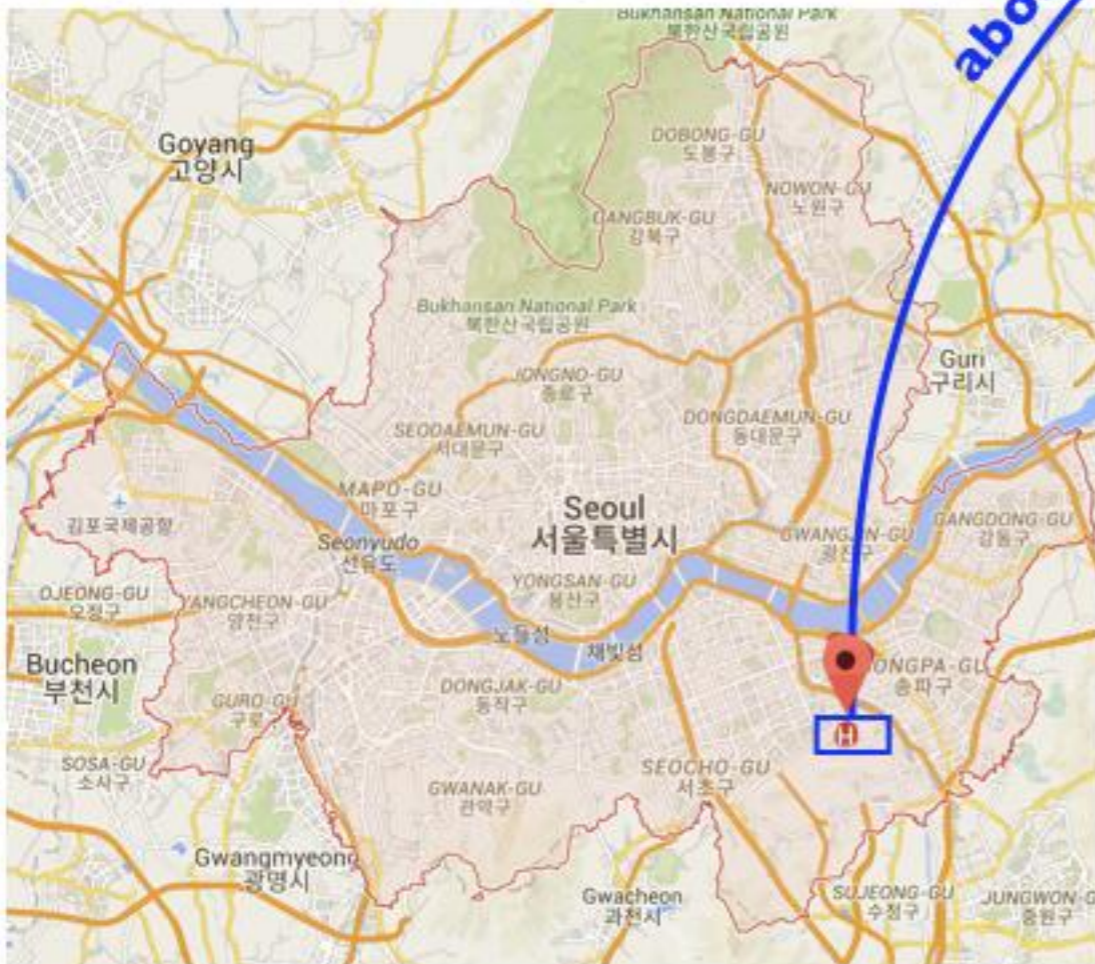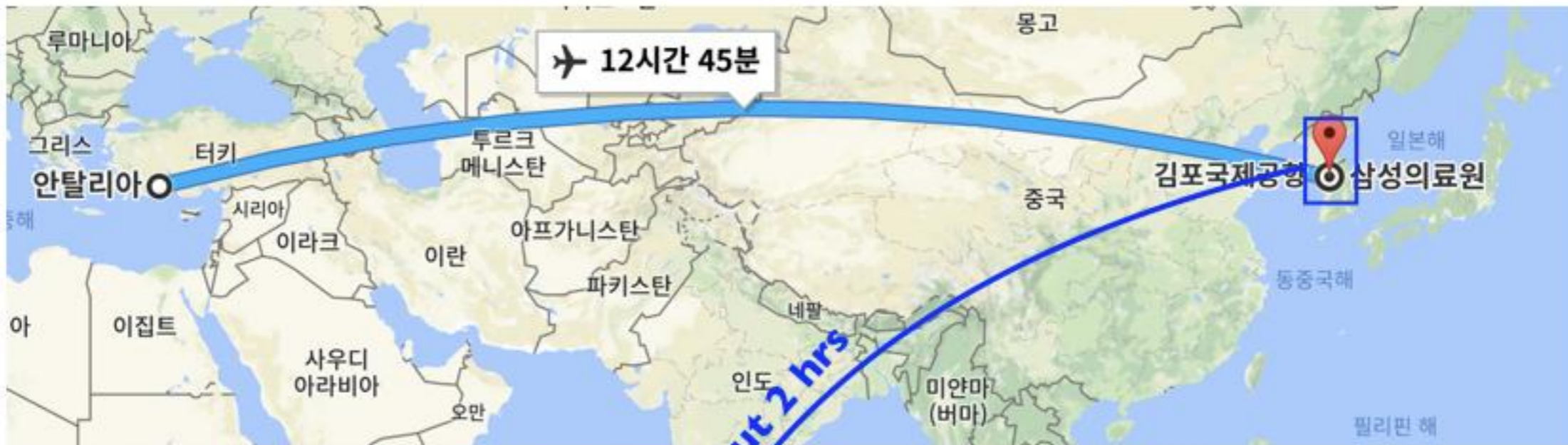# Integration of MRI in Radiotherapy

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Location of SMC (Dept. Radiation Oncology)

Comprehensive Cancer Center
B1

Proton Center
B1 ~ B3

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Resources in SMC

1994	2002	2008	2016
2 Faculty (MD)	4 Faculty (MD)	6 Faculty (MD)	11 Faculty (MD)
1 Physicist Faculty	1 Physicist Faculty	1 Physicist Faculty	4+5 Physicist Faculty (+2/+7)
			1 Biologist Faculty
	4 Trainee	10 Trainee	8 Trainee (Resid. & fellow)
9 RTT	18 RTT	35 RTT	56 RTT
19	37	68	121

Discovery 590RT, GE

Achieva 3.0T MR-RT, Philips

RayStation, RaySearch

Two Gantries with CBCT

Resources in SMC

LightSpeed RT16, GE

Discovery 590RT, GE

Acuity, Varian

TomoTherapy, Hi-ART

21Ex, Varian

Pinnacle3, Philips
iPlan, BrainLab

6Ex, Varian

6Ex, Varian

TomoTherapy, HD

NovalisTx, Varian

TrueBeamStx, Varian

21iX, Varian

Conventional Simulator: 1
CT simulators: 3
MR-RT simulator: 1
Linacs: 6
TomoTherapies: 2
Gantries with CBCT: 2

Discovery 590RT, GE

Achieva 3.0T MR-RT, Philips

RayStation, RaySearch

Two Gantries with CBCT

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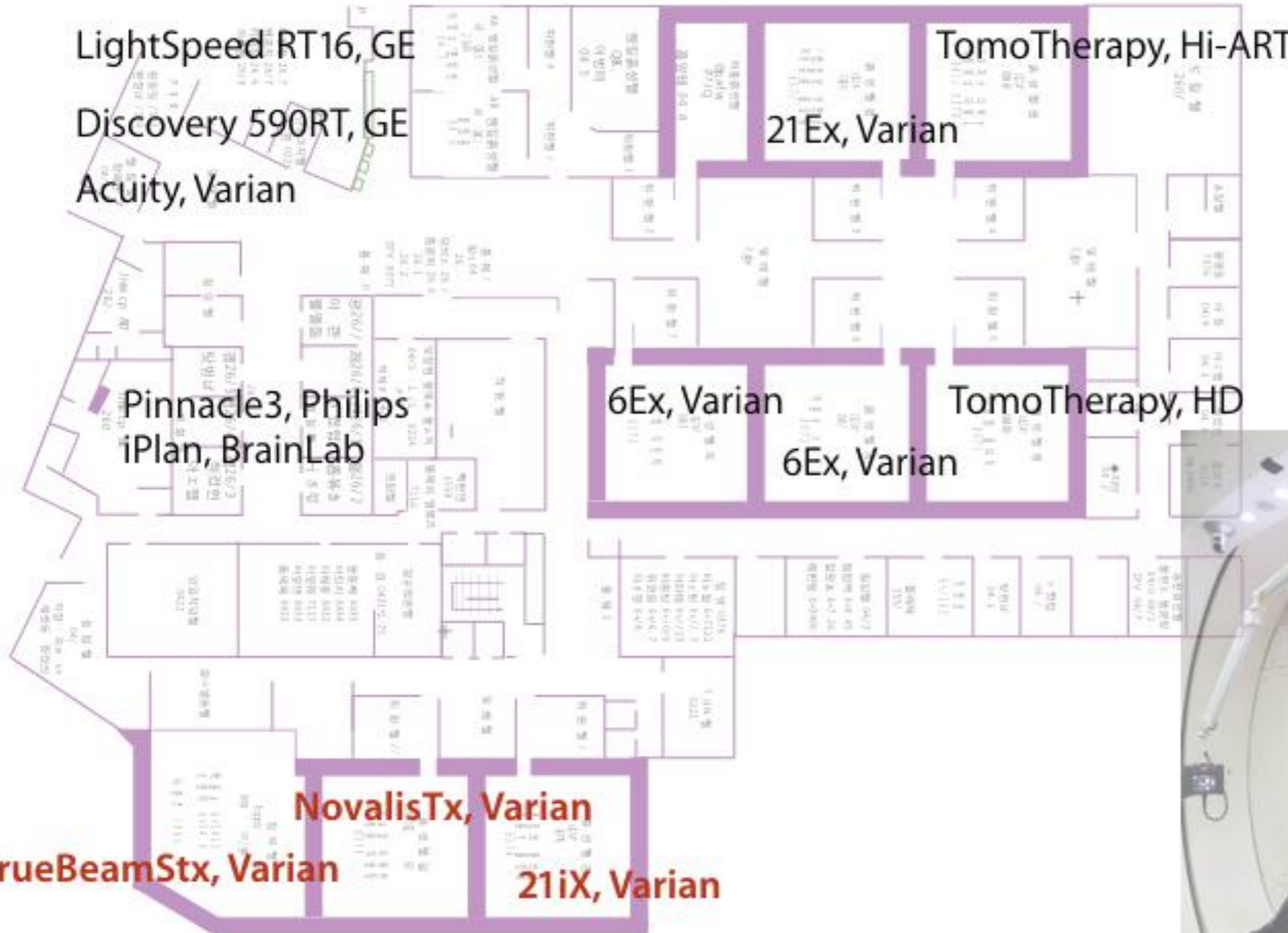
Multimodal images in radiotherapy

- A random sample of 1600 radiation oncologists in USA
- 393 responses
- Disease site - modality, delivery techniques.

as of 2009, [%]

	CNS	H/N	Lung	Breast	GI	GYN	GU	L/L	Ped
Target Delineation									
All	79	80	83	20	53	46	44	56	14
MR	68	37	4	4	7	18	33	4	11
PET	15	3	68	10	40	33	8	47	8
4DCT	2	4	37	5	17	3	3	3	2
In-Room Imaging									
All	72	74	67	44	60	58	91	40	24
Video	1	1	0	2	1	1	1	0	1
US	0	0	0	2	1	2	23	0	0
MV 2D	35	33	30	26	27	27	43	22	11
kV 2D	42	37	35	17	28	26	42	17	0
3D	35	38	37	12	33	27	45	15	12

D. R. Simpson, et al., Cancer **116**, 3953-3960 (2010).
D. R. Simpson, et al., JACR **6**, 876-883 (2009).

Multi-modal images in radiotherapy

- ## Computed Tomography
  - Attenuation coefficient
  - Energy, imaging protocol, contrast agent
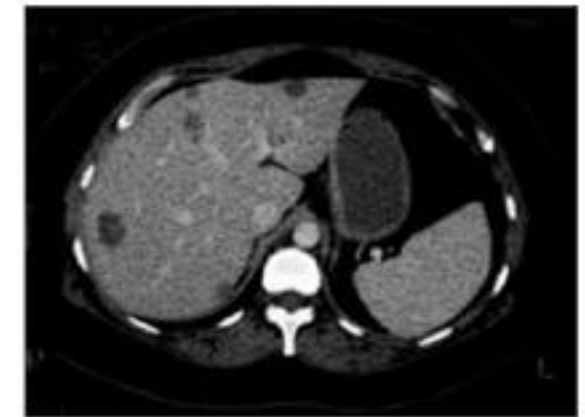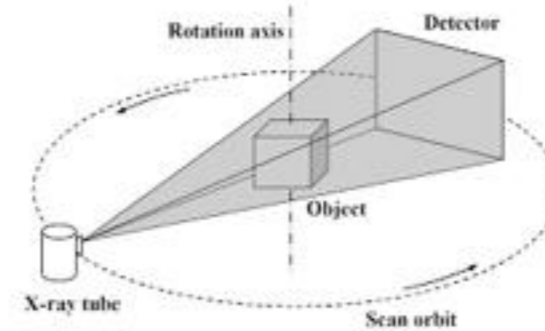
- ## Postiron Emission Tomography
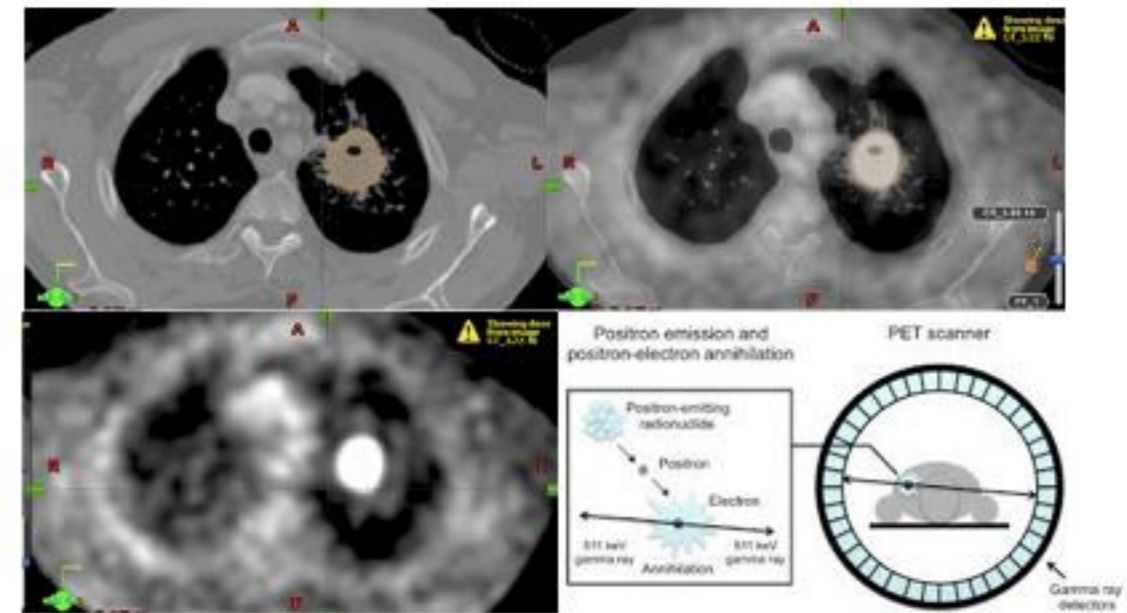 - Positron-emitting radionuclide
  - Agent, FDG, MISO, and so on

- ## Magnetic Resonance Imaging
  - Resonance pulse, Relaxation time, and so on
  - Contrast agent, imaging protocols, and so or

- ## Ultrasound, etc.

Figure 4 PET/CT fusion role in delineation of tumor. Left: CT image showing gross tumor. Right: PET image showing disease uptake. Middle: PET/CT fusion correlating gross tumor with uptake in PET.
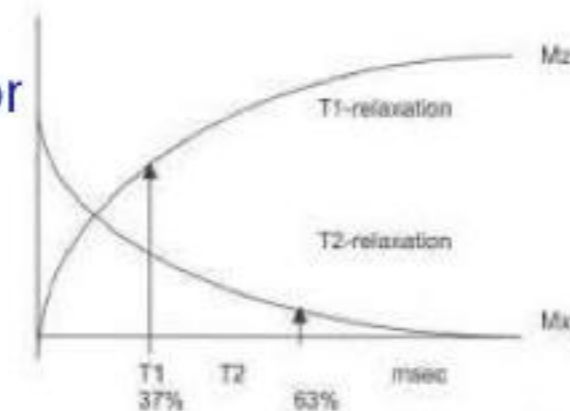
Tissue	T1 (msec)	T2 (msec)
Water/CSF	4000	2000
Gray matter	900	90
Muscle	900	50
Liver	500	40
Fat	250	70
Tendon	400	5
Proteins	250	0.1- 1.0
Ice	5000	0.001

Preliminary image in radiotherapy

- Computed tomography
  - Electron density converted to attenuation coefficient for radiotherapy
  - Geometrical accuracy of anatomy
  - **Lack of contrast resolution for differentiation between normal soft tissue structures and tutor extent**
- Advantages of MRI in radiotherapy
  - Superior contrast resolution and better soft tissue differentiation
  - No need - radiation exposure, iodinated contrast agent
  - Functional imaging sequences

	CT	PET	MRI
Signal intensity	Electron density	Uptake	Material composition and uptake
Resolution	Fine	Coarse	Fine
3D imaing	OK	OK	OK
Radiation	Exposure	Exposure	Non-ionizing
Acquisition time	less than 1 min	mins	a few seconds ~ mins (Imaging protocol)
Anatomy	OK	N/A	OK

History of MRI

- 1952 Herman Carr - Ph.D. Thesis

- 1973 Lauterbur PC

P. C. Lauterbur, "Image Formation by Induced Local Interactions: Examples Employing Nuclear Magnetic Resonance," Nature **242**, 190-191 (1973).

