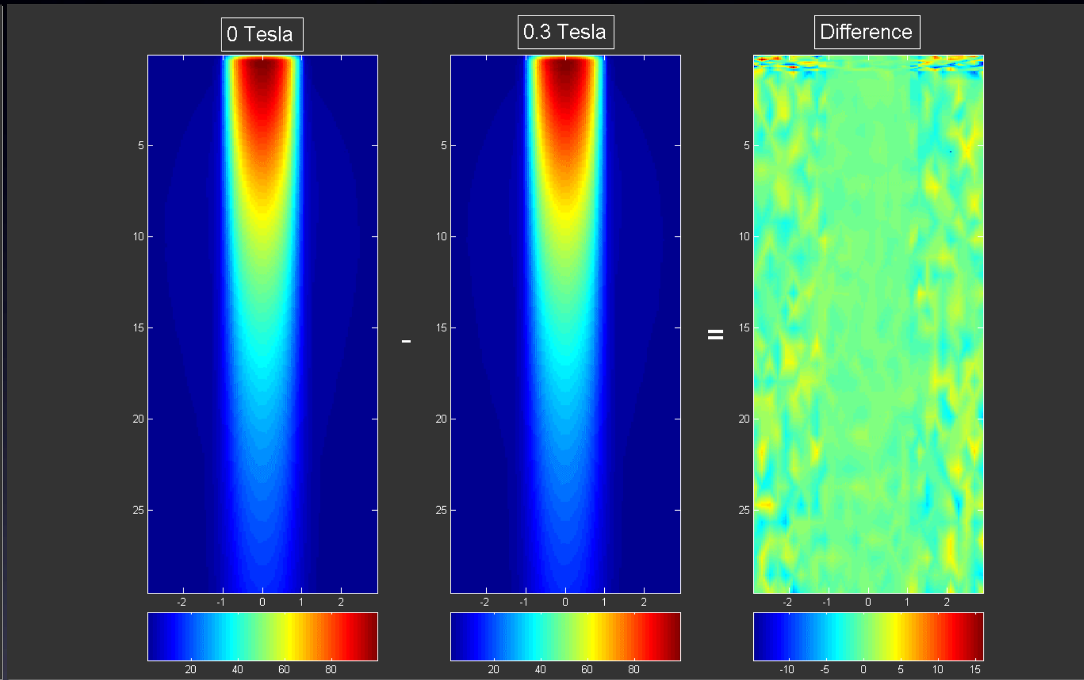
Raaysmaker et al. Phys. Med. Biol. **49** (2004) 4109–4118

Raaijmakers et al. Phys. Med. Biol. **50** (2005) 1363–1376



^{60}Co + Low-Field MRI @ 0.3 Tesla in Tissue (1g/cc)

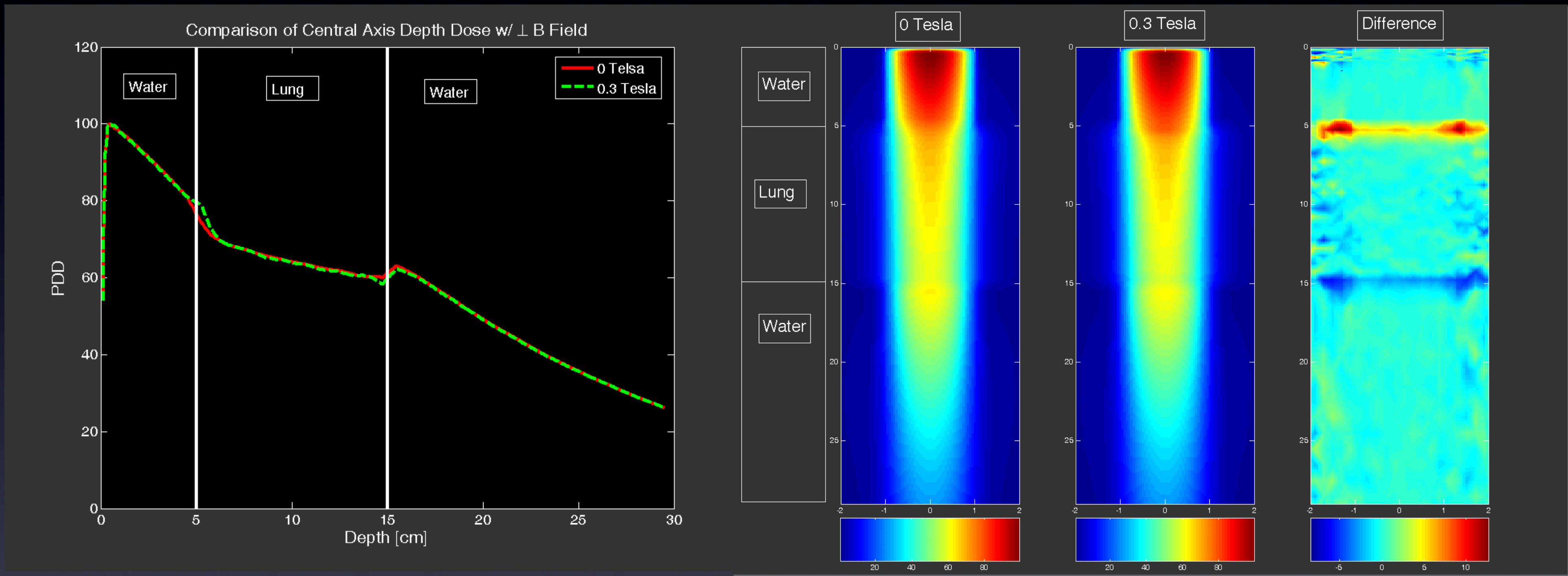




MC shows Essentially no distortion in tissue or water

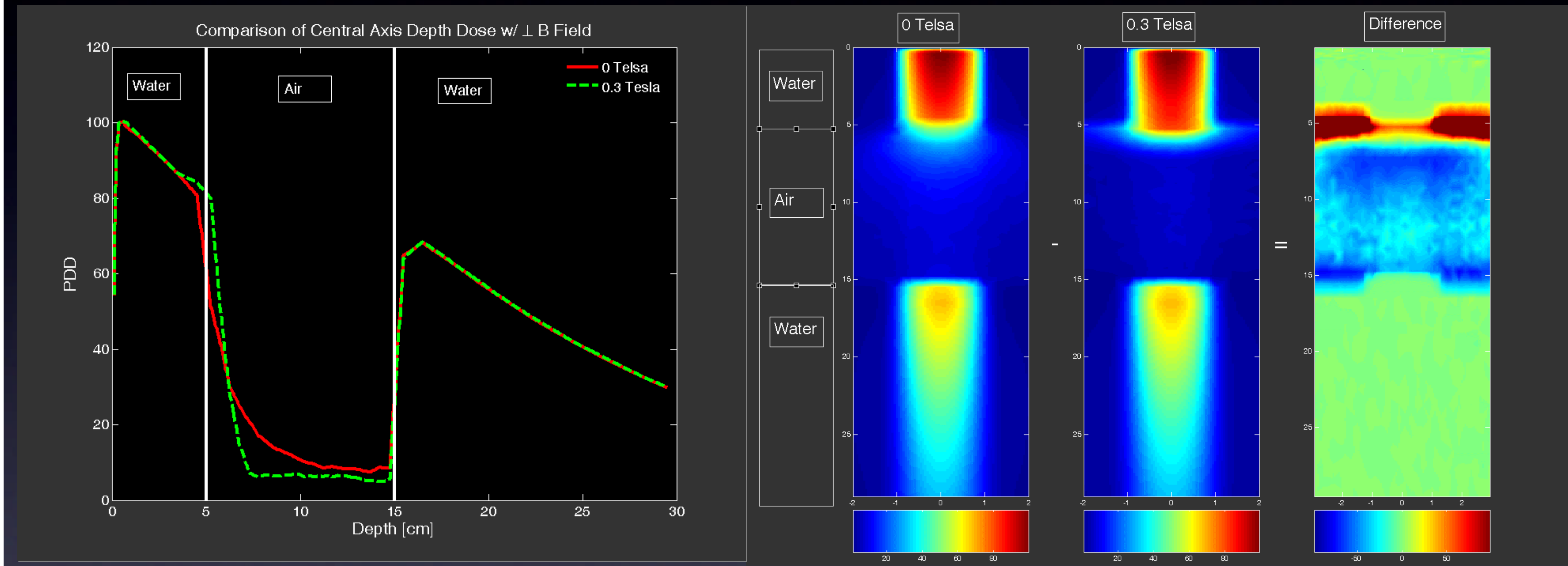
MFP for large angle collisions of secondary electrons much shorter than radius of gyration

^{60}Co + Low-Field MRI @ 0.3 Tesla in Lung (0.2 g/cc)



MC shows very small distortion in lung density material

^{60}Co + Low-Field MRI @ 0.3 Tesla in Air (0.002 g/cc)



MC shows sizable distortion only in air cavities only

hot spots at interface are greatly diminished

MRI Improves ^{60}Co IMRT Electron Contamination is Swept Away

MRI Sweeps Away the Contamination Electrons

Even a low-field Open MRI will provide enough field strength to sweep contamination electrons

In a 0.3 Tesla field the radius of curvature for a 1 Mev electron in vacuum is 1.3 cm