History – Integration of MRI into radiotherapy

- Initial reports in radiotherapy
  - Fabrikant JI, et al.(1985), Heavy charged-particle Bragg peak radiosurgery for intracranial vascular disorders.
  - HoudekPV, et al. (1989), MR technique for localization and verification procedures in episcleral brachytherapy.
- Fraass BA, et al (1987): **Integration of magnetic resonance imaging into radiation therapy treatment planning: I. Technical considerations**
  - mechanically-obtained external contour and simulator film data,
  - The study has shown that to use MRI data for RTTP,
  - (a) **use careful patient positioning and marking**,
  - (b) transfer information from CT to MRI and vice versa,
  - (c) determine the **geometrical consistency** between the CT and MR data sets,
  - (d) investigate the **unwarping of distorted MR images**, and
  - (e) have the ability to **use non-axial images** for determination of beam treatment technique, dose calculations, and plan evaluation.

History – Integration of MRI into radiotherapy

- **MRI simulator**
  - T. Mizowaki et al., 1996 (Kyoto University)
  - **0.2T permanent magnet system (Open type)**
  - **Off-axis 10 cm < geometrical error of 2 mm**
  - Clinical output and effectiveness for bone metastases (2001)

- **MRI based Treatment planning for prostate cancer (L. Chen et al., PMB, 2004)**
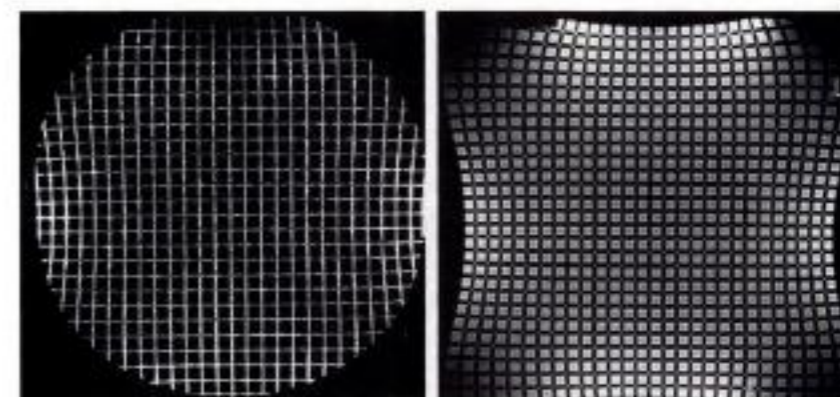
Figure 4. MR images of the two types of phantom. (a) T1-weighted axial images of the cylindrical phantom (FOV, 260 mm). (b) T1-weighted axial images of the cube-shaped phantom (FOV, 320 mm). Geometric distortion was generally observed in the peripheral area of the images. L = left.
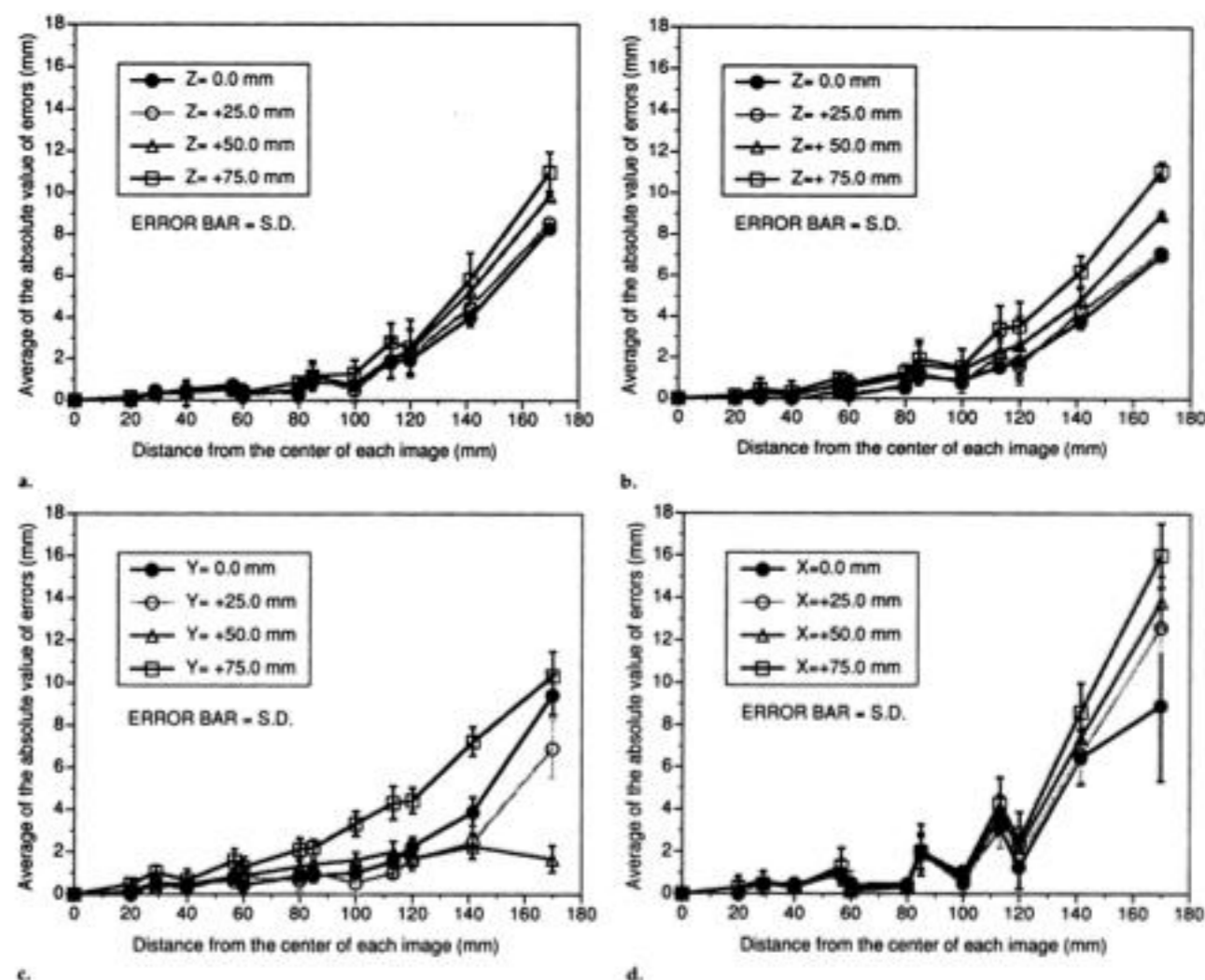
Figure 5. Positional errors in (a) T1-weighted axial, (b) T2-weighted axial, (c) T1-weighted coronal, and (d) T1-weighted sagittal MR images. Almost all positional errors within the 100-mm radius from the center of the image were within 2 mm. S.D. = standard deviation, X = coordinate of the x axis, perpendicular to the sagittal sections. Coordinates on the left side of the center are indicated by +. Y = coordinate of the y axis, perpendicular to the coronal sections. Coordinates on the upper side of the center are indicated by +. Z = coordinate of the z axis, perpendicular to the axial sections. Coordinates on the cranial side of the center are indicated by +.
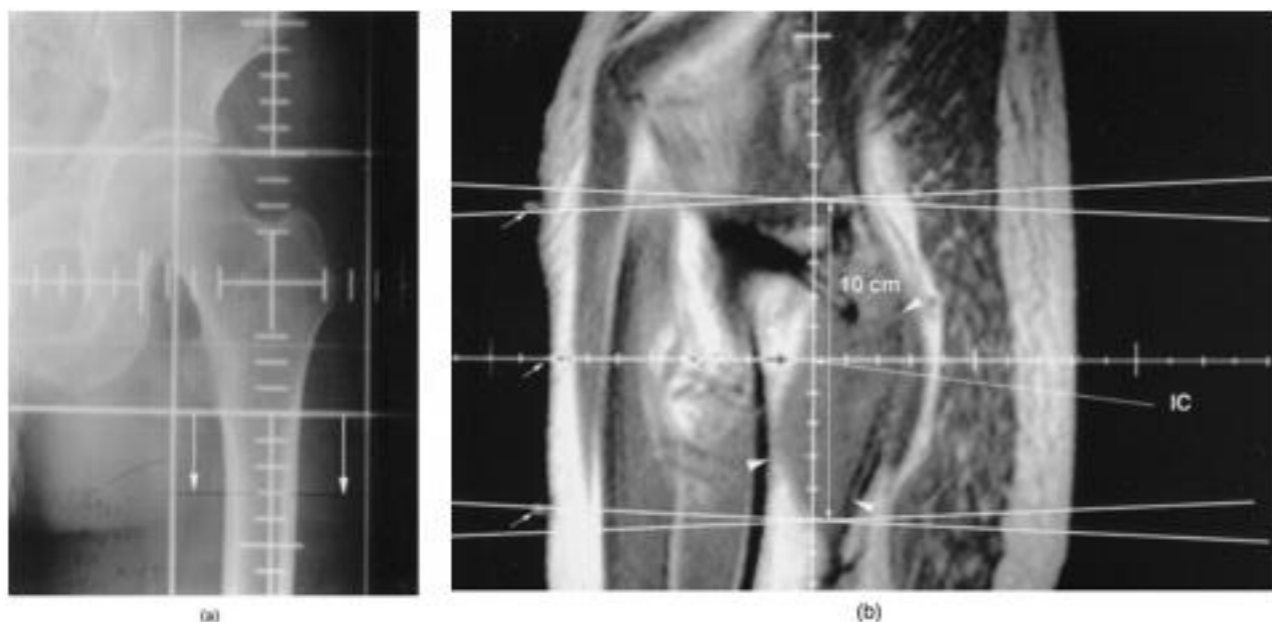
T. Mizowaki, Y. Nagata, K. Okajima, R. Murata, M. Yamamoto, M. Kokubo, M. Hiraoka and M. Abe, "Development of an MR simulator: experimental verification of geometric distortion and clinical application," Radiology **199**, 855-860 (1996).

MRI Integration in a CT–Based Radiotherapy Workflow

- Strategy I, Non constrast CT + constrast MRI
  - Target delineation
  - Visible outline of organ or landmark

MRI Image obtained with contrast

CT Image obtained without contrast

Image registration performed and evaluated using stent and liver boundary

Contours drawn on fused image with MRI visible, assigned to CT

MRI-based contour on CT for Tx Planning

K. K. Brock and L. A. Dawson, Seminars in Radiation Oncology **24**, 169-174 (2014).

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MRI Integration in a CT–Based Radiotherapy Workflow

- Strategy II, constrast CT + constrast MRI

  - Target delineation

  - Visible outline of organ or landmark

MRI Image obtained with contrast and tumor delineated

CT Image obtained with contrast and tumor delineated

Image registration performed and evaluated using tumor, vessels, and liver boundary

Contours combined, using information from both MRI and CT

MRI and CT-based contour on CT for Tx Planning

K. K. Brock and L. A. Dawson, Seminars in Radiation Oncology **24**, 169-174 (2014).

MRI Integration in a CT–Based Radiotherapy Workflow

- Accuracy of registration is the most important.
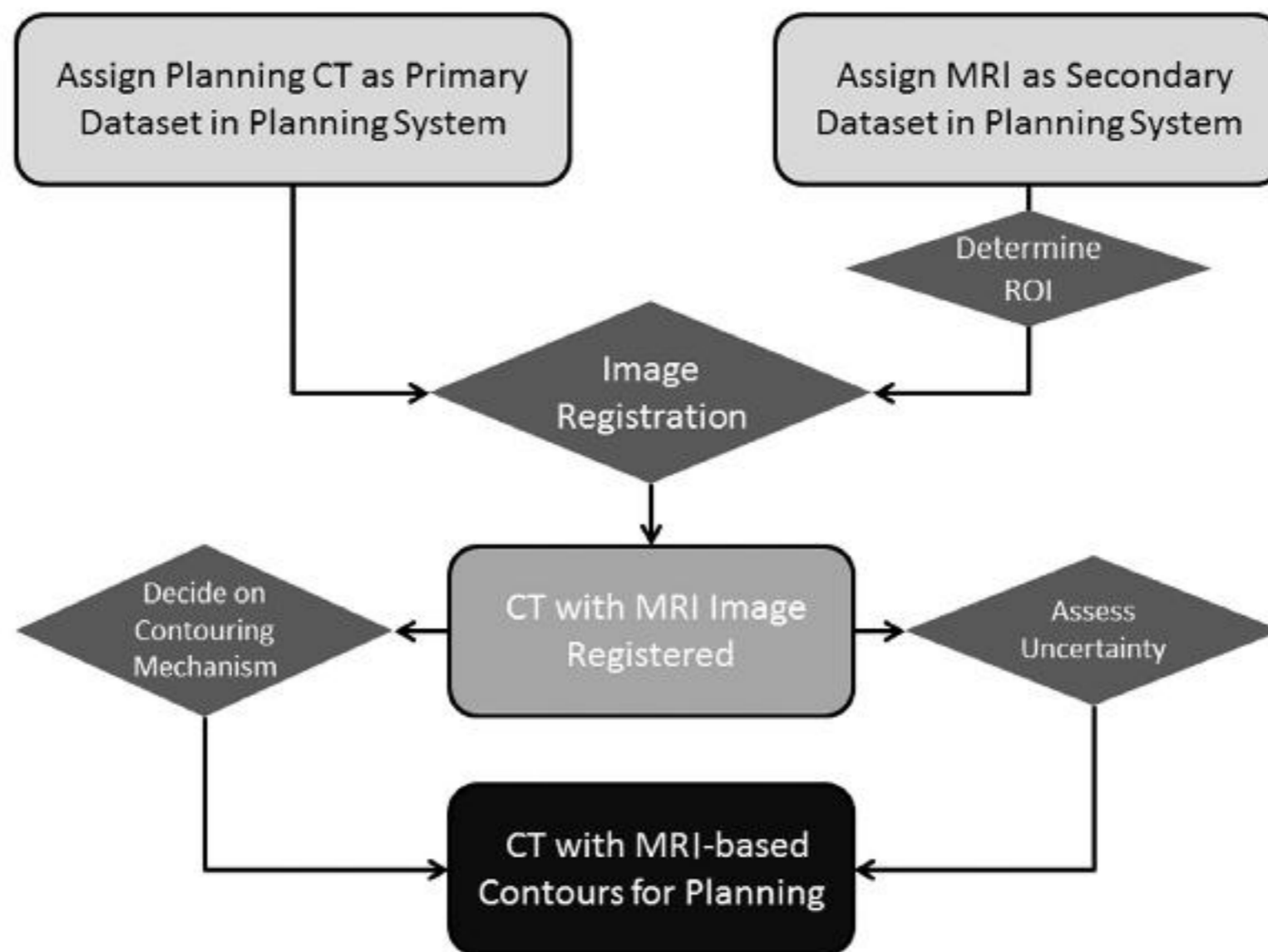
Figure 1 Overall workflow for integrating MRI into a CT-based treatment planning process.

K. K. Brock and L. A. Dawson, Seminars in Radiation Oncology **24**, 169-174 (2014).

Challenge: Generation of Synthetic CT

Unit Density

- The entire patient anatomy as a single bulk density, typically that of water or a mixture of adipose and muscle tissue

- Mean dose discrepancy less than 3%

Brain tumor
Gamma Knife radiosurgery
CT with heterogenous correction
CT without heterogenous correction
MRI with HU of 0
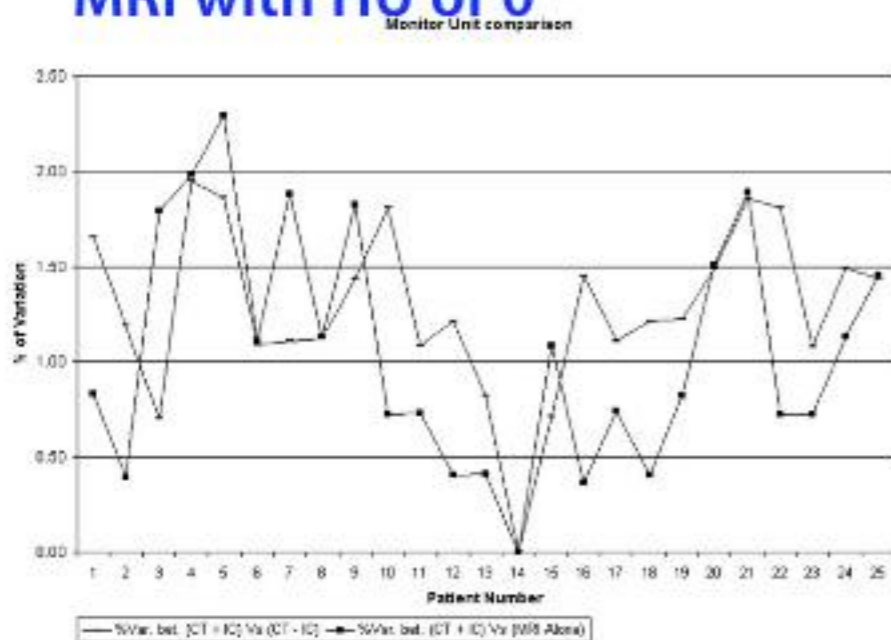
Figure 3. Monitor unit variation of CT without inhomogeneity and MRI alone with respect to CT with inhomogeneity. Var. bet, variation between; IC, inhomogeneity correction.

Comparison of mean value for different dosimeter parameters
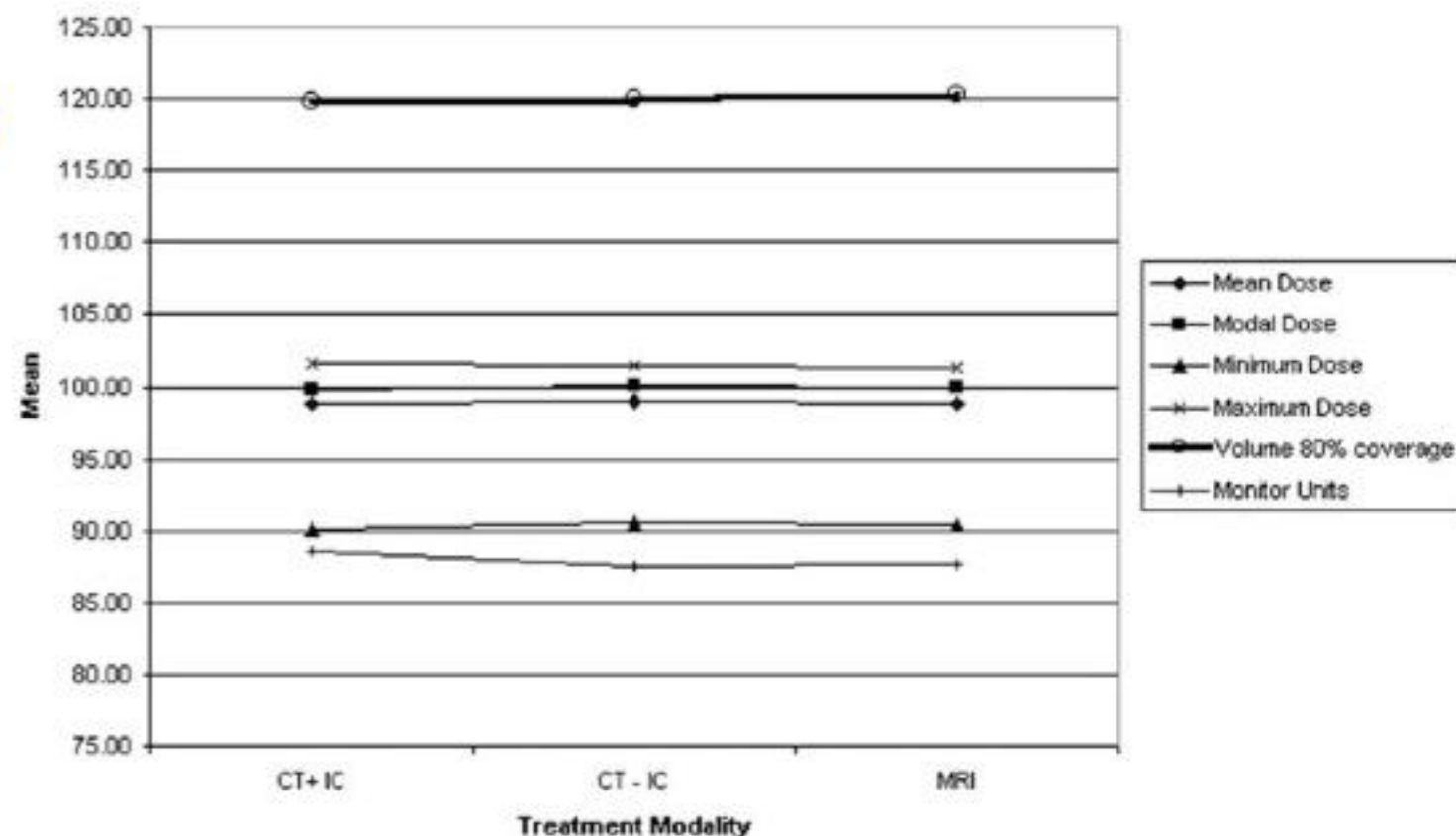
Figure 4. Comparison of mean value for different dosimetric parameters.

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Bulk Density with Bone

- Manual Bulk Density Assignment

    - The entire patient anatomy as a single bulk density, typically that of water or a mixture of adipose and muscle tissue

- Mean dose discrepancy less than 3%

- Different bulk density

    - Intracranial <1%

Table 4

Mean percentage point dose differences between the CT density corrected dose calculation and dose calculations based on unit density and bulk density, bone segmented mediums

Photon energy (MV)	Medium	Dose points			
		Isocenter	Norm	CT tumour center	MR tumour center
4	Unit density	1.5 ± 0.3	1.5 ± 0.3	1.2 ± 0.5	1.2 ± 0.4
	Bulk density (bone)	0.5 ± 0.2	0.3 ± 0.2	0.2 ± 0.4	0.2 ± 0.3
8	Unit density	1.0 ± 0.2	1.0 ± 0.3	1.1 ± 0.4	1.1 ± 0.5
	Bulk density (bone)	0.1 ± 0.1	0.2 ± 0.2	0.3 ± 0.3	0.3 ± 0.3
All	Unit density	1.4 ± 0.4	1.2 ± 0.3	1.2 ± 0.5	1.2 ± 0.4
	Bulk density (bone)	0.4 ± 0.3	0.3 ± 0.2	0.2 ± 0.4	0.2 ± 0.3

B. H. Kristensen, et al., Radiother Oncol **87**, 100-109 (2008).

Bulk Density with Bone

- Manual Bulk Density Assignment
  - The entire patient anatomy as a single bulk density, typically that of water or a mixture of adipose and muscle tissue
- Mean dose discrepancy less than 3% (Unit density), 1.5% (Bulk with Bone)

Prostate cancer

Pinnacle[3] and Eclipse

Four or Finve Fields with 18 MV

CT with bone, MR with bone

CT uniform density - HU of 0

MRI uniform density - HU of 0

Table 3

Summary of average point dose results for the four bulk electron density plans. The mean dose is the dose per fraction delivered by the plan, and the difference between this value and the full density CT plan is given as a percentage of the target dose delivered by the full density CT plan (200 cGy per fraction).

Plan	Mean dose (cGy)	% Variation from full density CT	Standard deviation (cGy)
CT-based with bone	200.2	+0.1	1.2 (0.6%)
MR-based with bone	197.5	−1.3	1.6 (0.8%)
CT-based, uniform density	197.2	−1.4	1.7 (0.9%)
MR-based, uniform density	194.8	−2.6	1.7 (0.9%)
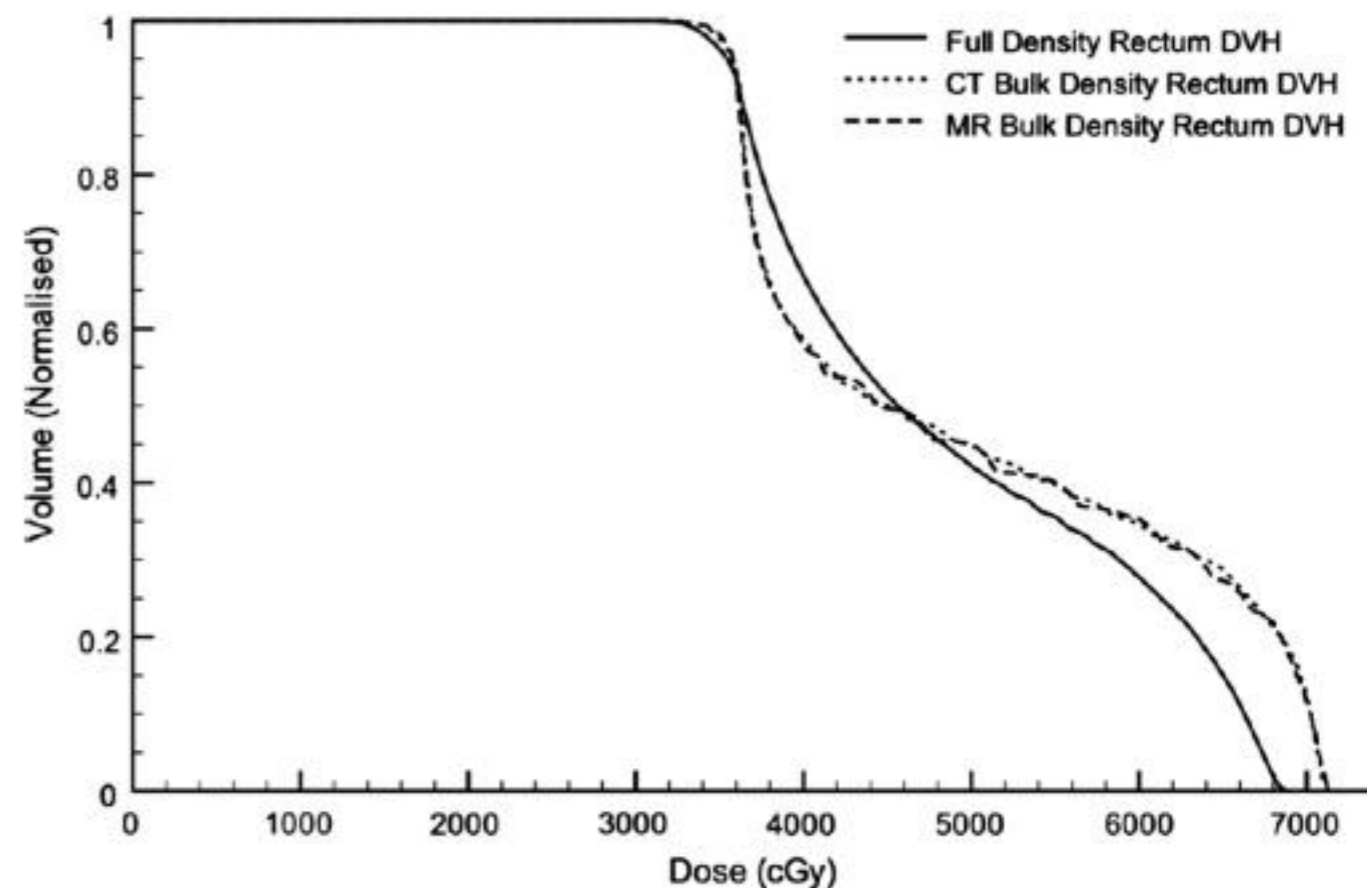
Fig. 1. Comparison of rectum DVHs from the bulk electron density plans to a full density CT plan when large gas pockets are present in the rectum.

J. Lambert, et al., Radiother Oncol 98, 330-334 (2011).

Bulk Density with Bone

- Manual Bulk Density Assignment

  - The entire patient anatomy as a single bulk density, typically that of water or a mixture of adipose and muscle tissue

- Mean Dose Discrepancy in Bone density, 1.3 g/cm³)

  - 0.2% for CTV, 4.1% for Bladder, and 5.3% for Rectum

Table I. Dose statistics for the CTV, bladder and rectum that shows the relative differences between clinically approved dose distribution (DD_{DP}) and the dose distributions based upon simulated MR images, DD_{WS} $DD_{W+B1.3}$, $DD_{W+B2.1}$ (refer to text for details). Prescribed target dose was 50 Gy.

| | CTV | | | | | | | Bladder | | | | Rectum | | | |
| | Volume [cm³] | Rel. diff. min. dose [%] | | | Rel. diff. mean. dose [%] | | | Volume [cm³] | Rel. diff. max. dose [%] | | | Volume [cm³] | Rel. diff. max. dose | | |
Pat. no.		DD_W	$DD_{W+B1.3}$	$DD_{W+B2.1}$	DD_W	$DD_{W+B1.3}$	$DD_{W+B2.1}$		DD_W	$DD_{W+B1.3}$	$DD_{W+B2.1}$		DD_W	$DD_{W+B1.3}$	$DD_{W+B2.1}$
1	88.0	−2.2	−1.1	−5.2	−1.0	0.5	5.8	64.2	3.8	3.9	7.5	84.9	4.2	4.9	8.5
2	123.0	−2.7	−2.0	−3.0	−0.7	0.0	2.5	219.8	9.6	9.6	9.5	53.7	7.2	7.4	8.6
3	141.2	−2.4	−1.6	−4.6	−0.9	0.2	4.2	127.2	7.0	7.2	8.6	88.6	5.9	6.2	8.1
4	139.7	−3.4	−2.0	−5.6	−1.2	0.2	4.9	113.2	1.5	1.9	8.8	94.8	5.8	6.3	8.3
5	146.2	−2.0	−1.4	−5.3	−0.7	0.2	3.6	72.1	3.3	3.4	4.6	78.9	5.5	6.9	12.2
6	125.9	−2.7	−1.6	−3.3	−0.7	0.2	3.4	88.5	3.4	3.6	4.7	122.3	4.6	5.3	9.3
7	99.8	−3.1	−1.8	−4.1	−1.3	0.1	5.5	232.0	2.2	2.2	11.0	64.2	4.3	5.0	9.7
8	107.1	−3.4	−1.5	−0.4	−0.8	0.3	4.4	58.6	2.5	2.6	5.2	56.6	−3.6	2.6	5.1
9	185.5	−3.4	−2.2	−5.4	−1.1	0.2	5.2	54.8	2.5	2.4	5.0	76.2	2.4	2.4	9.0
10	185.0	−2.4	−1.2	−6.3	−0.8	0.0	2.9	61.8	4.4	4.4	5.2	60.5	5.2	5.9	8.9
Avg.	134.1	−2.8	−1.6	−4.3	−0.9	0.2	4.2	109.2	4.0	4.1	7.0	78.0	4.2	5.3	8.8
Std.dev.		0.5	0.4	1.7	0.2	0.2	1.1		2.5	2.5	2.3	21.0	3.0	1.7	1.8
Population based mean		−2.7	−1.6	−4.3	−0.9	0.2	4.2		4.0	4.1	7.0		4.2	5.3	8.8

K. Eilertsen, L. Nilsen Tor Arne Vestad, O. Geier and A. Skretting, "A simulation of MRI based dose calculations on the basis of radiotherapy planning CT images," Acta Oncologica 47, 1294-1302 (2008).

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Atlas based synthetic CT

- Atlas based synthetic CT (or pseudo CT)
  - Atlas-based Segmentation on MR images
  - Generating New synthetic CT image from Average CT image
  - 1.5T, T2 FSE, GRE, FSE (Whole pelvis)
  - Five fields with nominal energy of 18MV
  - Dosimetric discrepancy < 2%
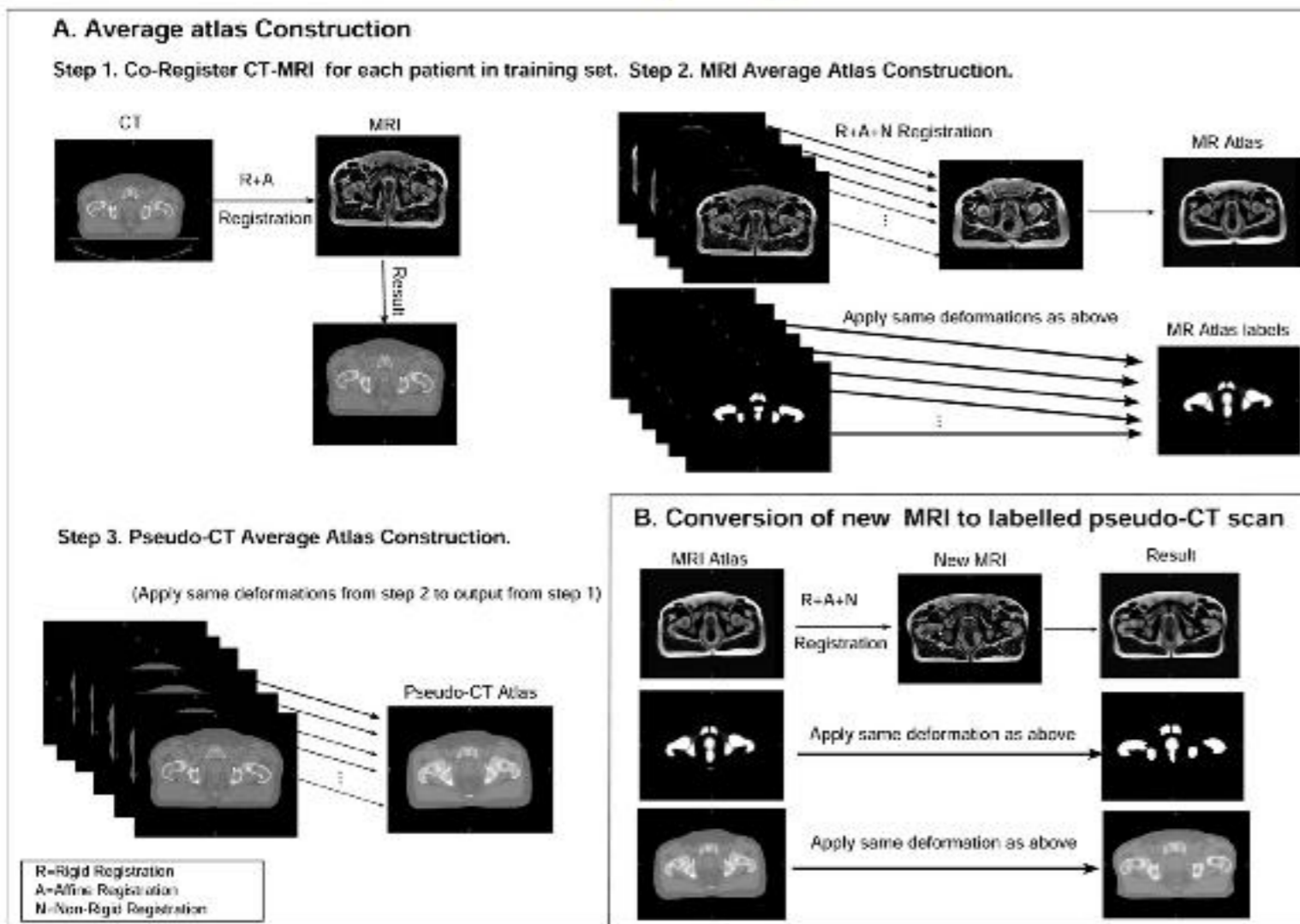
Table 2 Comparison of original CT and pseudo-CT-based HU ($n = 39$)*

Site	CT mean HU ($\pm$SD)	Pseudo-CT mean HU ($\pm$SD)	Two-tailed t-test p value result
Rectum	−54 (4)	−54 (143)	>0.9
Bladder	9 (0)	9 (6)	>0.9
Bone	339 (10)	340 (85)	>0.9
Prostate	42 (1)	42 (25)	>0.9

* The increased standard deviation (SD) in the pseudo-CT is due to the large number of CT scans used to generate the pseudo-CT atlas.