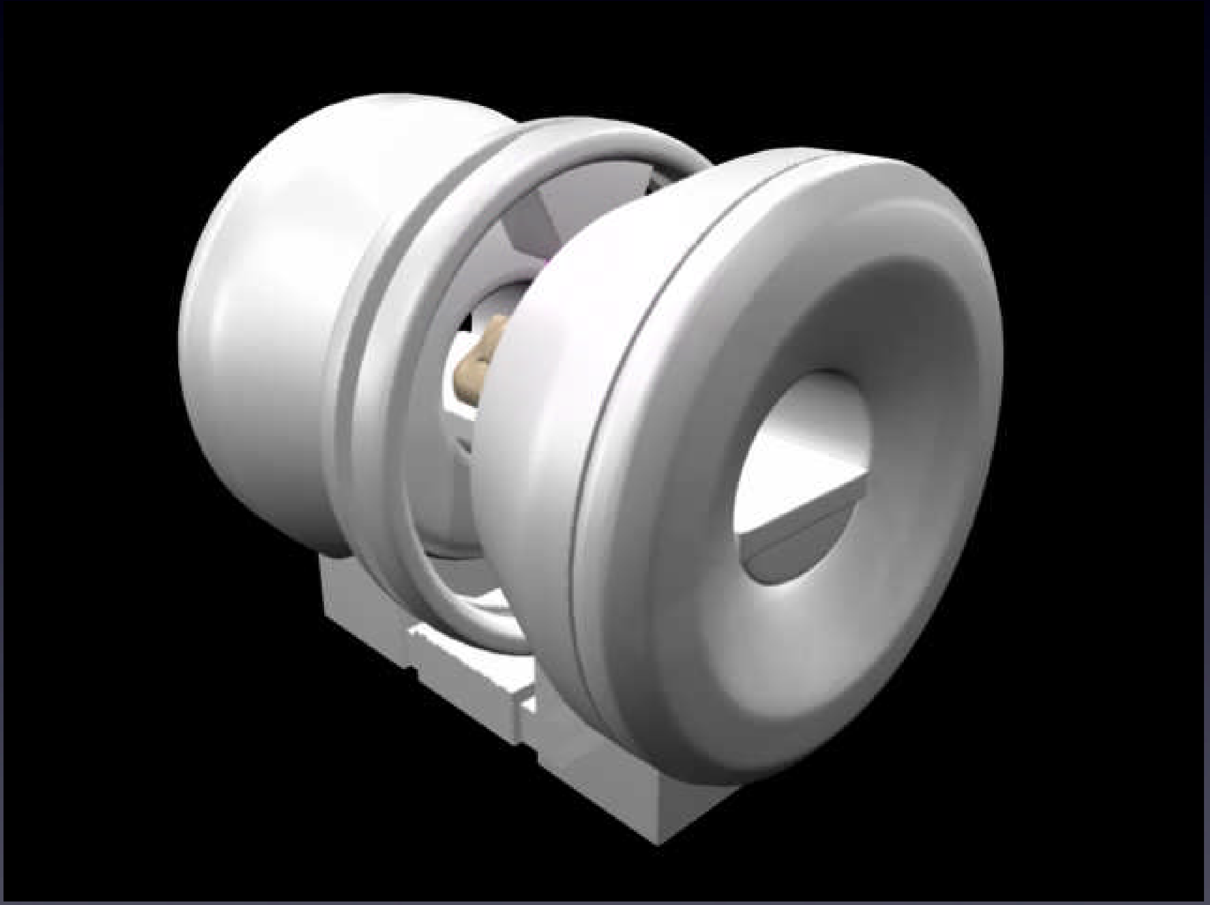
Contamination electrons cannot reach the patient: lower skin dose to patient

Can be modeled by Monte Carlo Simulation

See paper for measurements of sweeping effect:
Jursinic and Mackie Phys. Med. Biol. 41 (1996) 1499–1509.

Elimination of Contamination Electrons

Electrons are shown in blue/white
Photons are shown in pink



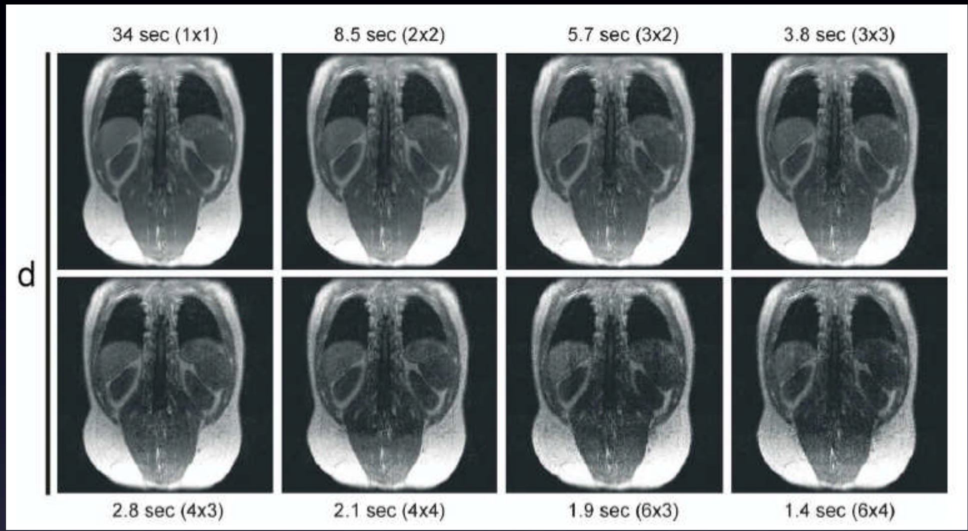
How to Make MRI Fast @ Low Field:Parallel MRI (pMRI)

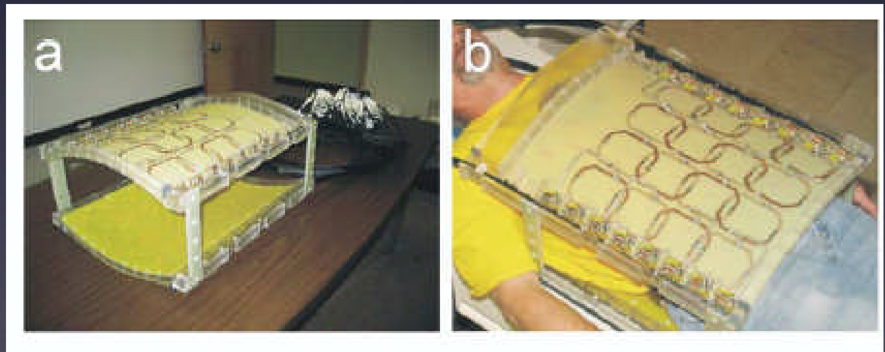
Current MRI scanners already operate at the limits of potential imaging speed based on rapidly switched gradient systems (for safety concerns).

Huge advances from pMRI

– Commercially, up to 32 independent receiver channels available which theoretically allows order-of-magnitude increased image acquisition speed

Sodickson *et al. Acad Radiol. 2005 May;12(5):626-35*.



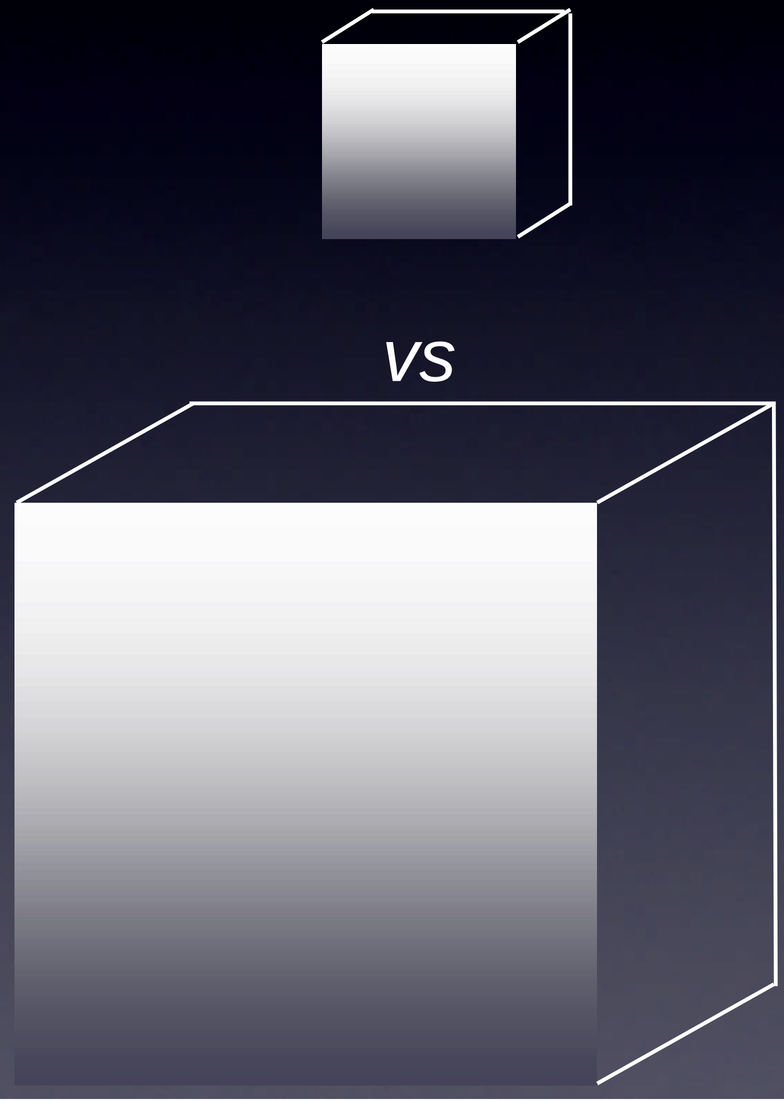


What About Signal?