Table 3 Dice similarity coefficient overlapping scores between manual and automatic segmentations for each pelvic organ ($n = 39$)

Site	Mean DSC ($\pm$SD)
Bone	0.79 (0.12)
Prostate	0.70 (0.14)
Bladder	0.64 (0.16)
Rectum	0.63 (0.16)

Abbreviations: DSC= Dice similarity coefficient; SD = standard deviation.

J. A. Dowling, et al., Red Journal **83**, e5-e11 (2012).

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Voxelwise Conversion

- Ultrashort echo time imaging (UTE)

- No contribution of cortical bone in imaging
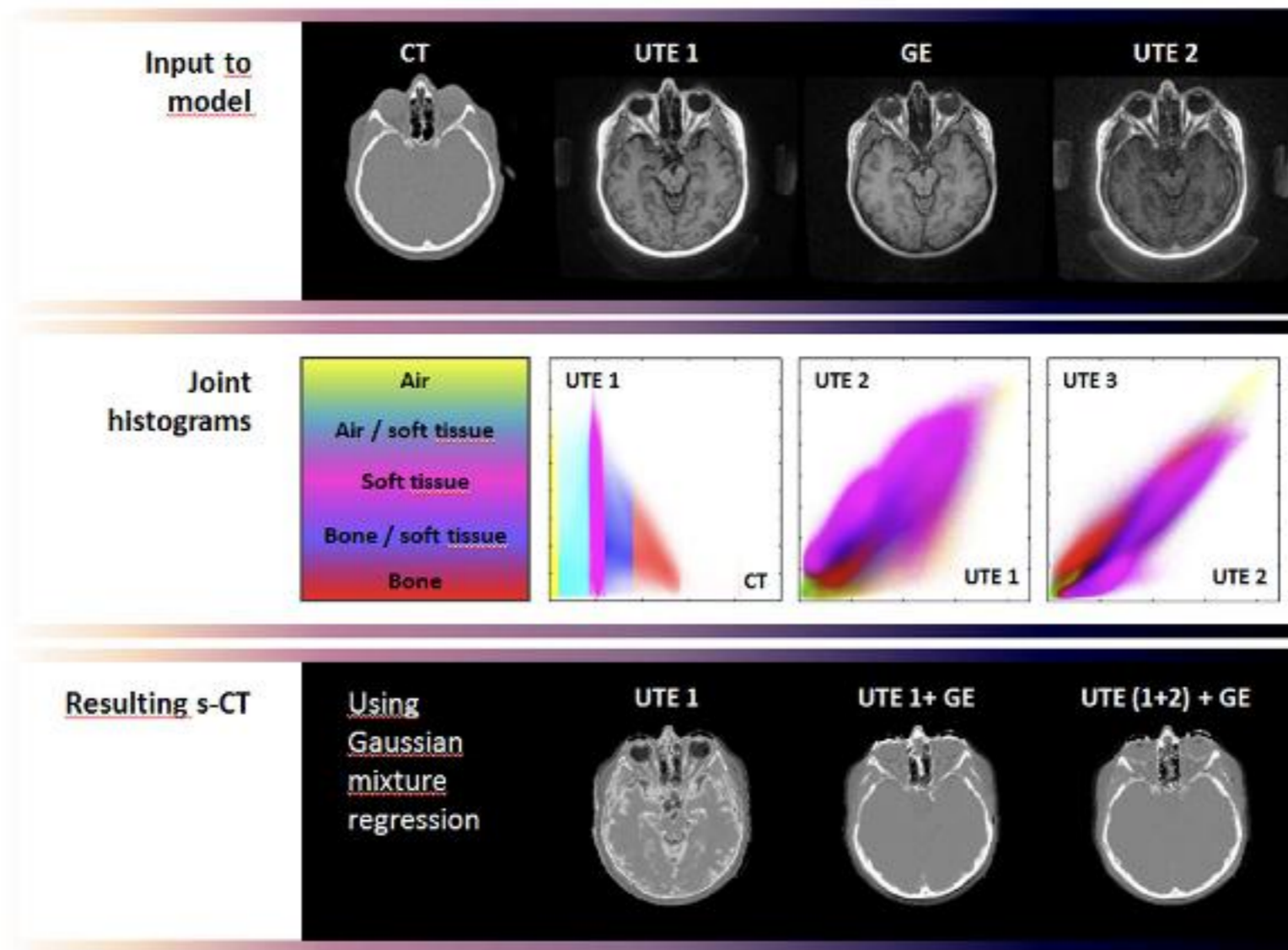
J. H. Jonsson, et al., Radiother Oncol **108**, 118-122 (2013).

Voxelwise Conversion

- Ultrashort echo time imaging (UTE)

- No contribution of cortical bone in imaging

- Intracranial < 0.5%
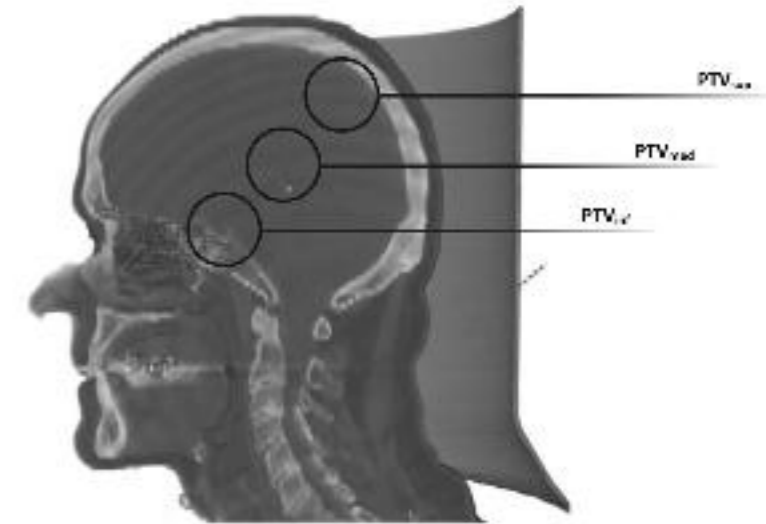
Fig. 1. The placement of the 3 spherical target volumes used in the study.

Table 3
Results from the treatment planning study summarized as the mean percentage point deviation from the CT calculation for each target and image data set over all 5 patients. The gamma index is presented as a mean percentage over all patients.

Target	Data	Isocenter [pp]	D(90) [pp]	V(100) [pp]	Gamma index%		
					3%/3 mm	2%/2 mm	1%/1 mm
PTV$_{inf}$	SCT	0.41	0.86[a]	15.41	97.67	89.29	67.86
	Water	1.62	2.65[b]	46.40[a]	87.23	47.23	20.85
	Bulk	0.00	0.42	6.23	98.18	91.19	68.01
PTV$_{med}$	SCT	0.10	0.23[a]	8.87	97.70	88.74	71.90
	Water	2.59[b]	2.51[b]	50.19[a]	93.00	53.60	22.01
	Bulk	−0.20	0.17	−1.49	98.34	90.41	69.77
PTV$_{sup}$	SCT	0.40	0.10	6.41	97.92	88.22	67.61
	Water	2.71[b]	2.11[b]	31.79[b]	88.41	42.66	16.82
	Bulk	−0.60	−0.69	−12.42	98.37	88.46	64.42

[a] Significant at the 1% level.
[b] Significant at the 0.1% level.

J. H. Jonsson, et al., Radiother Oncol **108**, 118-122 (2013).

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Voxelwise Conversion

- ## Voxelwise conversion, sCT

  - ## Ultrashort echo time imaging (UTE)

  - ## Dual model, Prostate < 0.5%
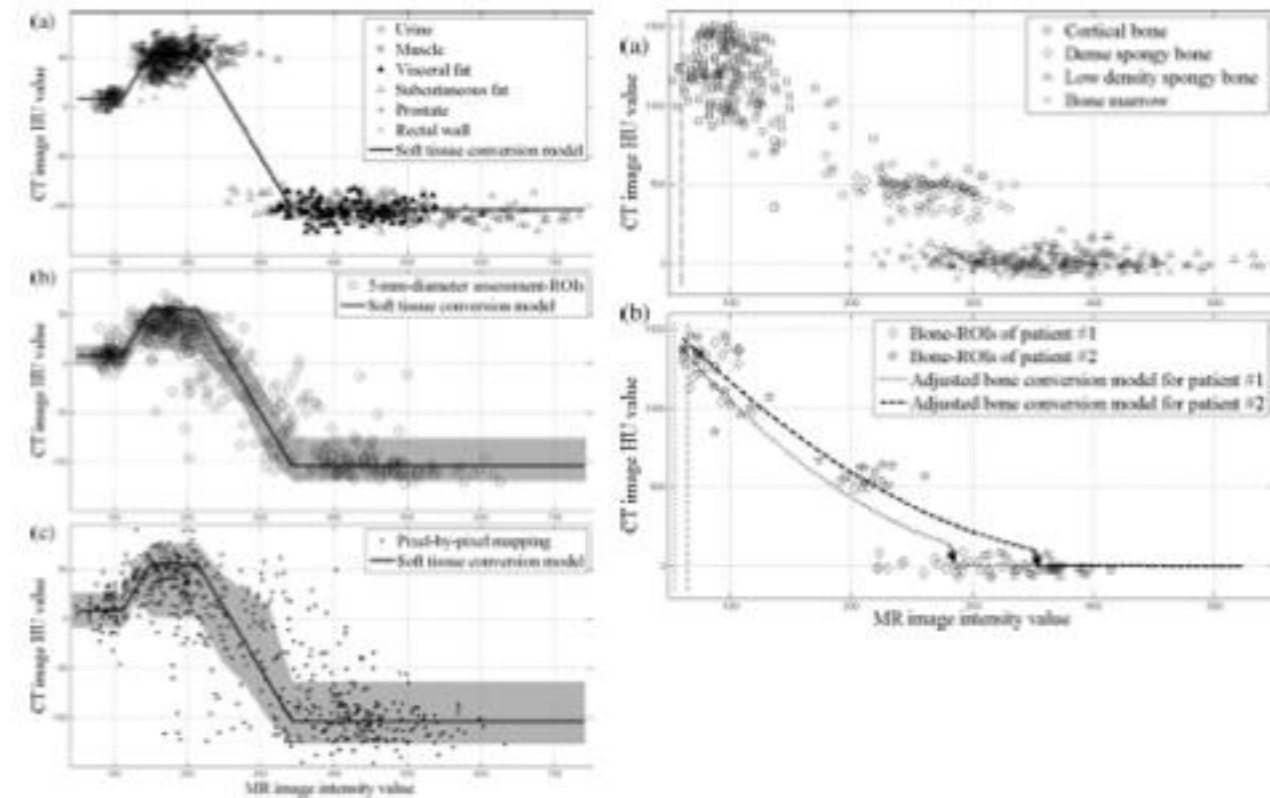
TABLE III. Absolute value deviations in PTV DVH-parameters between RTP images as averages with ± SDs [and ranges] of the test patients.

Plan	PTV volume (%)	CT vs Pseudo (dual model) (%)	CT vs Pseudo (bones only) (%)	t- and F-tests[a] (p_t / p_F)	Pseudo (dual model) vs pseudo (bones only) (%)
IMRT	95	0.3 ± 0.2 [0.1–0.7]	0.8 ± 0.7 [0.2–2.2]	0.01/0.05	0.8 ± 0.5 [0.0–1.5]
	50	0.3 ± 0.2 [0.0–0.7]	0.9 ± 0.7 [0.1–2.3]	0.00/0.04	0.8 ± 0.6 [0.0–1.6]
	5	0.3 ± 0.2 [0.0–0.7]	0.8 ± 0.7 [0.0–2.4]	0.02/0.02	0.8 ± 0.5 [0.0–1.7]
VMAT	95	0.3 ± 0.2 [0.0–0.7]	0.5 ± 0.4 [0.1–1.3]	0.89/0.04	0.4 ± 0.2 [0.0–0.6]
	50	0.3 ± 0.2 [0.0–0.8]	0.7 ± 0.6 [0.0–2.0]	0.05/0.02	0.6 ± 0.4 [0.2–1.4]
	5	0.3 ± 0.3 [0.0–0.8]	0.7 ± 0.7 [0.1–2.2]	0.05/0.02	0.7 ± 0.4 [0.1–1.4]

[a]Statistical tests were conducted to deviations (including signs) in DVH parameters by comparing the deviations between CT and the dual model HU conversion pseudo-CT image with the deviations between CT and bones-only HU conversion pseudo-CT image.

J. Korhonen, et al., Med Phys 41, 011704 (2014).

Conventional Direct Conversion Methods

- Brain and prostate

- Bulk density, <3% in the target

- Recent techniques, <1% in the target

Table Selection of Presented Dosimetric Results for MR-Based Dose Calculations

References	Method	Region	#*	Difference†	Quantification Parameter
Lee et al[15]	Bulk density assignment	Prostate	4	<2.0%	Volume within 60%, 70%, 80%, and 90% isodose levels
Chen et al[32]	Nonheterogeneity corrected	Prostate	15	<2.0%	D95 of prostate volume
Chen et al[4]	Nonheterogeneity corrected	Prostate	15	<2.0%	Isocenter point dose
Prabhakar et al[7]	Nonheterogeneity corrected	Brain	25	< ±1.9%	Mean dose to target volume
Kristensen et al[18]	Bulk density assignment	Brain	11	0.4 ± 0.3%	Isocenter point dose
Eilertsen et al[19]	Bulk density assignment	Prostate	10	<0.5%	Mean dose to CTV
Jonsson et al[17]	Bulk density assignment	Prostate	10	0.2% ± 0.5%	Monitor units to reach prescribed isocenter point dose
Jonsson et al[17]	Bulk density assignment	Thorax	10	0.2% ± 0.4%	Monitor units to reach prescribed isocenter point dose
Lambert et al[13]	Bulk density assignment	Prostate	39	1.6% ± 0.8%	ICRU point dose
Dowling et al[9]	Atlas conversion	Prostate	37	<2.0%	Isocenter point dose
Kapanen and Tenhunen[8]	Direct conversion of bones and density-assigned soft tissue	Prostate	10	< ±1.3%	Dose for all points within PTV
Jonsson et al[28]	Direct conversion	Brain	5	0.4%	Mean isocenter point dose

CTV, clinical target volume; ICRU, International Commission on Radiation Units and Measurements, PTV, planning target volume.
*Number of patients.
†Difference compared with clinical treatment planning.

Machine-Learning based synthetic CT

- Factors which can affect accuracy could be overcome using machine-learning from big-data sets.