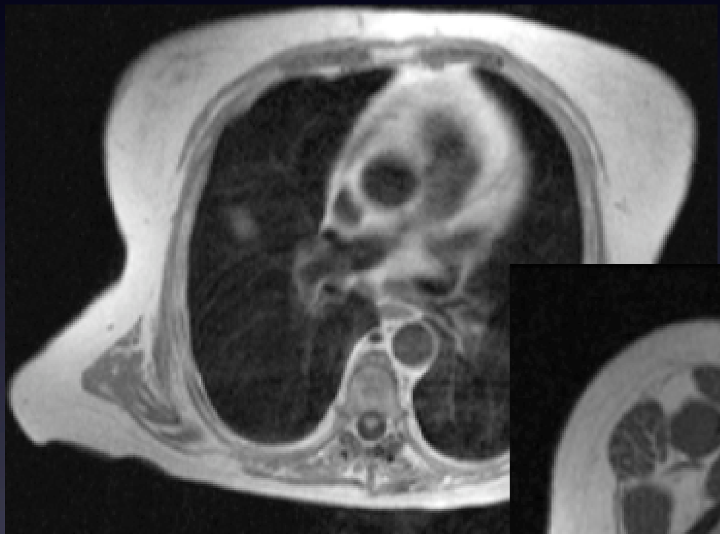
Low field MRI is a must for radiation therapy

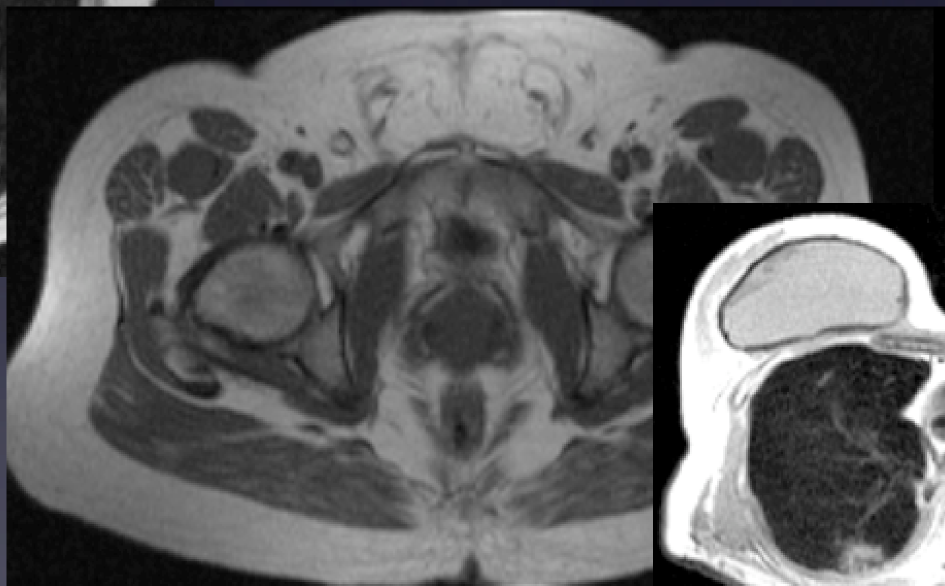
1.5T => 0.3T
Factor of 5 loss of signal

But,
1mm voxel => 3 mm voxel
gives 27 times more signal
still 5.4 times more



Low Field MRI for Simulation & Planning





Examples of 0.2 T Open MRI Simulation Data of Lung & Prostate Cancer atients

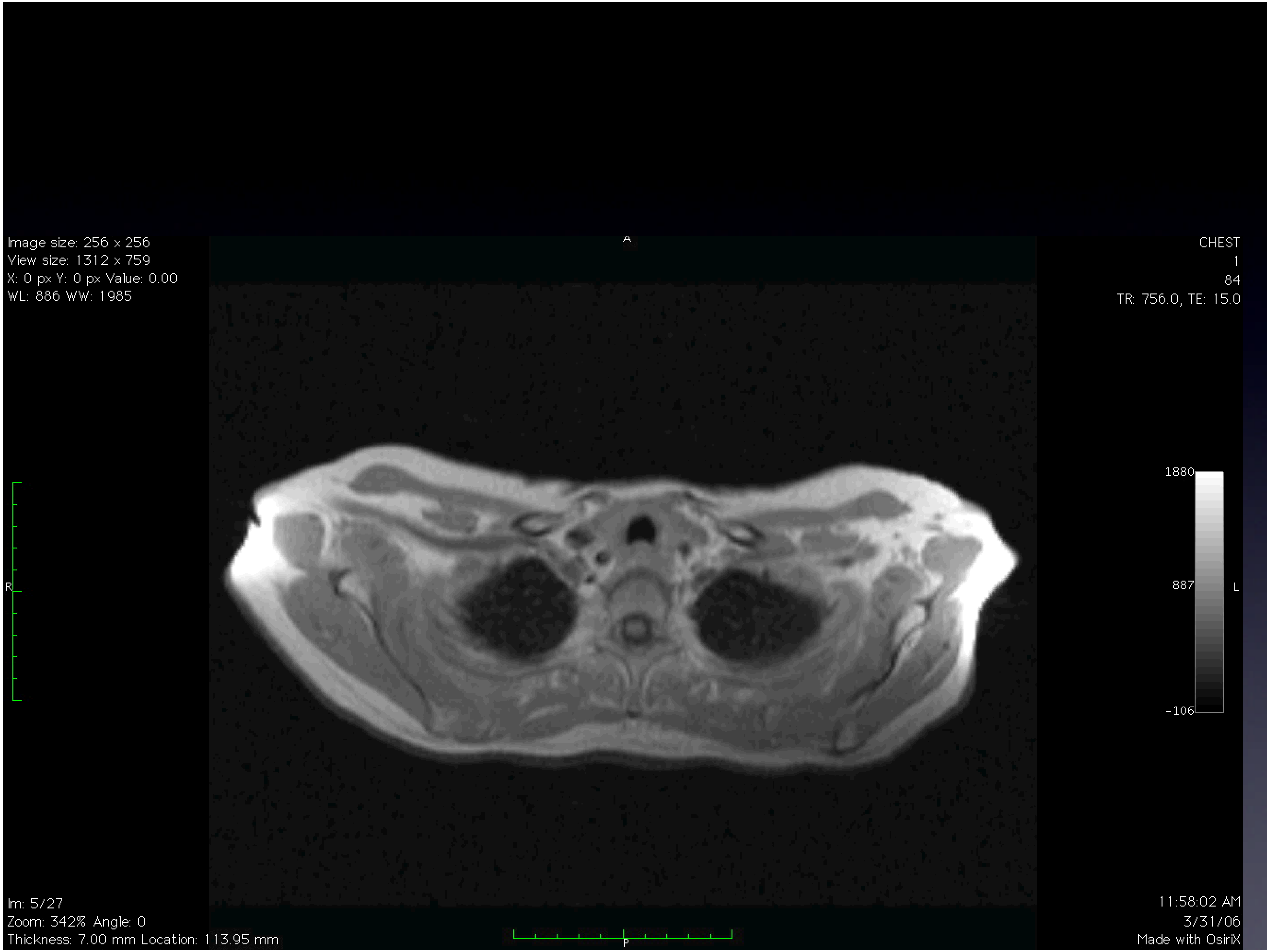


Image size: 256 x 256
View size: 1312 x 759
X: 0 px Y: 0 px Value: 0.00
WL: 886 WW: 1985
A
CHEST
1
84
TR: 756.0, TE: 15.0
R
L
1880
887
-106
P
Im: 5/27
Zoom: 342% Angle: 0
Thickness: 7.00 mm Location: 113.95 mm
11:58:02 AM
3/31/06
Made with OsiriX

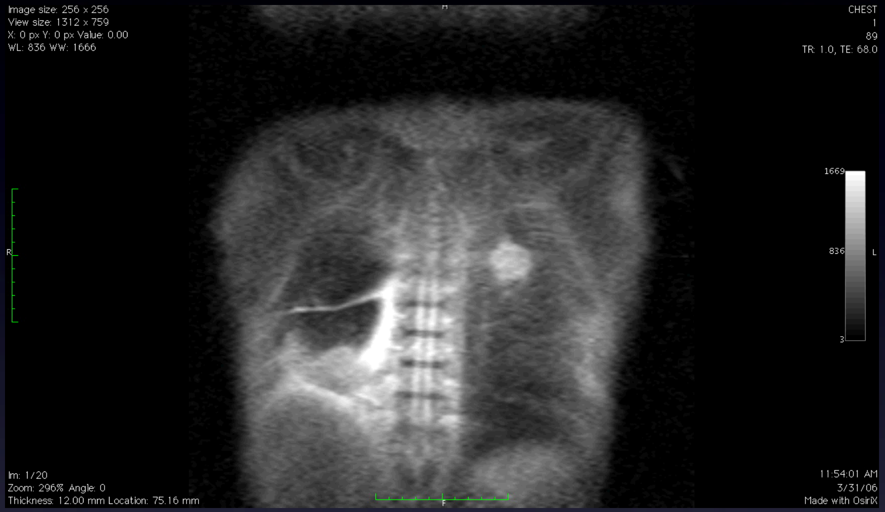
Real-time MRI: Lung

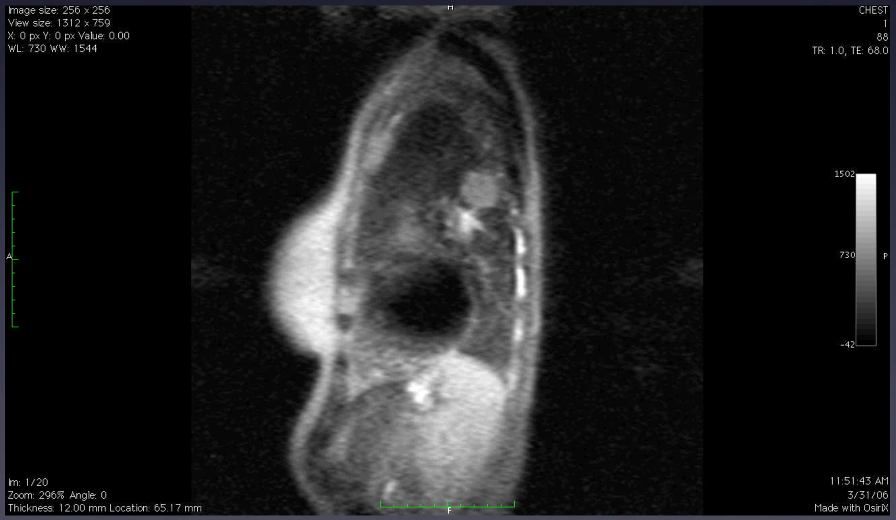
Coronal & Sagittal 2D MRI taken every 0.5 seconds on an existing 0.2 T open MRI

Benefits:

Capture 4D target every day

Gate therapy on motion of soft tissues





Real-time MRI

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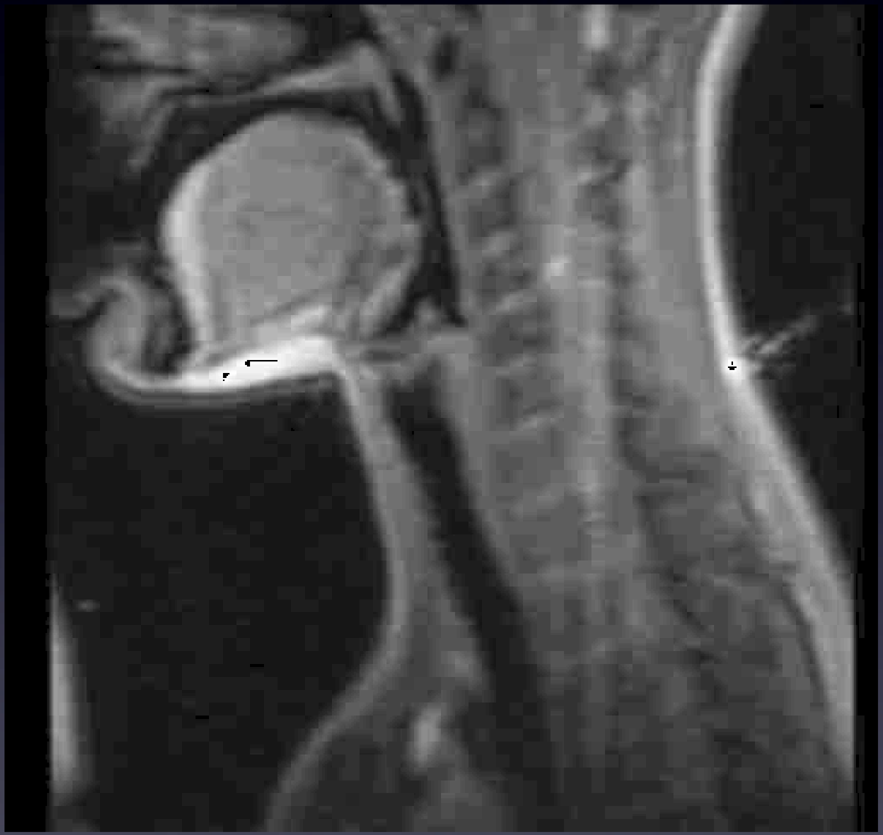
Real-time MRI

Coronal 2D MRI taken every 0.5 seconds on an existing 0.2 T open MRI

Benefits:

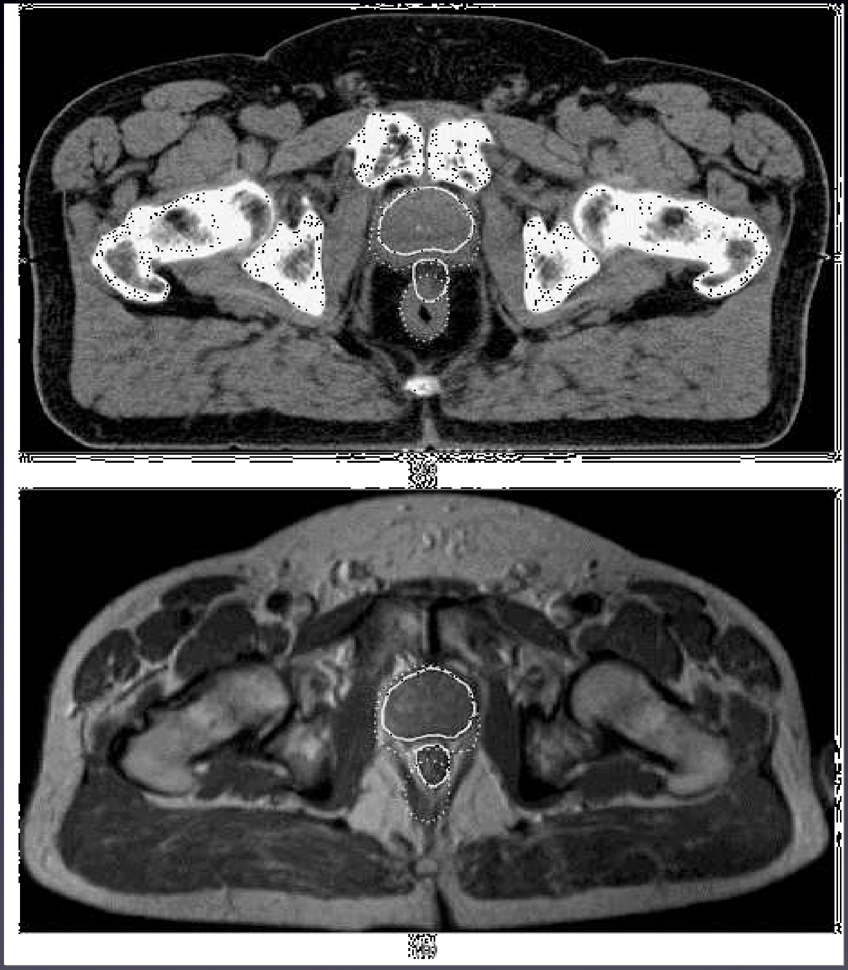
Capture 4D target every day

Observe effects like blood flow, coughing, swallowing, voluntary motion, IMRT aliasing w/ motion, etc.



What else can MRI currently bring to the table?!

MRI can provide
Better soft tissue contrast
T1
T2
Proton density
Bold Perfusion imaging
Spectroscopy

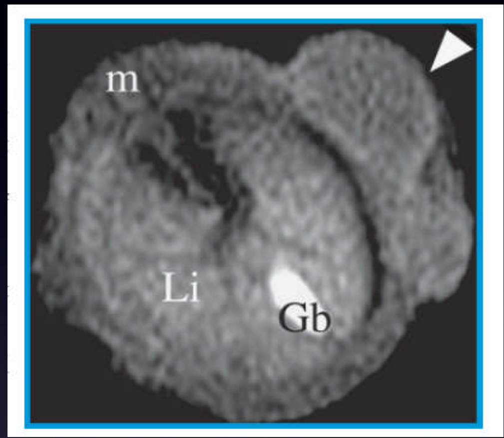


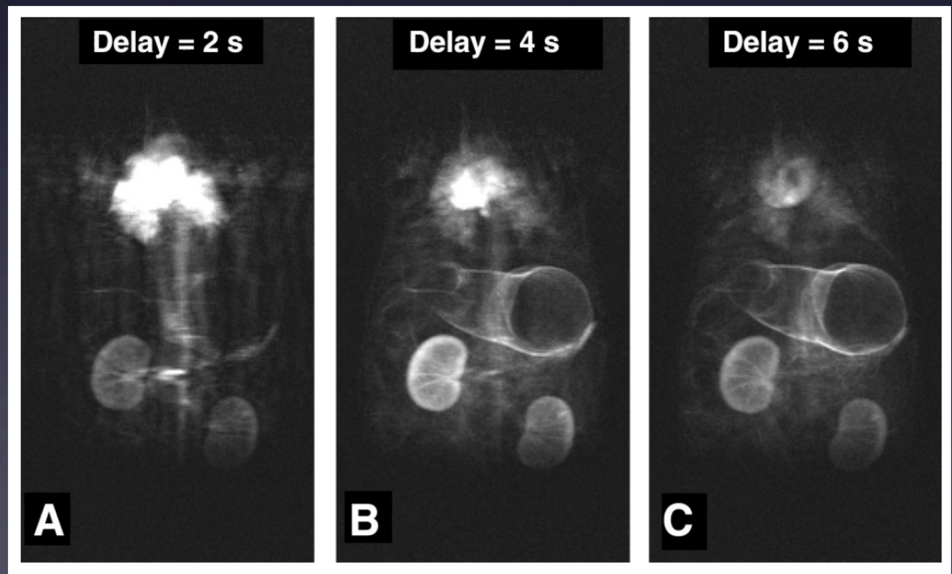
What else will MRI bring to the table in the future?!

Exciting MRI contrasting agents that can provide "nuclear medicine"-like metabolic information are being developed

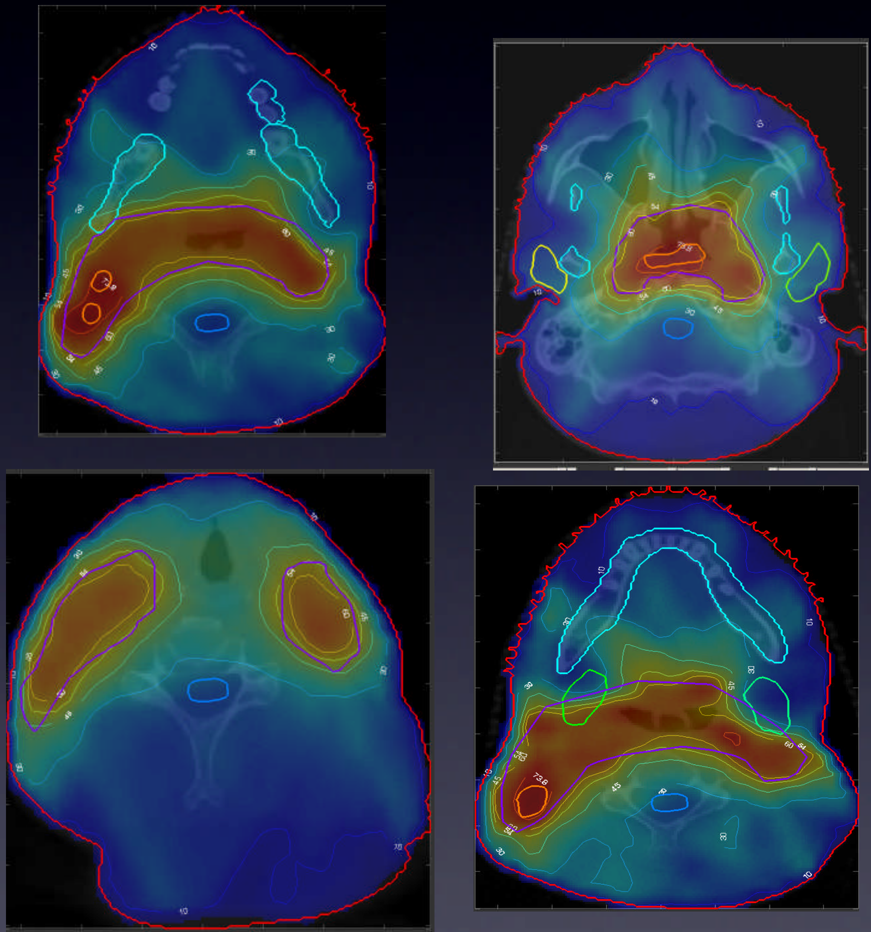
Hyperpolarized liquids
Liposome-based agents

Come for the organ motion, stay for the metabolic imaging!