Red: False Negative
Blue: False Positive

Brain dataset

Prostate dataset

Real CT plan (100% = 7000)
Synthetic CT plan (100% = 7000)
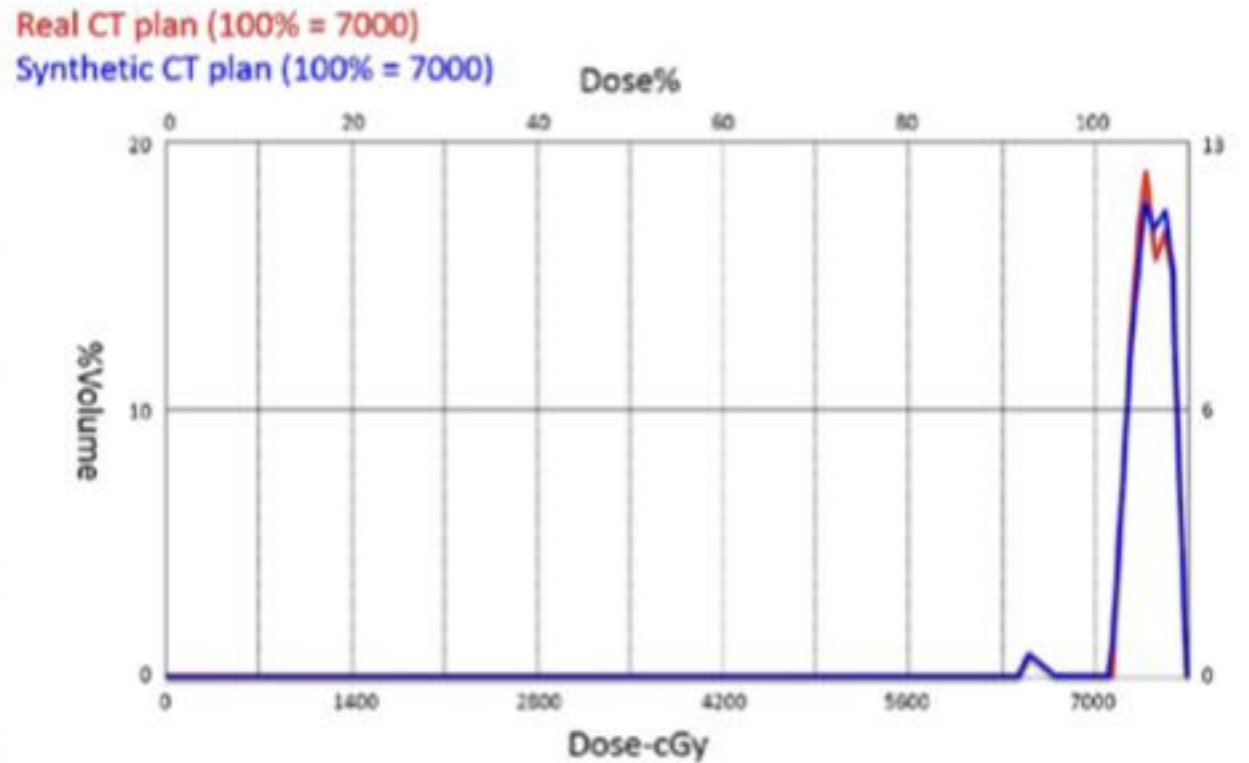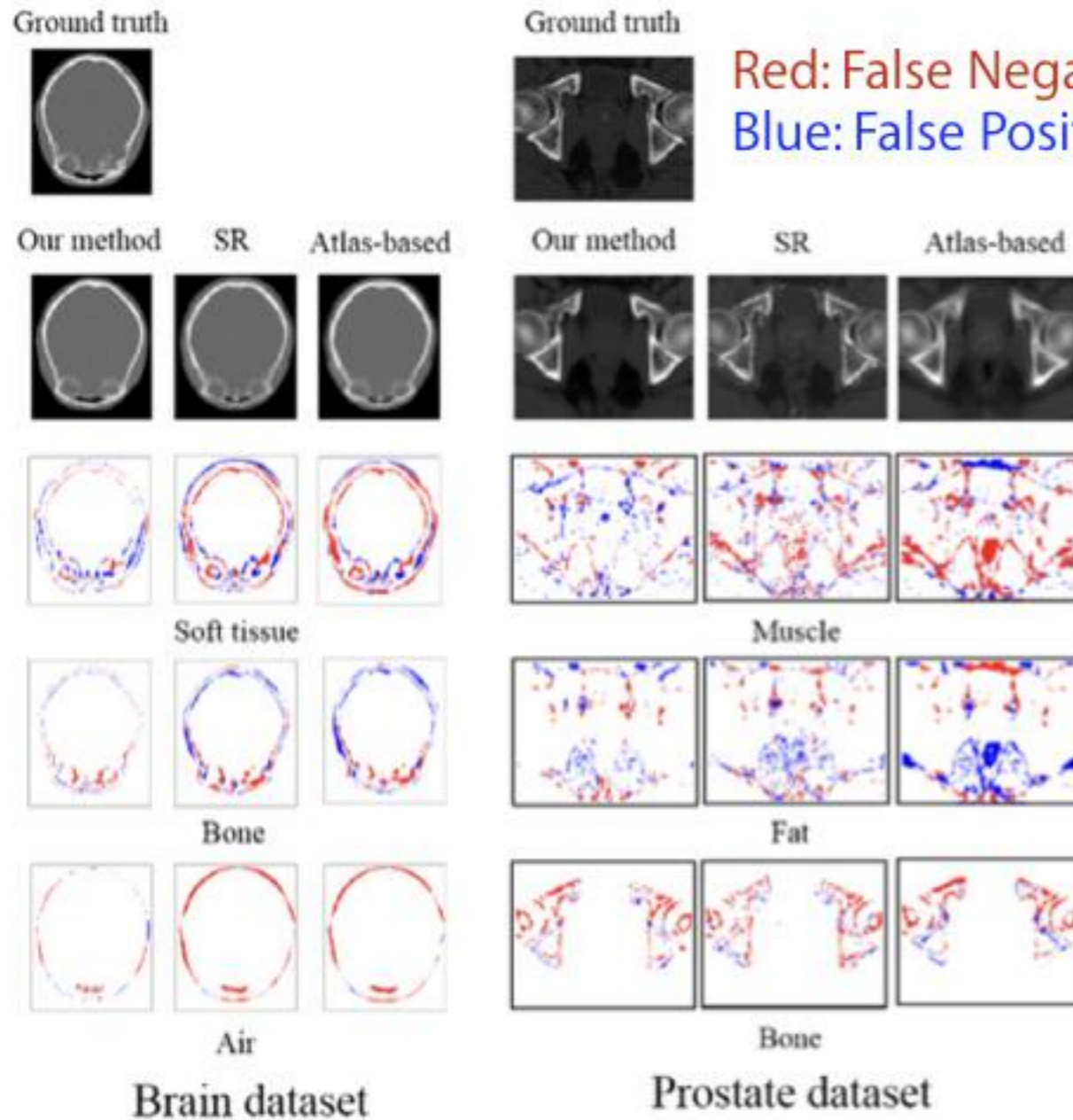
Tri Huynh, et al., IEEE Trans MED Imaging 35 (1) (2016).

Challenge: Four-Dimensional MR

Cine-MRI
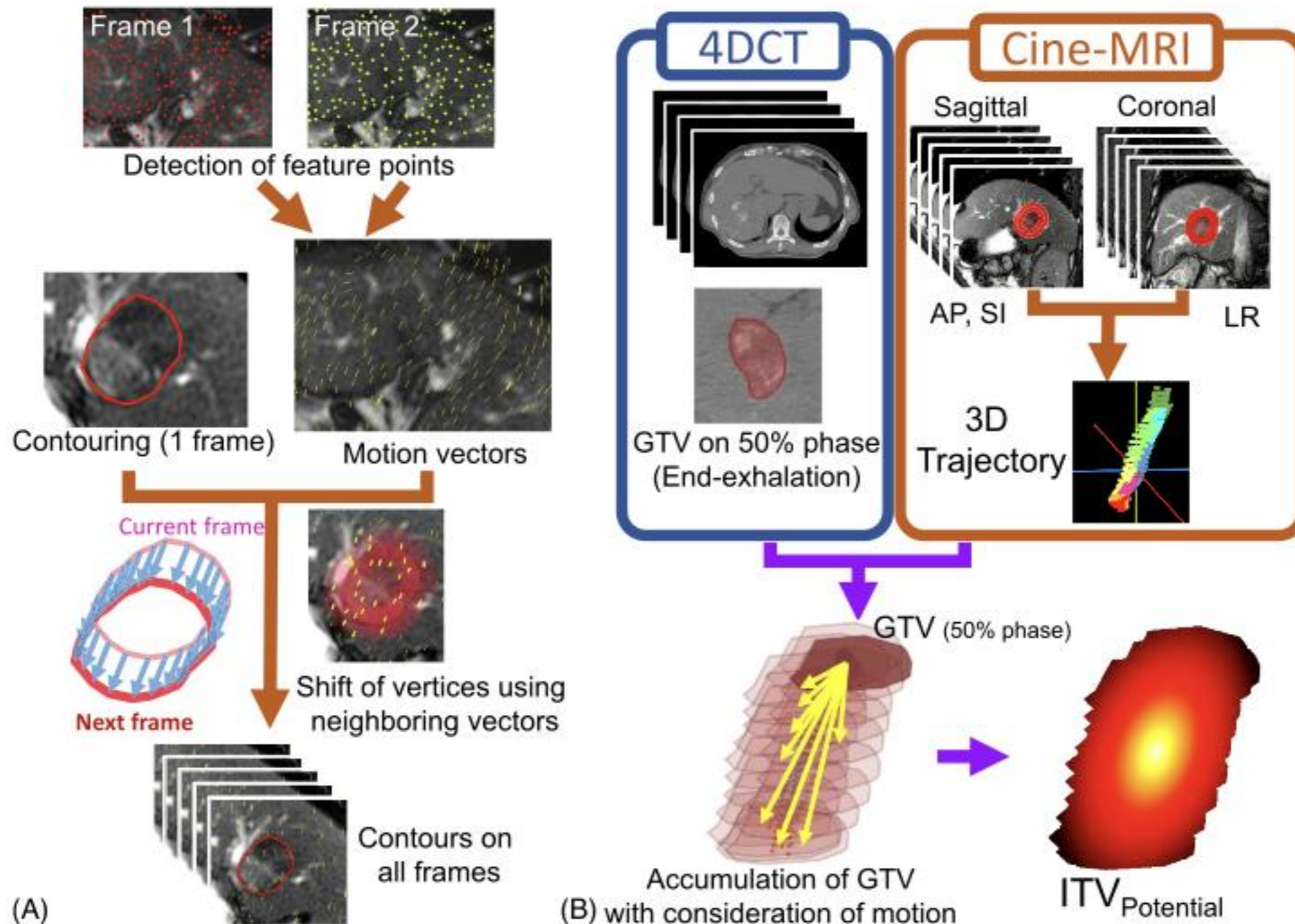
FIG. 1. A flowchart of the (A) automatic estimation of tumor motion on cine-MRI images and (B) calculation of potential ITV (ITV$_{Potential}$) using GTV delineated on 4DCT and motion data derived from orthogonal cine-MRI images. Abbreviation: LR, left–right; AP, anterior–posterior; SI, superior–inferior.

Y. Akino, et al., Med Phys **41**, 111704 (2014).

Body Area with 2D Axial Image
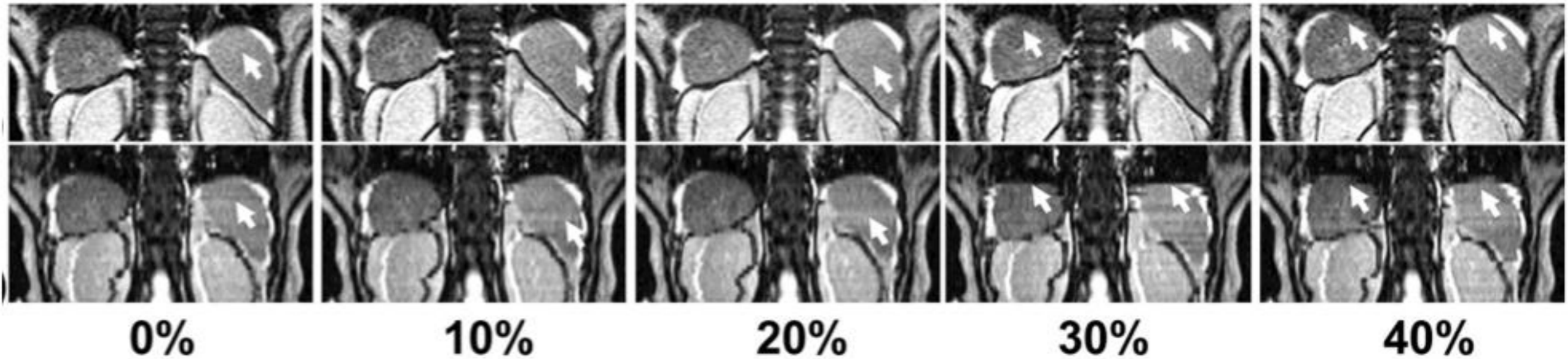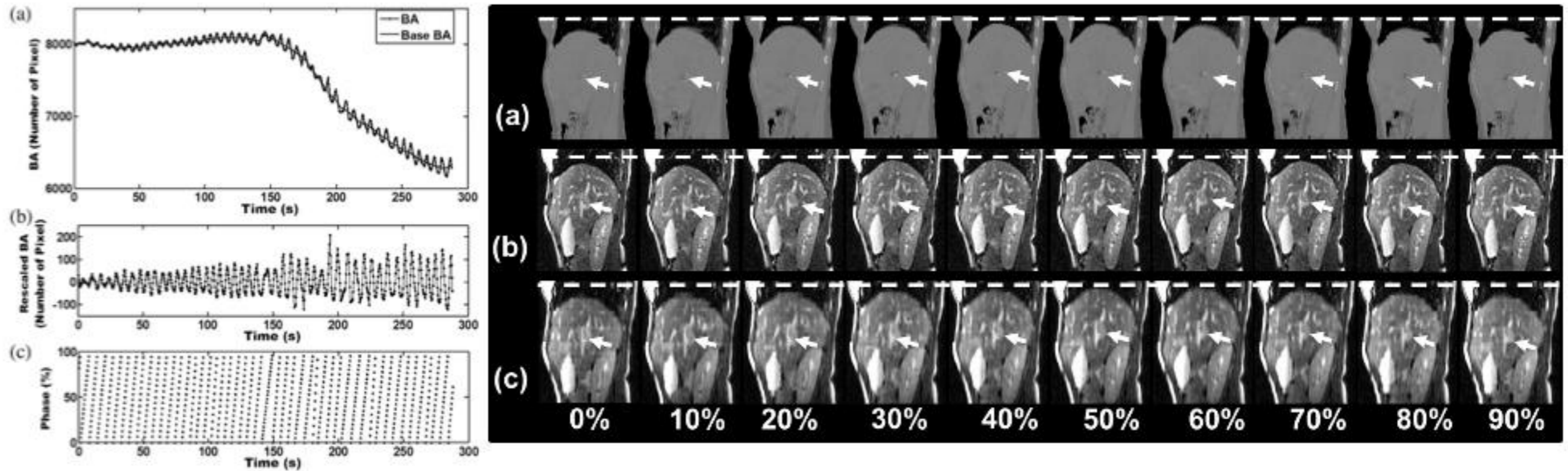
J. Yang, et al., Int J Radiat Oncol Biol Phys **88**, 907-912 (2014).

Navigation Slice
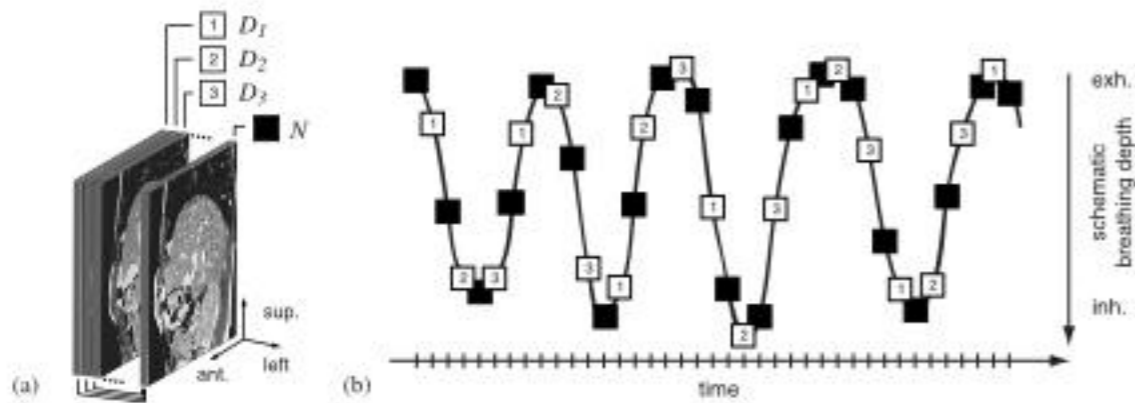
Figure 1. (a) Sagittal slices covering the volume of interest. One dedicated slice N is used as navigator slice for image sorting. (b) Interleaved acquisition of data and navigator frames.