Why ©-Ray IMRT?



Because it works!!!

High quality optimization enables gamma-ray IMRT

40 seconds to optimize on single PC

Compatible w/ MRI

1.5 cm =diameter ^{60}Co source

300R/min. @ 1 meter

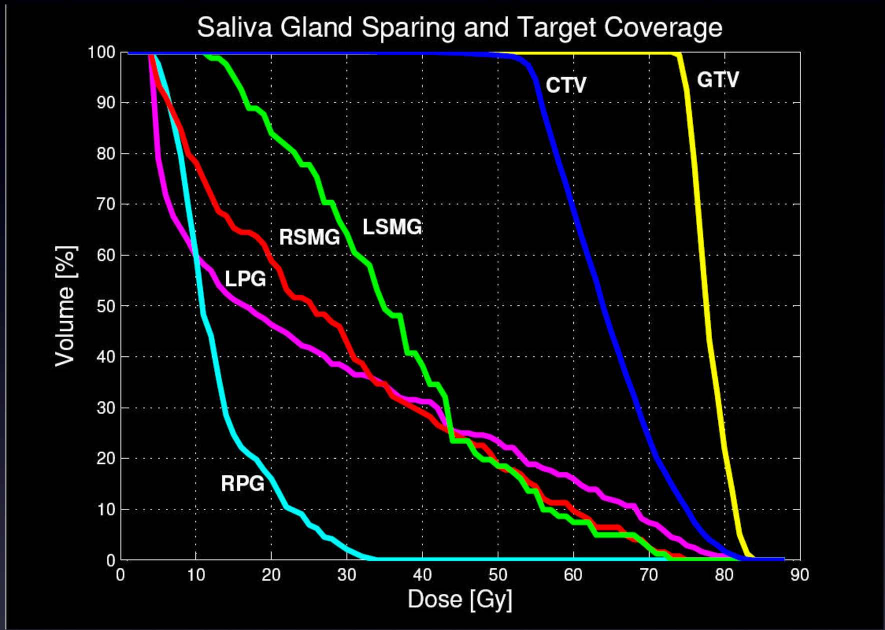
MLC @ 60 cm

7 beam plan

Targets to 73.8 and 54 Gy

Spare tissue, saliva glands, cord, brain stem, and mandible

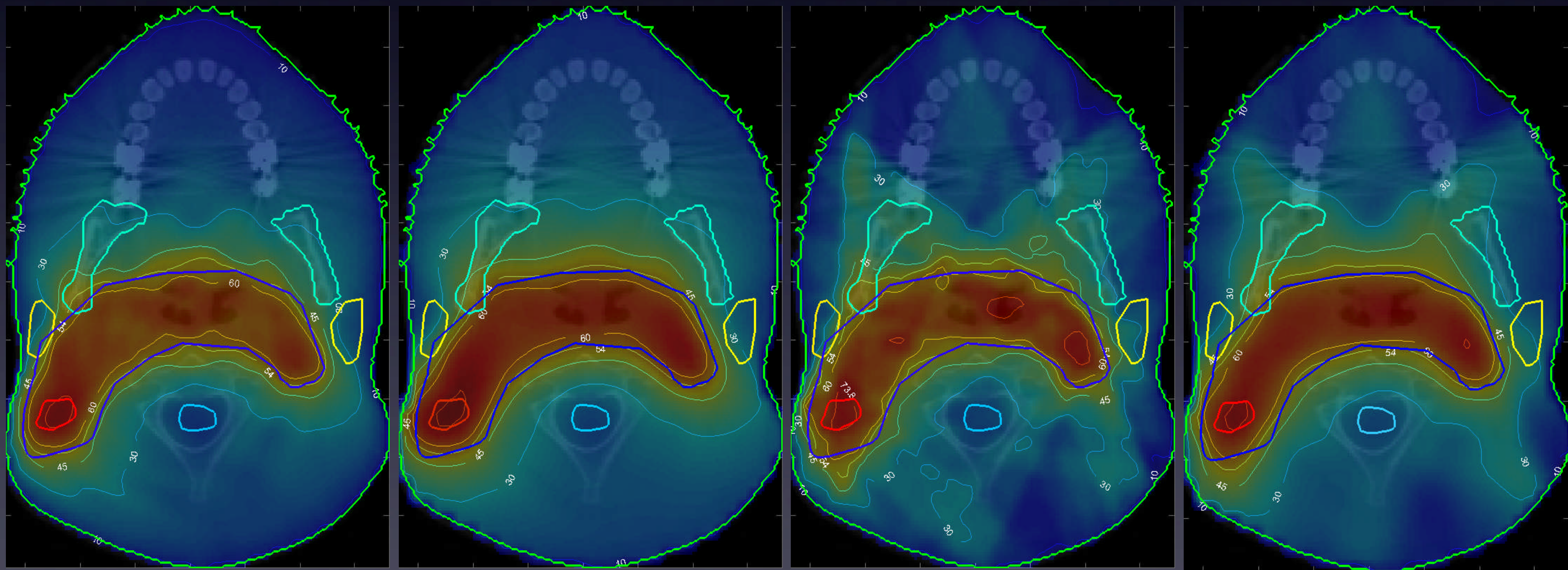
Head&Neck Case: DVHs



Targets w/ >95% Vol. coverage
<12% hot spot for high dose target
Sparing for 3 out of 4 saliva glands <50% vol. @ 30 Gy
<3% Tissue > 50 Gy
Cord, brain stem, and mandible below tolerance

Renaissance Goes “Toe-to-Toe” with the Best

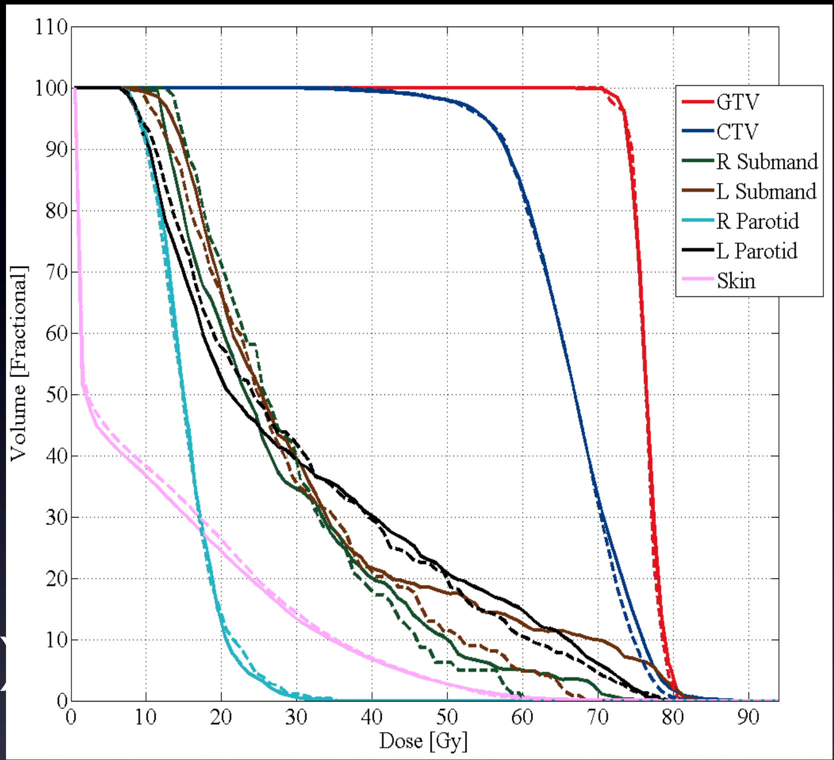
6MV 71 beams	Co60 71 beams	6MV 7 beams	Co60 7 beams



a) b) c) d)

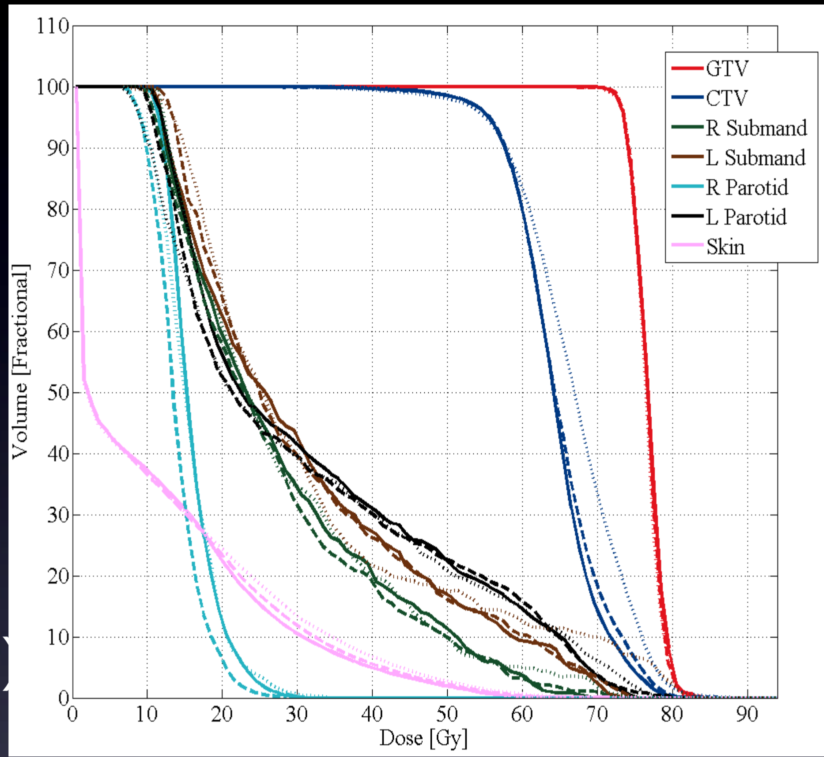
By Every Measure Co60 Makes Great Plans

a)

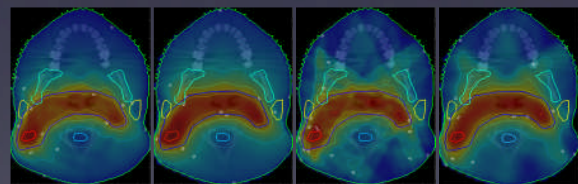


$6MV^{solid}$ vs $^{60}Co^{dashed}$ 7 beams

b)



6MV 71^{solid}, 11^{dashed}, 5^{dotted}



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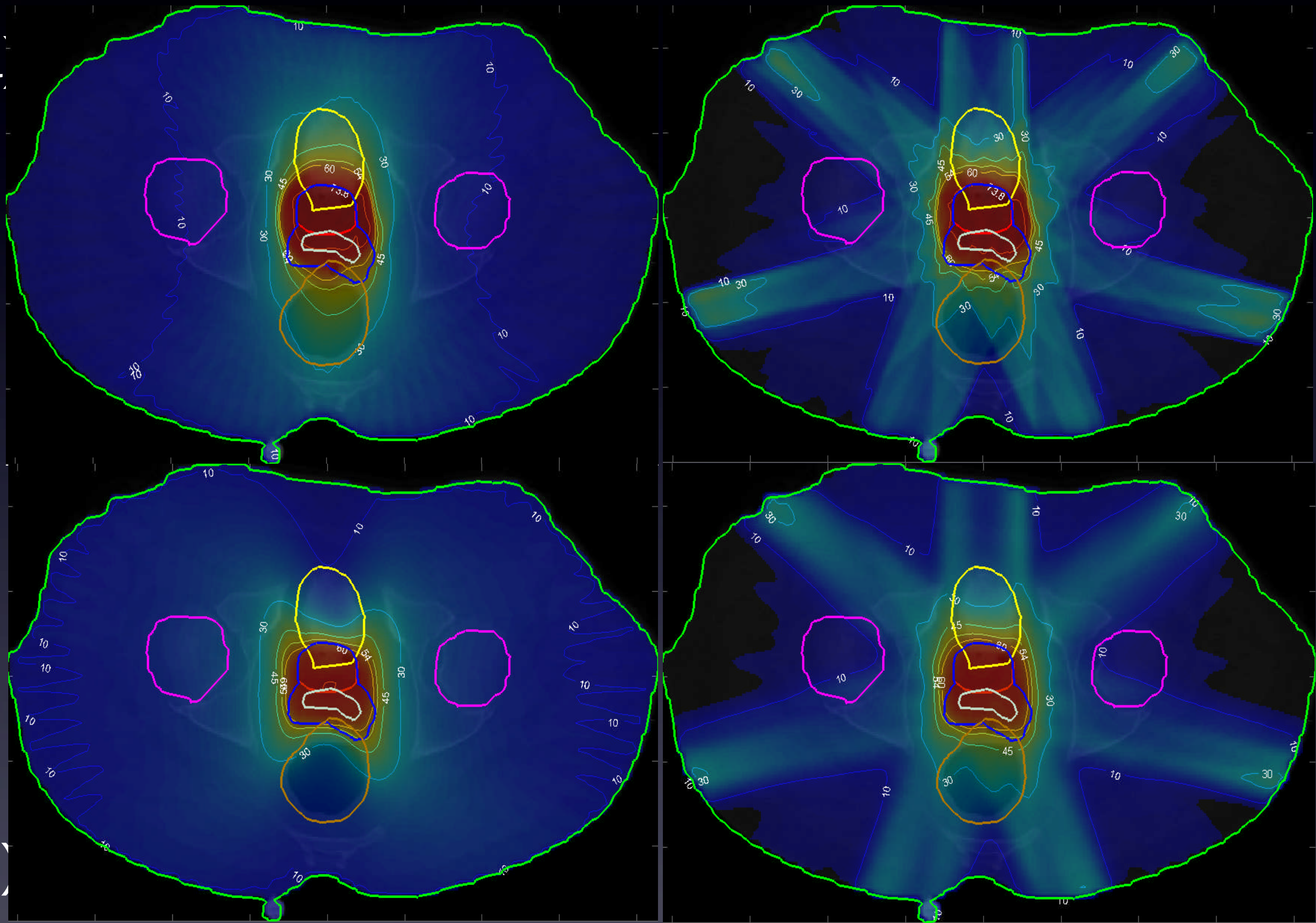
Prostate - Dose Dist.

a) 6MV 71 beams

b) 6MV 7 beams

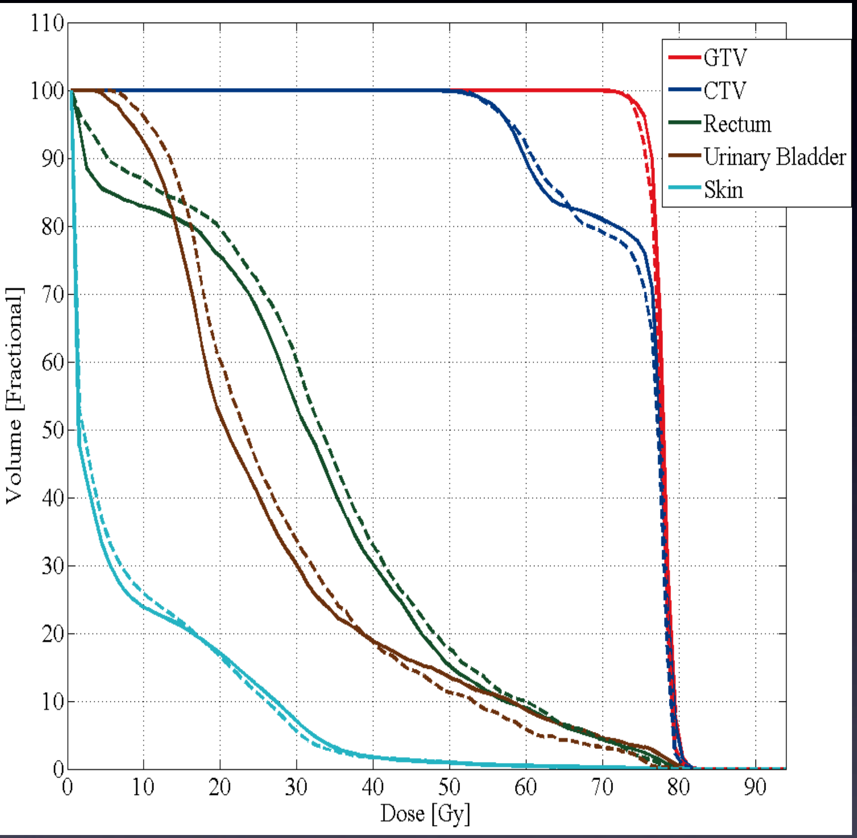
c) Co60 71 beams

d) Co60 7 beams



Prostate -DVHs

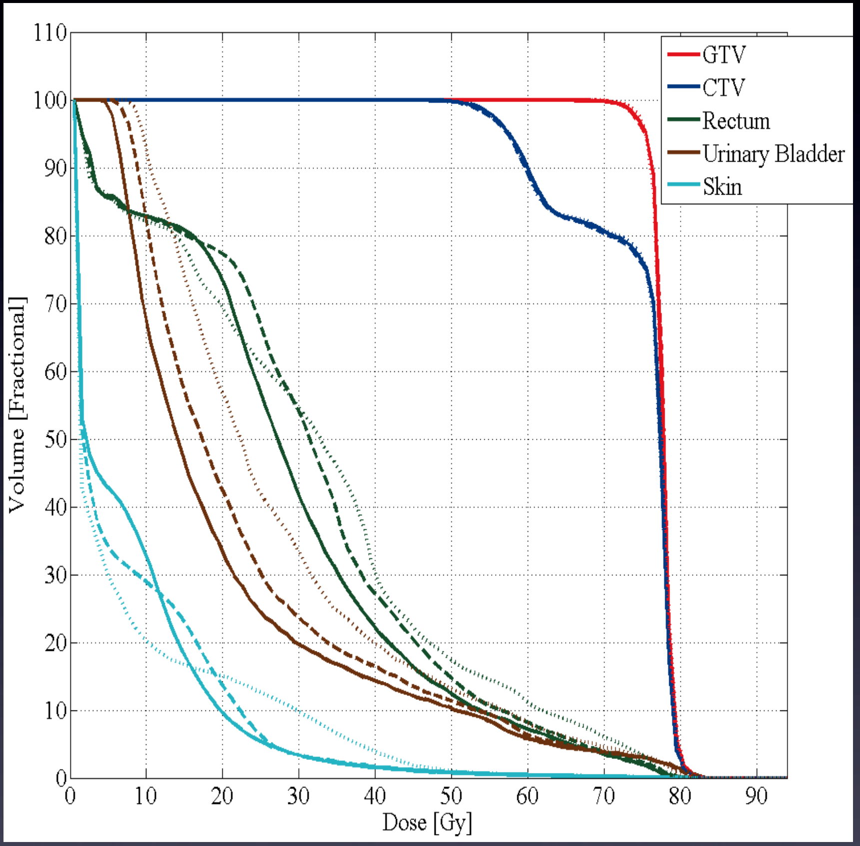
6MV[solid] vs [60]Co[dashed] 7 beams



a)

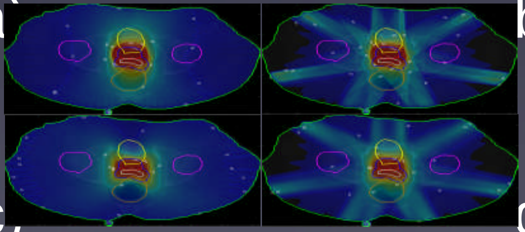
b)

6MV 71[solid], 11[dashed], 5[dotted]



a)

b)



c)

d)

Is Cobalt a Problem?