Diaphragm Only

Multi-point Navigation
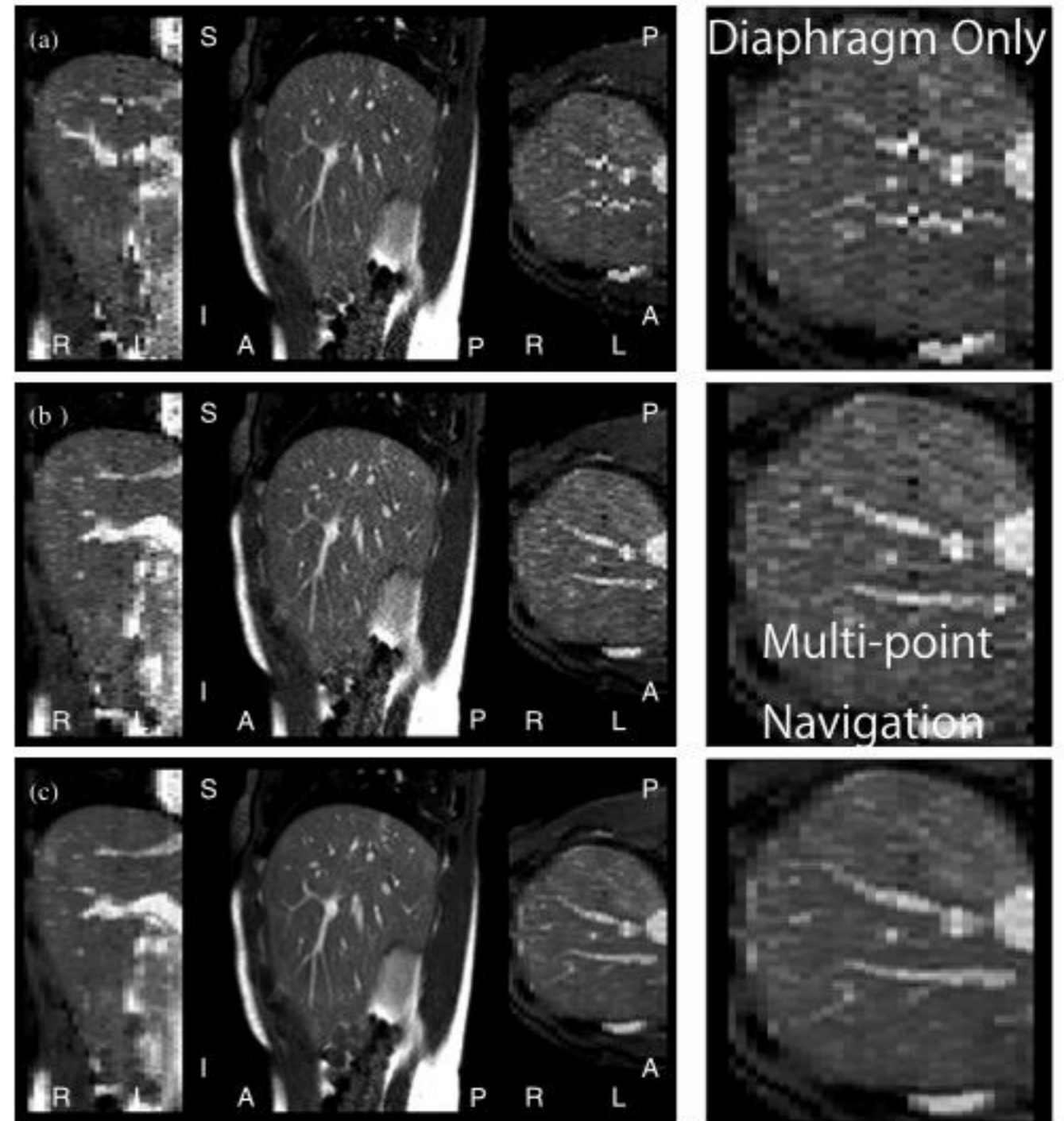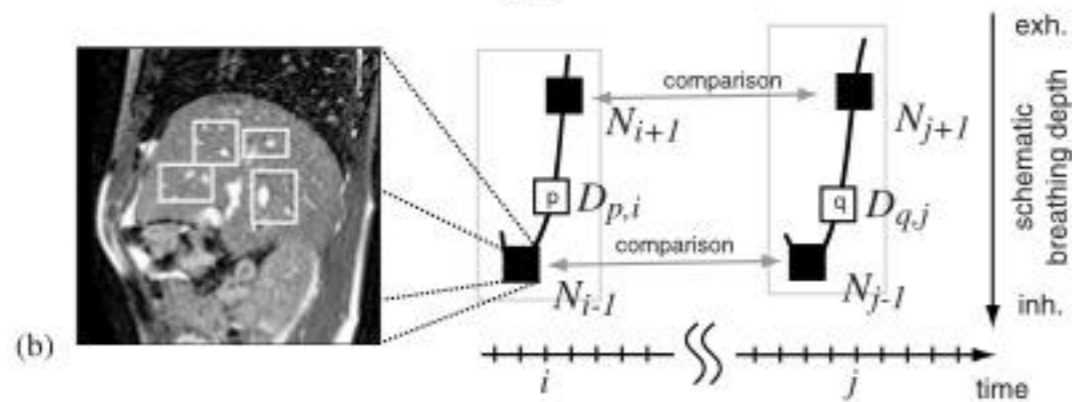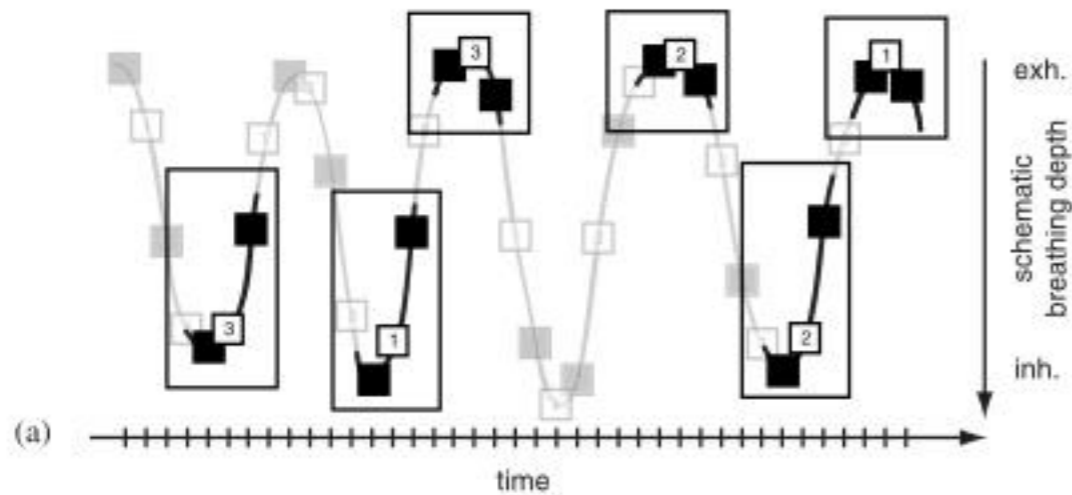
M. von Siebenthal, Phys Med Biol **52**, 1547-1564 (2007).

Our experience

- Physiology signal was used as like 4DCT using RPM.

- However, the axial image were acquired prospectively.
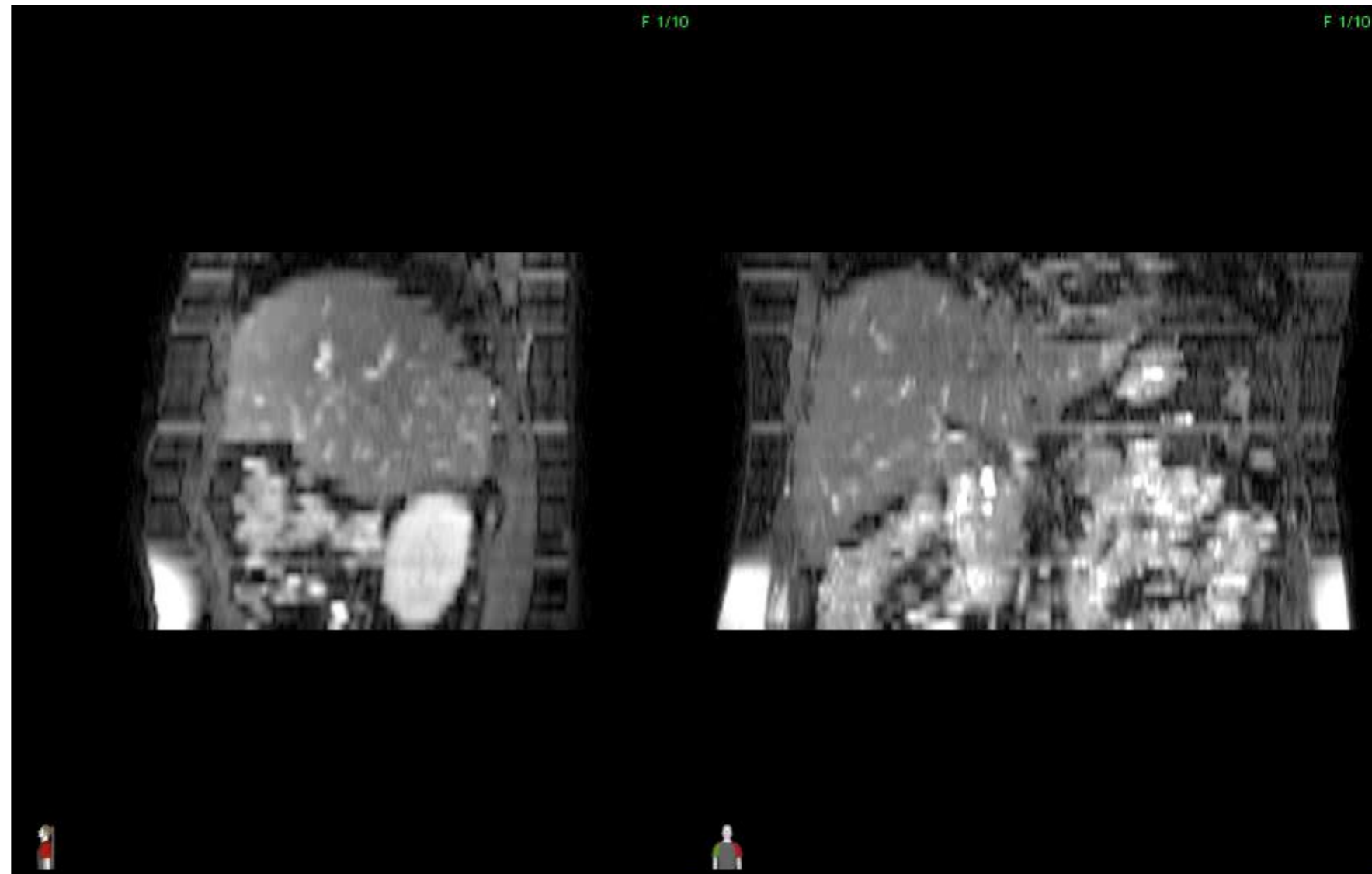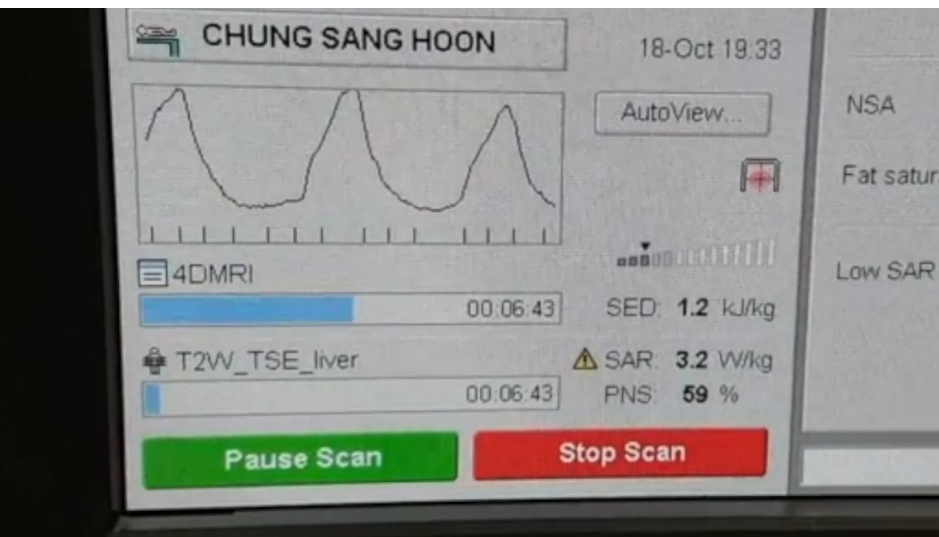
Challenge: Response Evaluation

Response Evaluation

- Role of Diffusion MRI in radiotherapy

    - Mobility of water within tissue at the cellular level without the need of any exogenous contrast agent

    - A sensitive marker for alterations in tumor cellularity and the early assessment of treatment response.

- ADC (Apparent Diffusion Coefficient)

    - DWI acquired with 2 (or more) b-values reflect the local mobility of water molecules calculated on a pixel-by-pixel basis

- DAI (Diffusion Abnormality Index)

    - A diffusion abnormal probability accounting for both of these changes was generated for each tumor voxel and then summed altogether

DAI and DWI
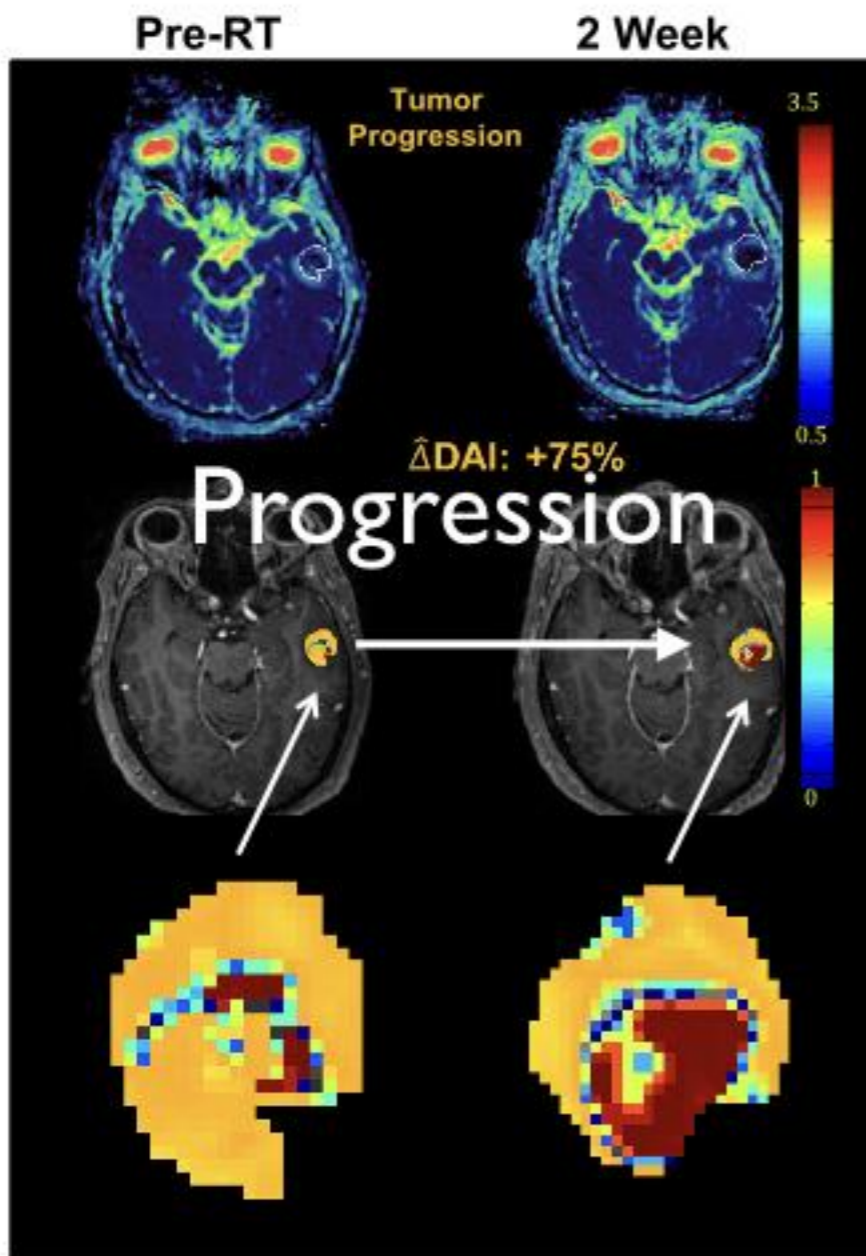
Diffusion abnormality index (DAI) of a patient with a brain metastasis treated with whole-brain radiation therapy. DW-MRI was obtained both pre-RT (left column) and post-RT (right column). Top row: color-coded ADC maps, middle row: DAI maps, and bottom row: zoomed DAI maps of the tumor. The tumor volume showed no significant change between pre-RT and post-RT. However, the DAI increased by 75% from pre-RT to post-RT, suggesting tumor progression which was confirmed by post-Gd T1-weighted MRI 1 month post-RT.

R. Farjam, et al., Practical radiation oncology **3**, S5 (2013).

Region of interest (ROI) drawing on an apparent diffusion coefficient (ADC) map. Two radiation oncologists measured ADC values of target hepatocellular carcinoma (HCC) in reference to other diffusion images.