^{60}Co is undoubtedly the best isotope for external beam therapy
Cobalt is a ferromagnetic metal
Ferromagnetic materials magnify magnetic fields
Magnetic field inhomogeneities can destroy the performance of the MRI

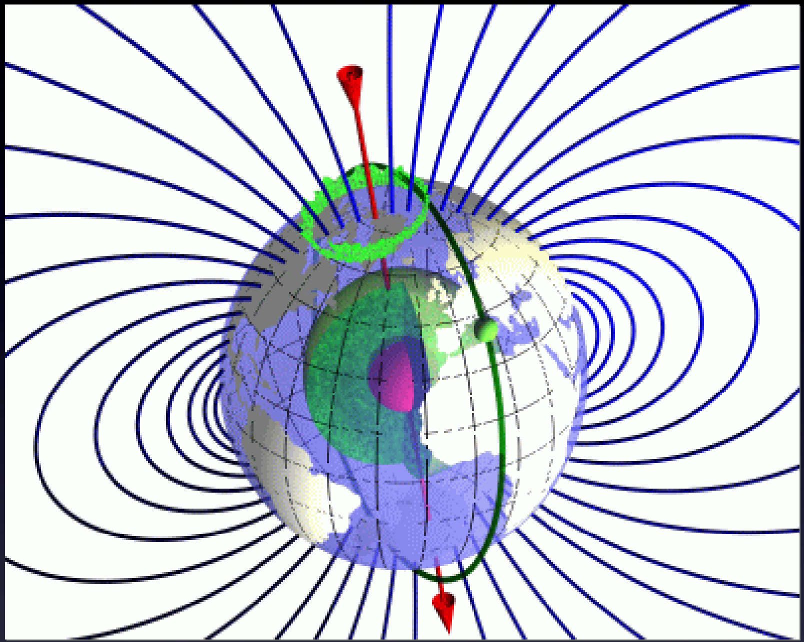
How big is this effect?!

No! Co Has Negligible Effect on MRI!

Consider a small 1.5 cm dia. sphere of cobalt in a uniform 0.3T field 1 m away from a 70 cm field of view.
Cobalt acts like a soft ferromagnetic material.
The magnitude of the magnetic field can be found exactly by solving Poisson's Eqn. for the magnetic potential

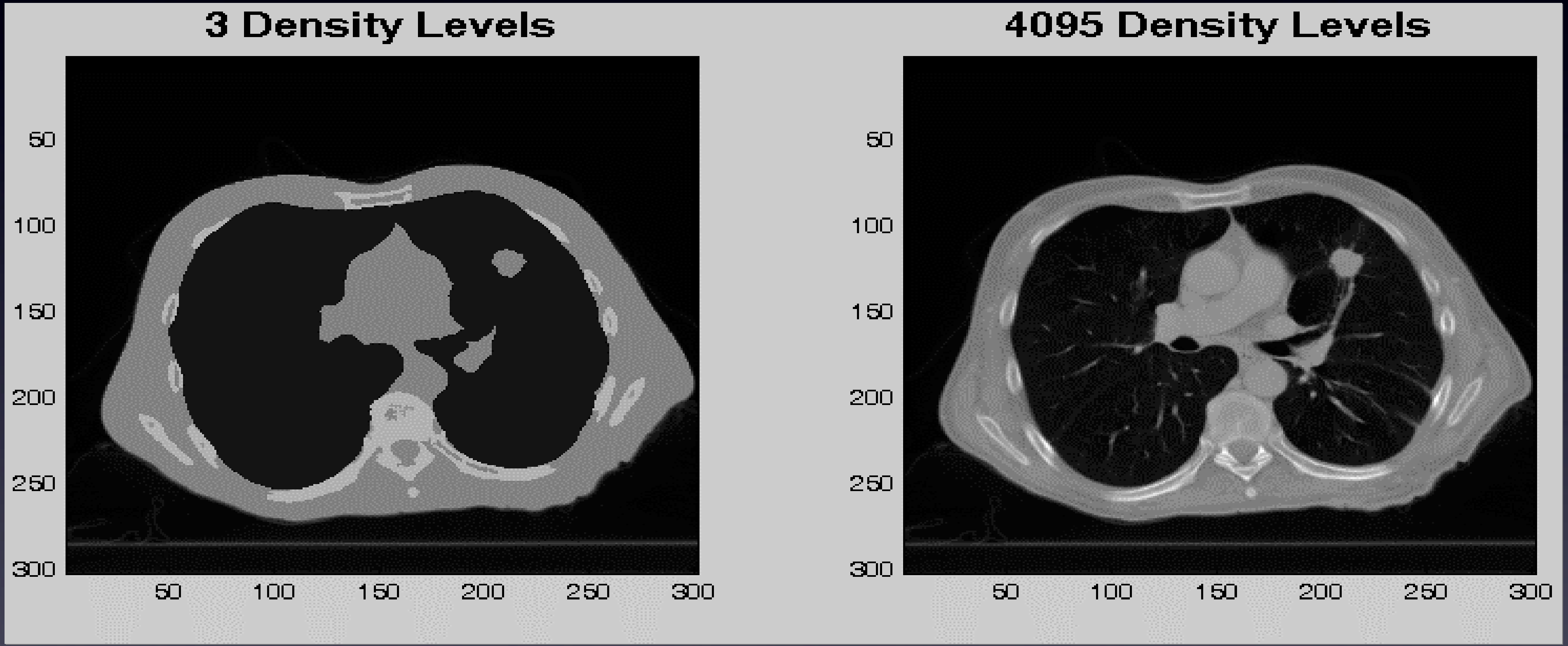
Inside the sphere & on its surface the field is 0.9 T
The excess magnetic field falls off as a dipole, i.e., with $1/r^3$

- Less than chemical shift



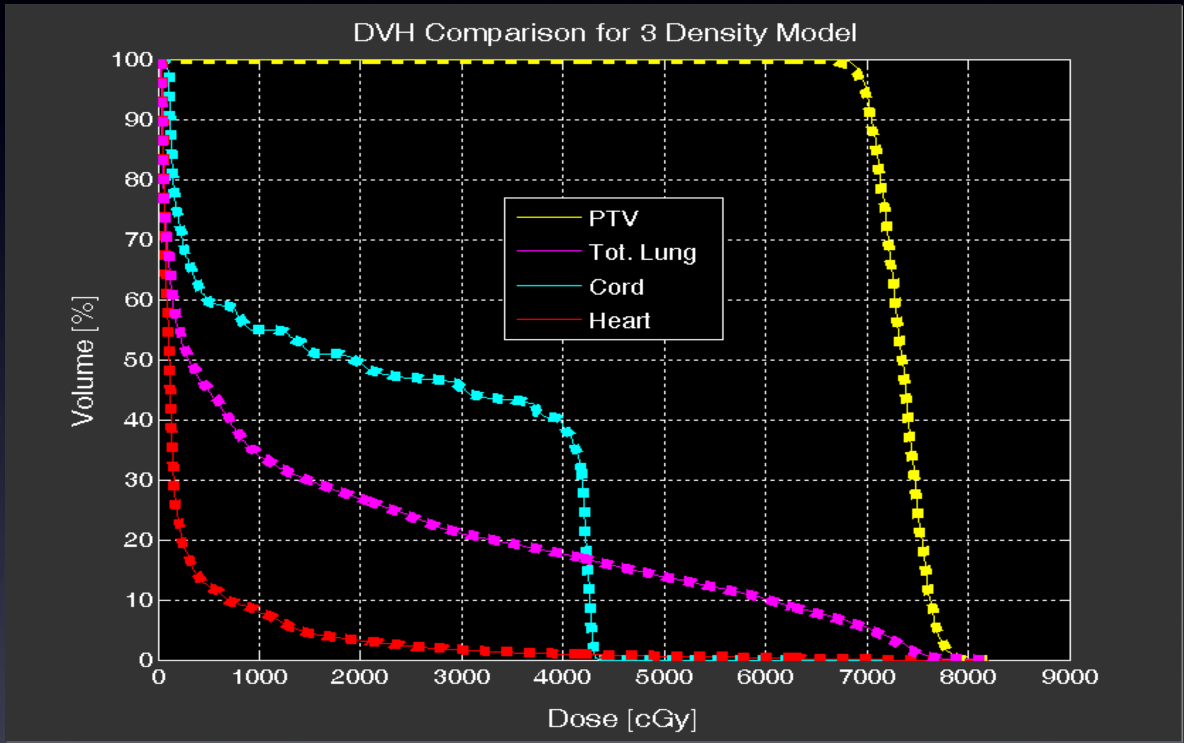
Where the cobalt induced field meets the MRI FOV is already ~ 2ppm and rapidly dropping!!!

Can We Compute Dose Without CT Densities ?



Conformal Lung treatment plan: take CT data & reduce to 3 values: lung; bone; and soft tissue; having 0.15,

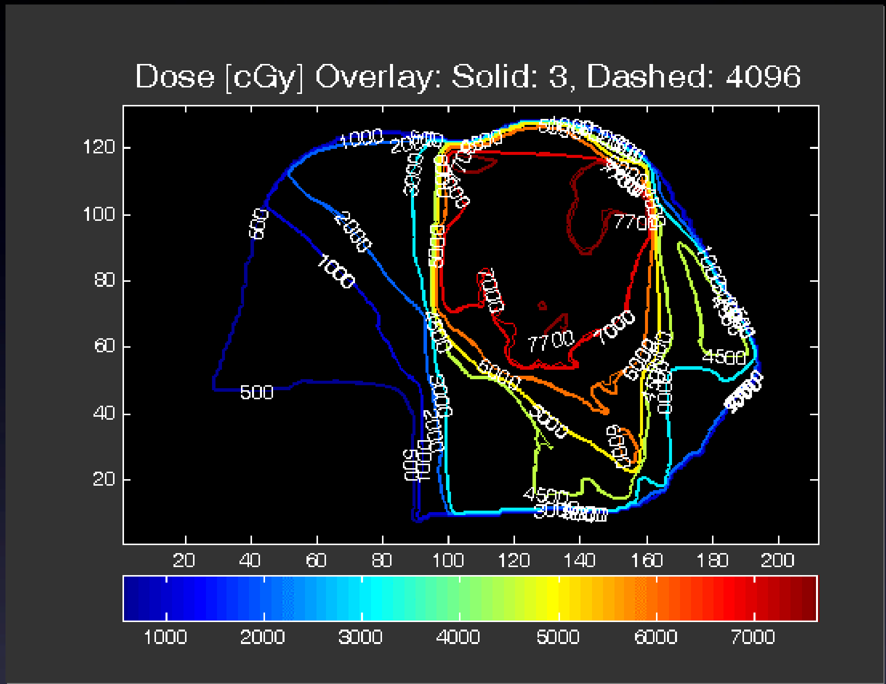
Computing Dose Without CT

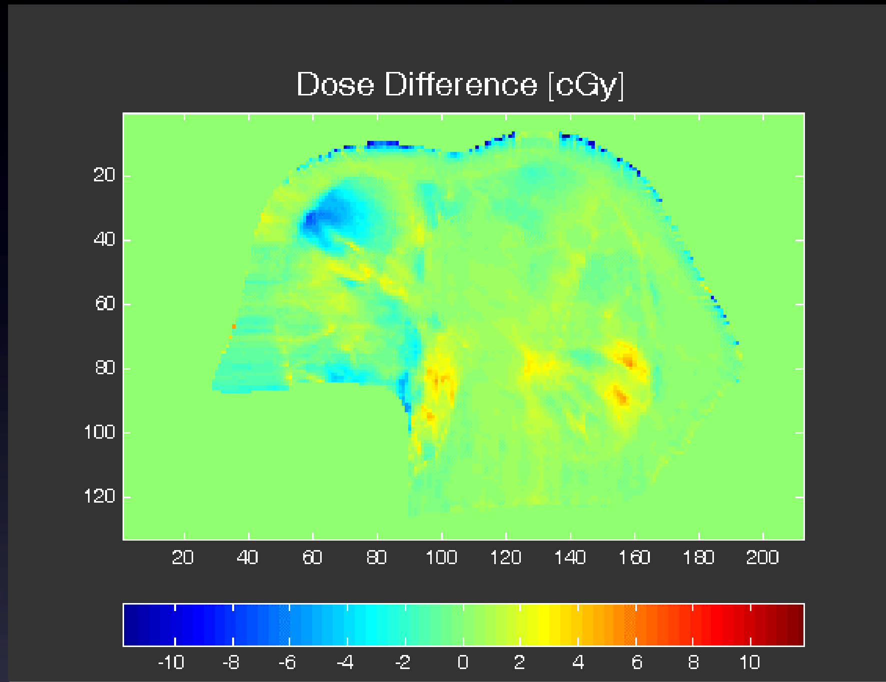


DVH overlay of full CT calc. and 3 density calc.

No observable difference in the DVHs

Computing Dose Without CT



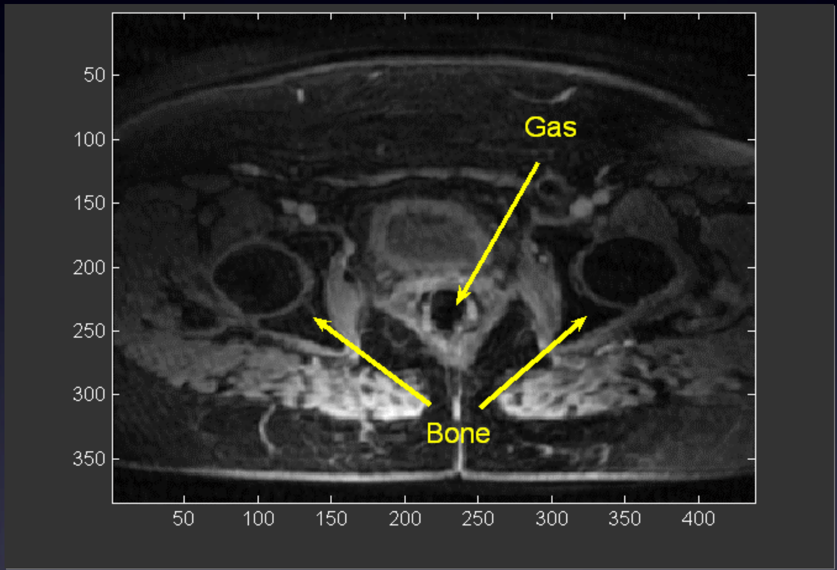


We just need to know where the air, lung, soft tissue, and bone are

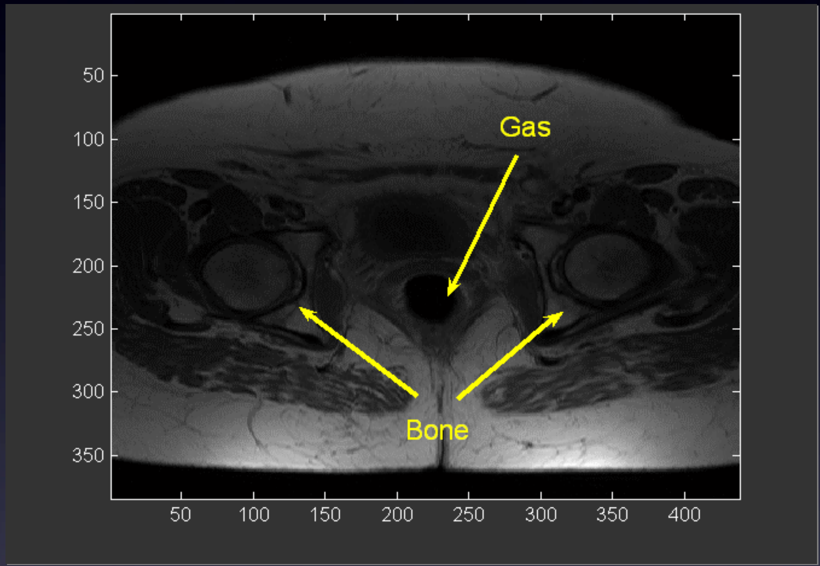
Dose Difference < ±34 cGy or 0.5% everywhere

By the way, you can use this with CBCT…

Can We Differentiate Tissues in MRI?



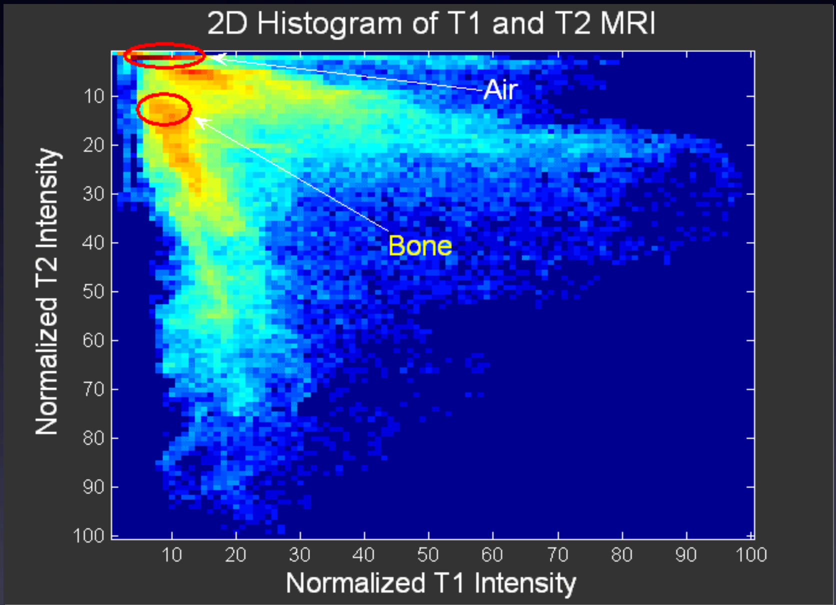
T2

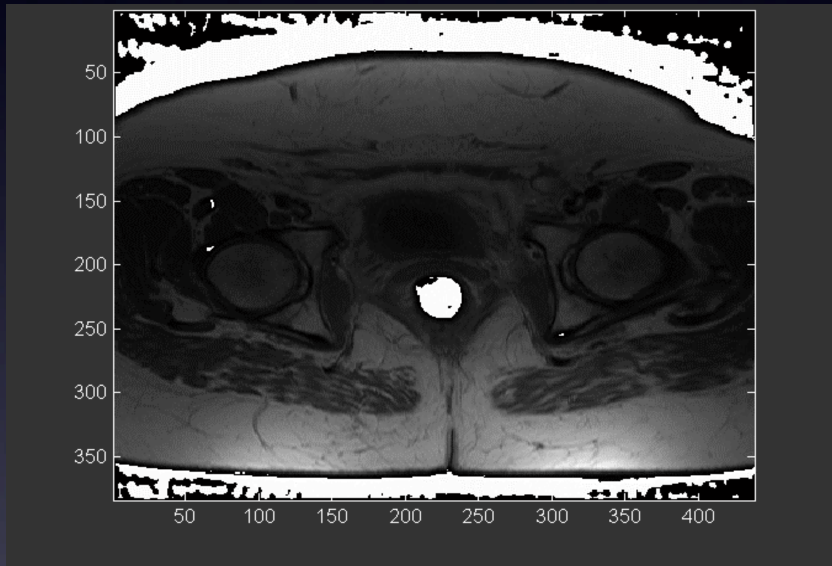


T1

Yes, Using the information in both T1 & T2 pretreatment MRIs we can differentiate bone from air

Differentiating Tissues in MRI





The rectal gas and air selected over pelvis & femurs

Roadmap

- The Generation of the Renaissance^{TM}
  - Gen-1 - daily reoptimization & dose recording
  - Gen-2 - closed loop beam-by-beam reoptimization
  - Gen-3 - real-time reoptimization driven tracking
- Metabolic Imaging

Summary & Outlook

Viewray, Inc. Formed w/ experienced management

Patent pending

Feasibility Studies Completed

Forming scientific board of advisors

Design team established

Strong Corporate Partners with experience in: whole body MRI, Cobalt Therapy, MLC systems, control systems, gantry & couch design

Seeking strong clinical institutions & strategic partners for collaboration on ViewRay development for

Adaptive treatment planning algorithms in HPC system
MRI metabolic imaging
Deformable image registration
pMRI development
Metabolic imaging

Collaborators

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