J. I. Yu, et al., Red Journal **89**, 814-821 (2014).

Normal Tissue Damage

- Radiation-induced hepatocytes injury

- Hepatobiliary phase images of Promovist enhanced MRI

- Correlation of dose to changes in signal intensity between pretreatment and follow-up MRI
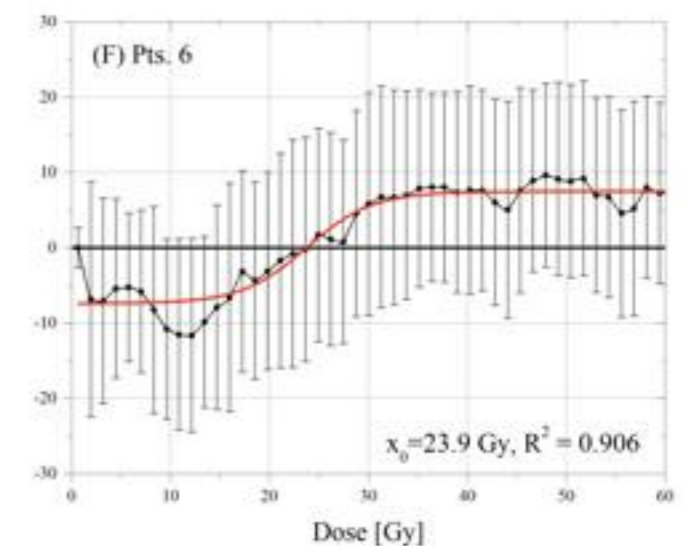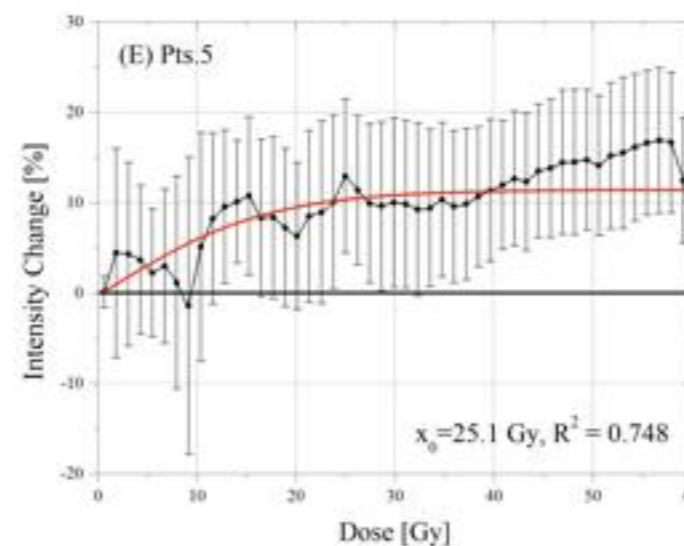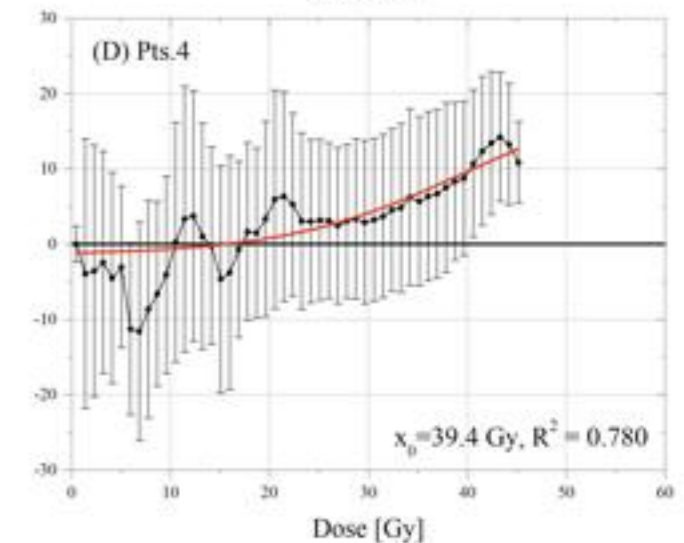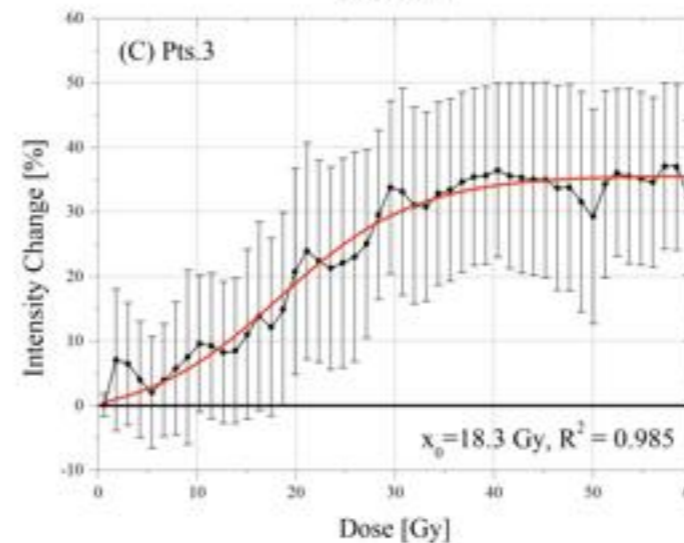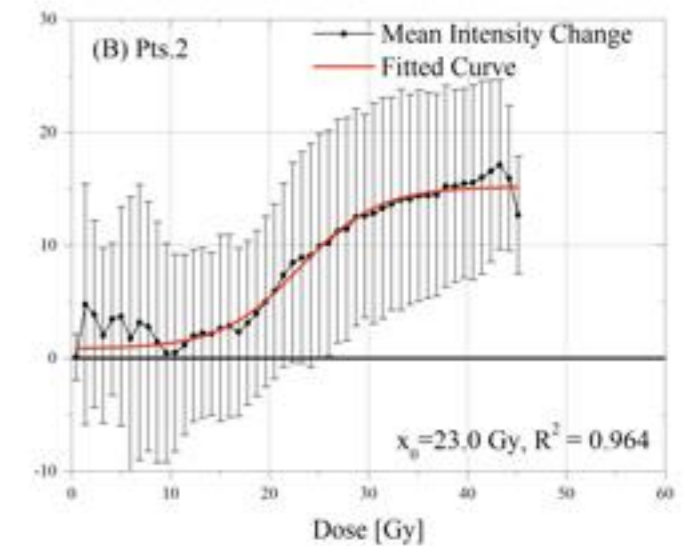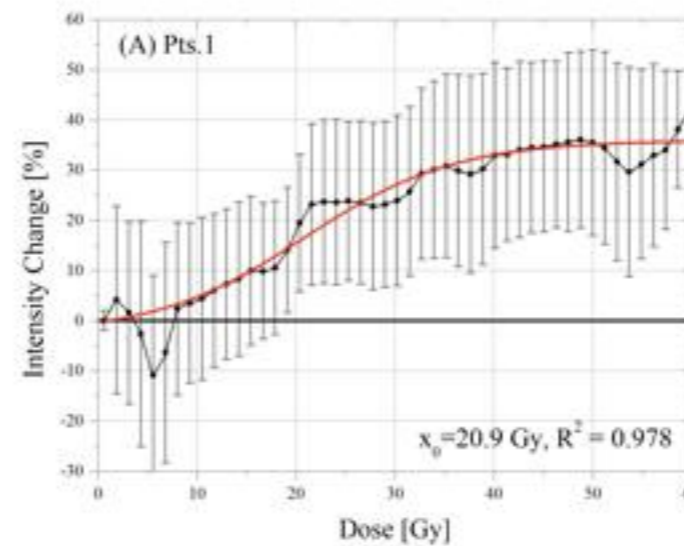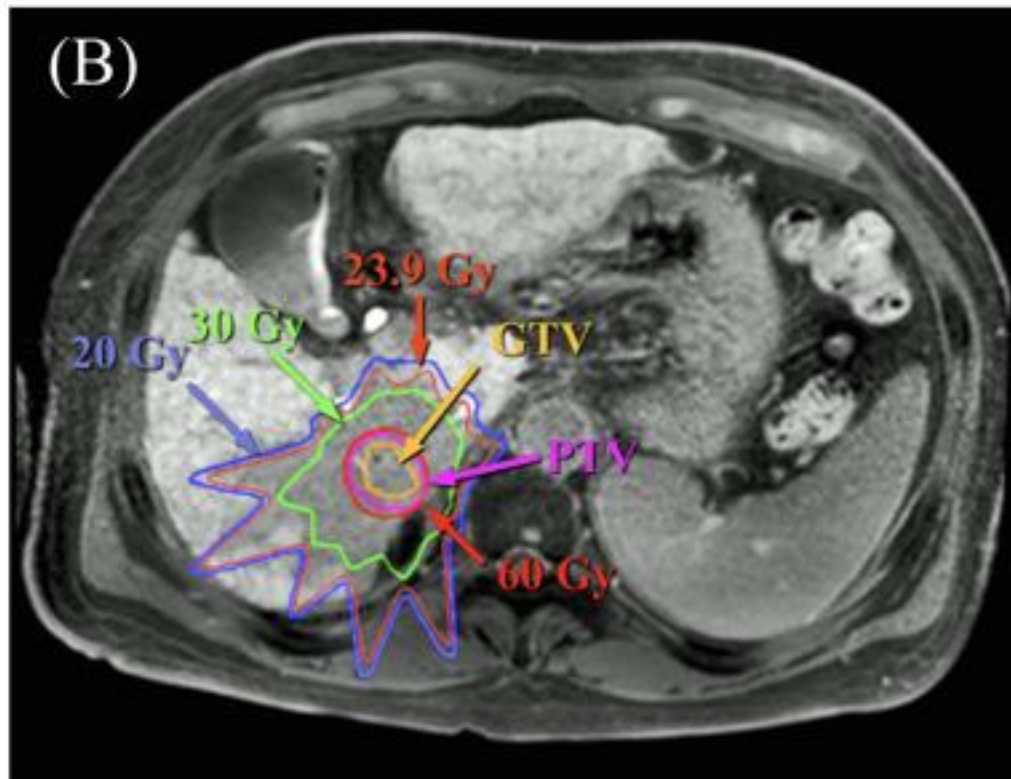
Estimation of Normal Liver Function

Quantitative signal intensity

$$ER\text{-}SI\text{-}s = \frac{(SI_{liver}/SI_{spleen})_{post} - (SI_{liver}/SI_{spleen})_{pre}}{(SI_{liver}/SI_{spleen})_{pre}} \quad (2)$$

$$ER\text{-}SI\text{-}m = \frac{(SI_{liver}/SI_{muscle})_{post} - (SI_{liver}/SI_{muscle})_{pre}}{(SI_{liver}/SI_{muscle})_{pre}} \quad (3)$$

$$ER\text{-}SI\text{-}c = \frac{(SI_{liver}/[SS \cdot RSS])_{post} - (SI_{liver}/[SS \cdot RSS])_{pre}}{(SI_{liver}/[SS \cdot RSS])_{pre}} \quad (4)$$
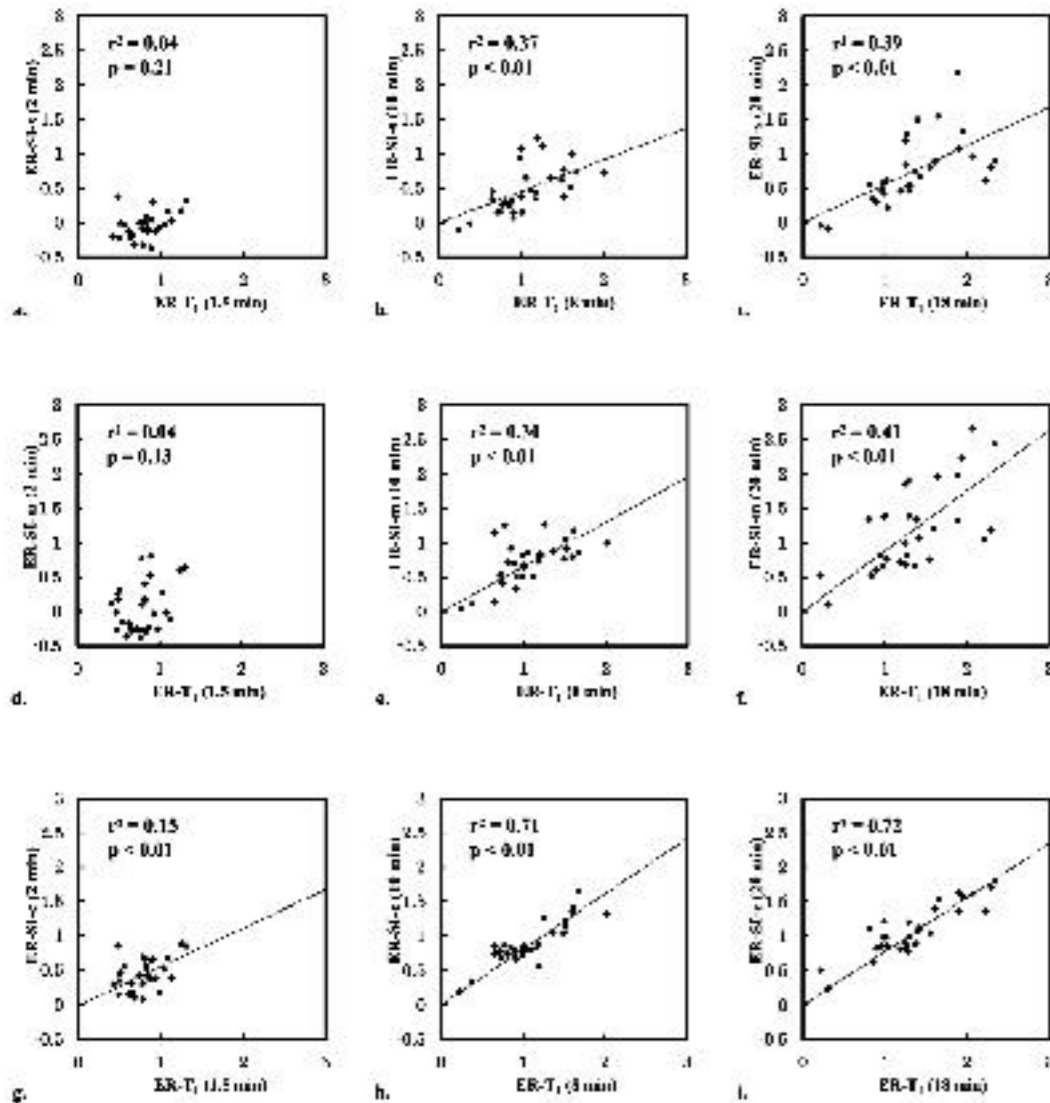
Fig. 3. Graphs showing the correlation of ER-T1 with ER-SI-s (a)-(c), ER-SI-m (d)-(f), and ER-SI-c (g)-(i) determined by liner regression analysis (a, d, g) for all 30 patients. Comparison of ER-T1 at 1.5 min and ER based on signal intensity (SI) 2 min after Gd-EOB-DTPA administration. (b, e, h) Comparison of ER-T1 at 8 min and ER based on SI 10 min after administration. (c, f, i) Comparison of ER-T1 at 18 min and ER based on signal intensity 20 min after administration. Dotted lines are the regression lines.

M. Onoda, et al., Eur J Radiol **84**, 339-345 (2015).

Contrast agent specific T1 relaxometry
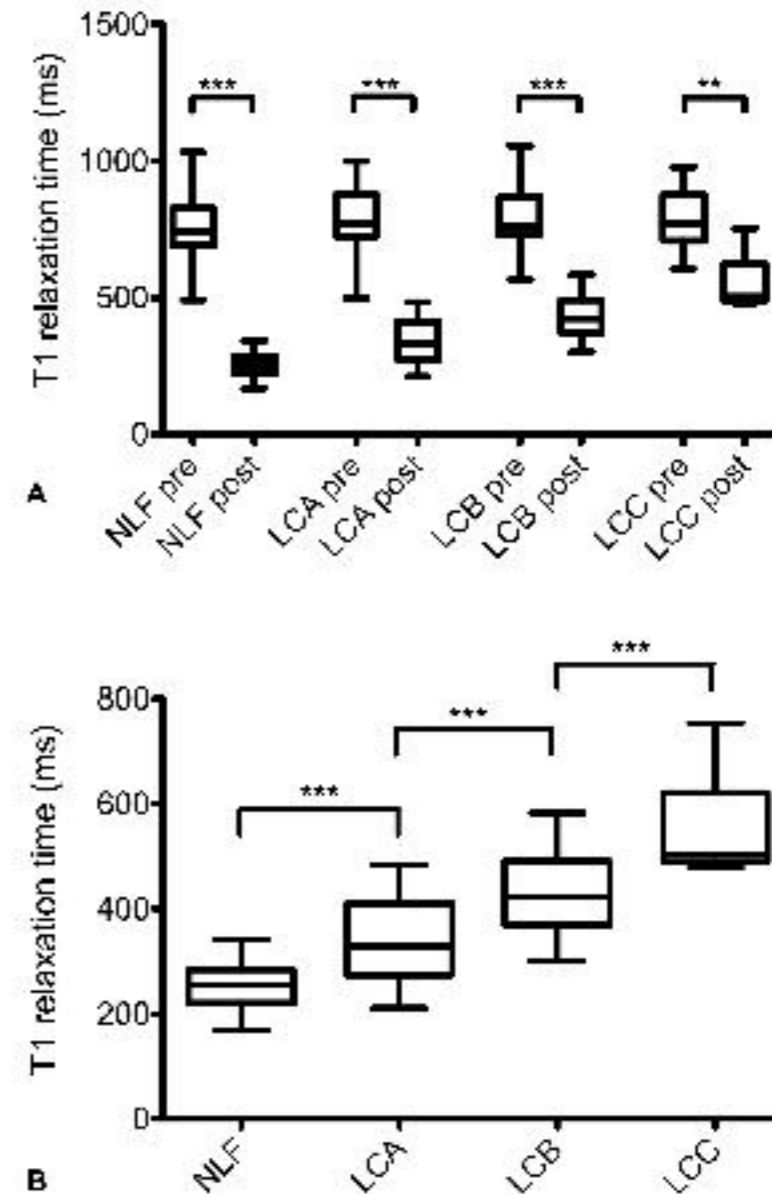
Figure 1. Pre- and post-contrast T1 relaxation times. (A) Boxplots indicating T1 relaxation times before (pre) and after (post) Gd-EOB-DTPA administration in patients with normal liver function and in patients with liver cirrhosis Child-Pugh A, Child-Pugh B, and Child-Pugh C. After contrast medium administration, T1 relaxation times were significantly reduced in each group. (B) Boxplots indicating T1 relaxation times after Gd-EOB-DTPA administration in patients with normal liver function and in patients with liver cirrhosis Child-Pugh A, Child-Pugh B, and Child-Pugh C. T1 relaxation times increased significantly with increased progression of liver cirrhosis.
NLF: normal liver function; LCA: liver cirrhosis Child-Pugh A; LCB: liver cirrhosis Child-Pugh B; LCC: liver cirrhosis Child-Pugh C. Data given as mean T1 reduction rate ± standard deviation. Tukey's adjustment was used to generate Boxplots, and the Wilcoxon-Test was used to compare groups.

M. Haimerl, et al.,PloS one **8**, e85658 (2013).

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Challenge: MR-Guided RT

MRgRT

- MRgRT in Princess Margaret Cancer Centre

- 1.5T MRI based external radiotherapy and brachytherapy
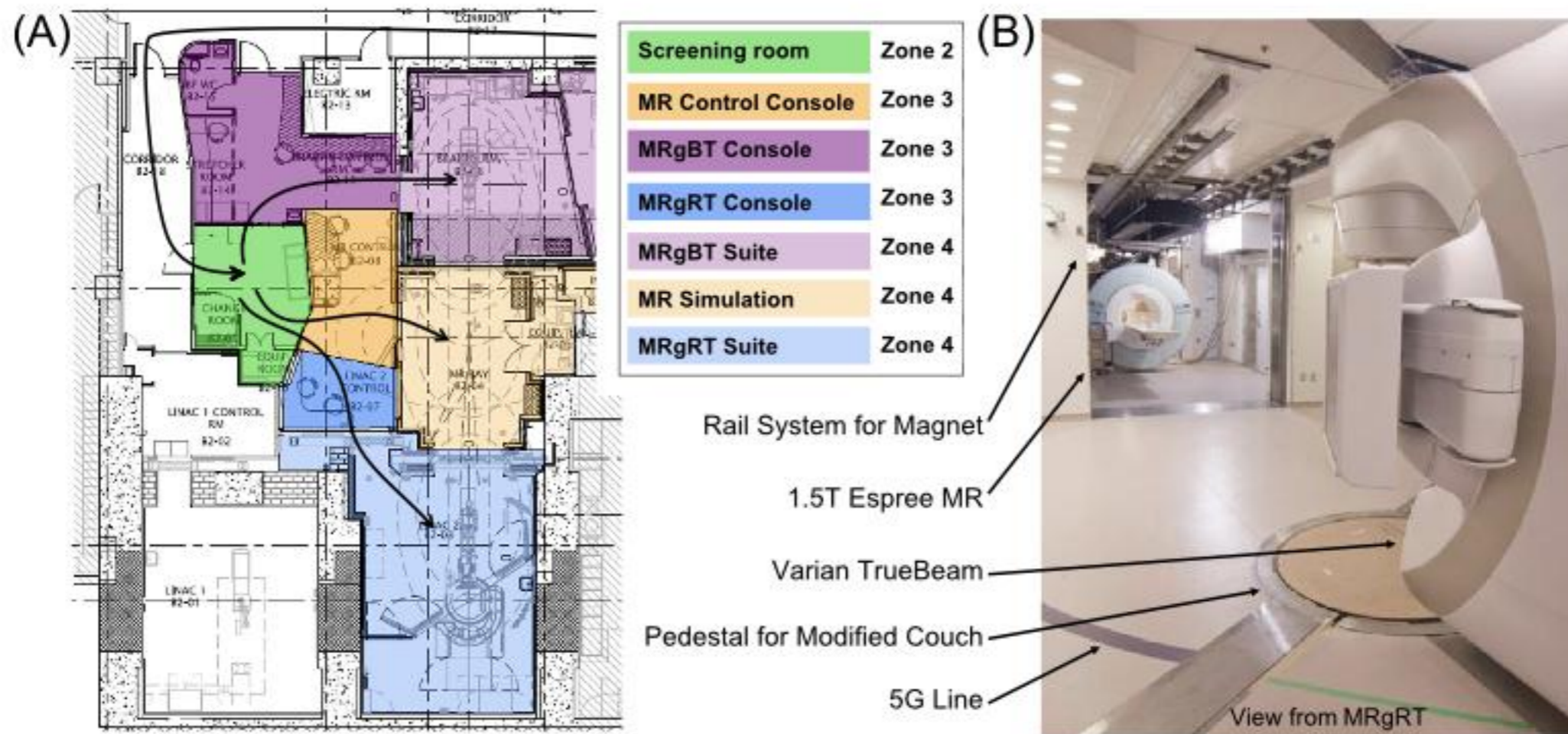
Figure (A) Floor plan and safety zones of the MR-guided RT facility at the Princess Margaret Cancer Centre showing brachytherapy, imaging, and external-beam RT suites. (B) Photograph of the accelerator and MR scanner in the facility. The magnet is advanced on the rail system into the MRgRT suite, and the patient is positioned via a modified treatment couch. At nearest approach, the magnet to linear accelerator isocenter distance is 3.1 m.

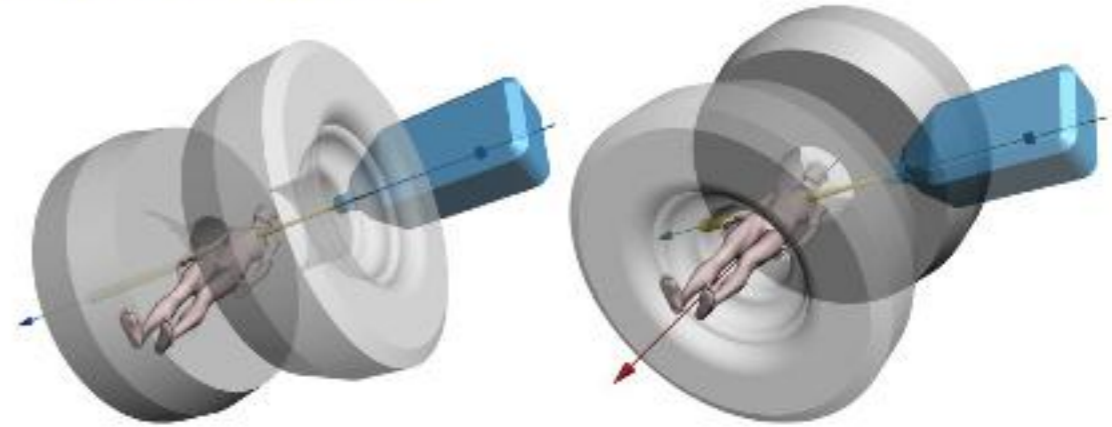# Challenges: Rotating biplanar linac

Cross Cancer Institute, University of Alberta, Edmonton, Alberta, Canada.

Sydney Medical School, The University of Sydney, New South Wales, Australia.
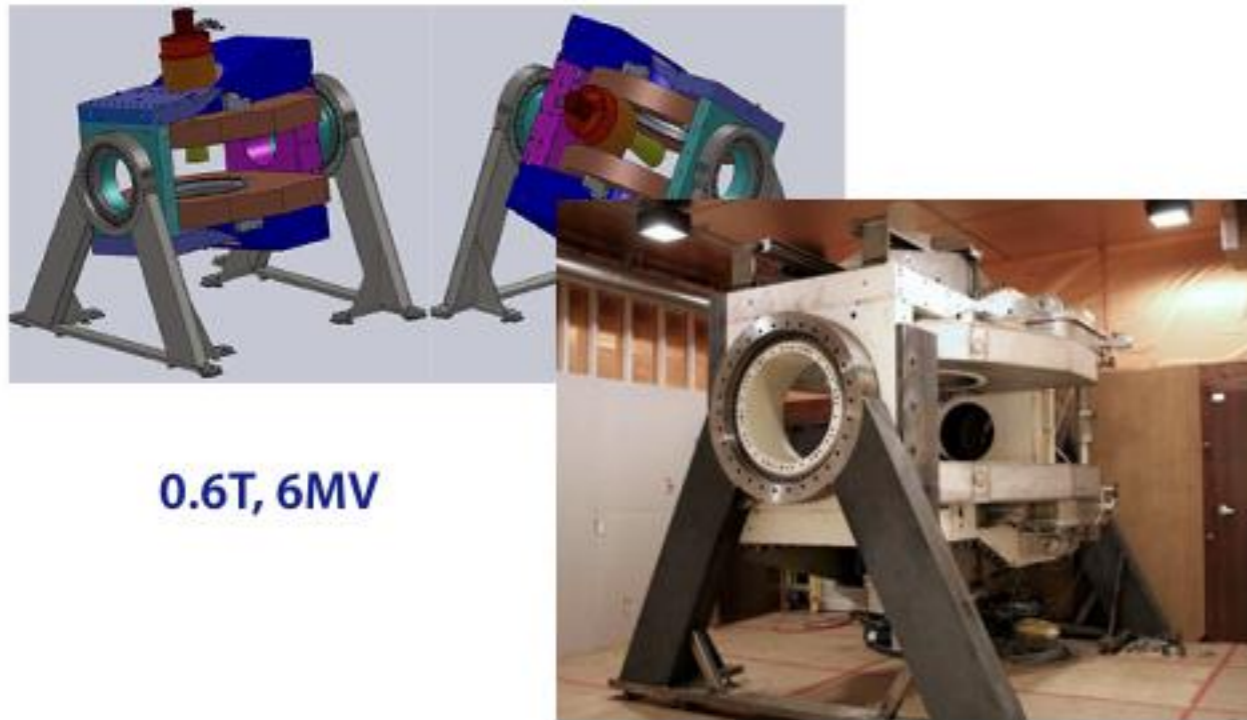
0.6T, 6MV

Figure 1 (Left) The inline orientation, that is, linac aligned with B_0. (Right) The perpendicular orientation, that is, linac perpendicular to B_0. Both the orientations are to be experimentally investigated. (Adapted with permission from Constantin et al.[5]) (Color version of figure is available online.)

1.0T, 6MV

Table 2 A Comparison of the Advantages of the Inline and the Perpendicular Approaches that Will be Experimentally Investigated

Advantages of the Inline Approach (Fig. 1, Left)	Advantages of the Perpendicular Approach (Fig. 1, Right)
No beam attenuation and Compton scatter to the patient from irradiation through the cryostat (if closed bore)	More similar design to mass-produced conventional MRI systems (if closed bore)
Less effect of the B field on electron gun operation	Lower constraints on magnet, gradient coil, and RF design, resulting in higher potential imaging performance and higher B field (if closed bore)
Less effect of the B field on waveguide operation	Lower skin dose
Less effect of the B field on electron transport within the patient: sharper penumbra and no electron return effect	No need to rotate the magnet or the patient
Lower exit dose	
Linac fixed with respect to the magnet. This reduces the need to manage eddy currents or dynamic shimming requirements, where the linac moves with respect to the magnet	

Abbreviation: RF, radiofrequency.

Challenges: MRI with linac

- UMC Utrecht, Utrecht, The Netherlands.

- 1.5T MRI and 6MV (Philips and Elekta)

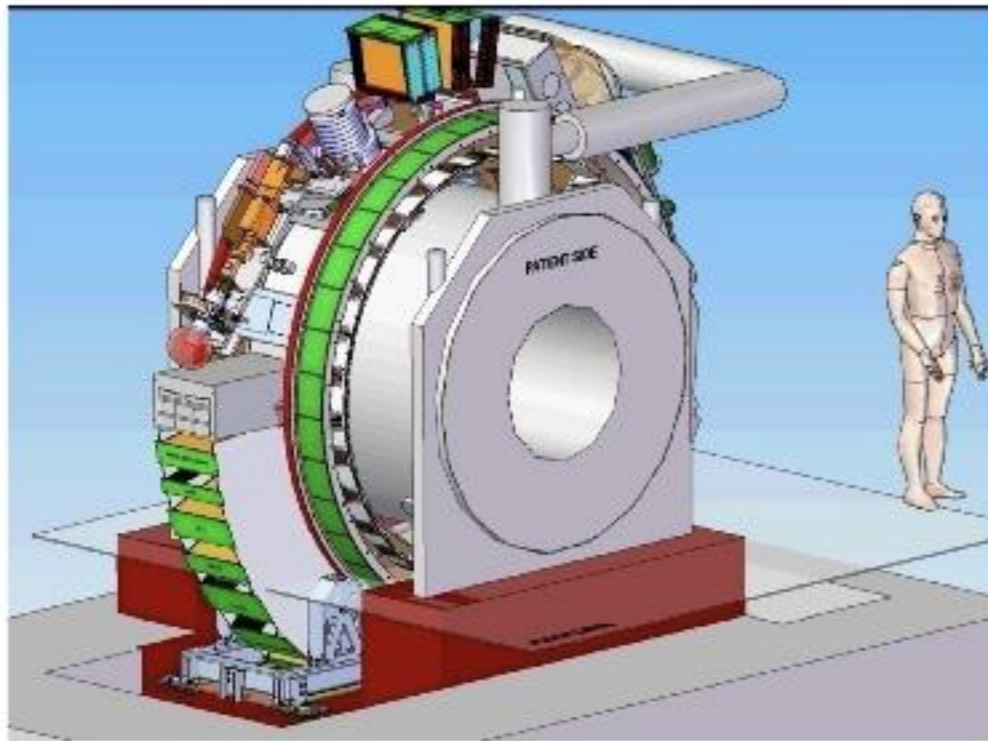- Installation started at June 12, 2014

Figure 2 Schematic design of the combined MRI-linac system. (Color version of figure is available online.)

S. Crijns and B. Raaymakers, "From static to dynamic 1.5T MRI-linac prototype: impact of gantry position related magnetic field variation on image fidelity," Phys Med Biol **59**, 3241-3247 (2014).

MRI-Linac

- Canada, Australia, and Netherland (USA)

- Realtime imaging with higher contrast and resolution

- Clinical effectiveness - Being validated

- Technical aspects - Potential benefits

Table 1

Authors	Jaffray et al	Mutic et al	Fallone	Keall et al	Lagendijk et al
Field strength (Tesla)	1.5	0.35	0.56	1	1.5
Radiation source	6 MV	Co-60	6 MV	6 MV	6 MV
In-line imaging	No	Yes	Yes	Yes	Yes
Clearance	70-cm bore	70-cm bore	85-cm open bore	82-cm open bore	70-cm bore
Install requirement	Adjacent MRI suite	Conventional bunker	Conventional bunker	Conventional bunker	Conventional bunker

ViewRay

- Three ^{60}Co sources and 0.35T MRI

- Cons

  - Low T (increasing SNR)

  - ^{60}Co - lower output, less penetration, larger penumbra, and higher surface doses

- Pros

  - IMRT optimization mitigates the issues with penetration and penumbra

  - Surface dose is greatly lowered by the MRI magnetic field sweeping away contamination electrons

MRIdian.avi

MRIdian

- 0.35T MRI, 70 cm bore, 6MV FFF Beam linac, 1100 MU/min

- 27.4 cm x 24.1 cm

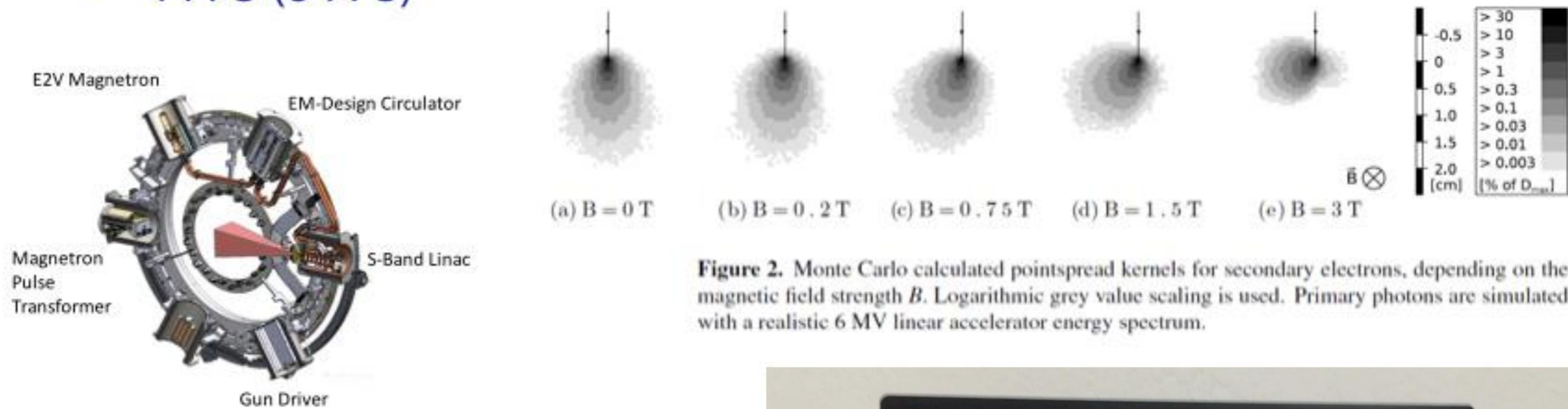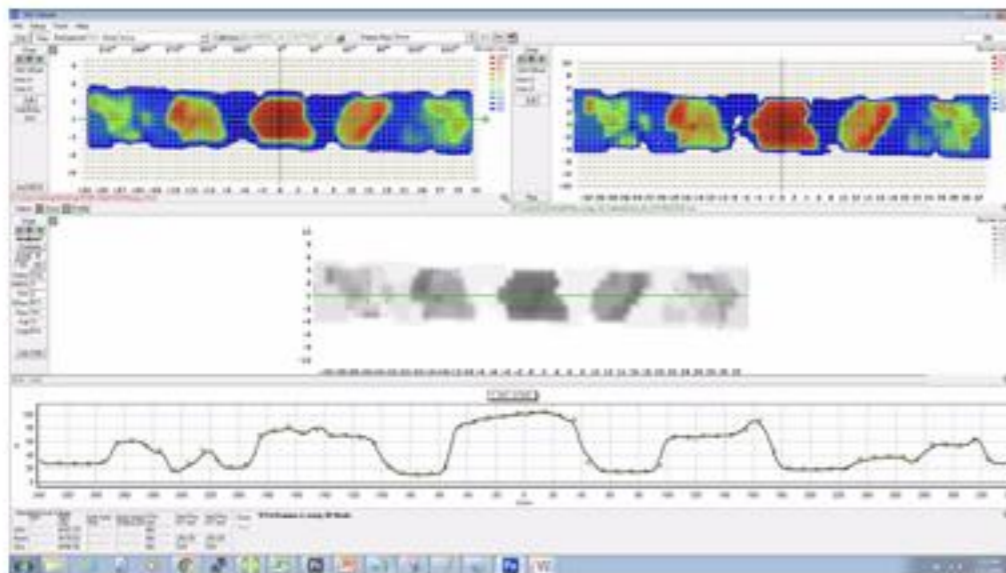- Conventional (3D), IMRT, and SBRT delivery

- 4 FPS (8 FPS)

Figure 2. Monte Carlo calculated pointspread kernels for secondary electrons, depending on the magnetic field strength *B*. Logarithmic grey value scaling is used. Primary photons are simulated with a realistic 6 MV linear accelerator energy spectrum.

Courtesy of Justin C Park

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Summary

- Use of MRI in RT process could increase accuracy of delineation of target volume, and could be reduce complication of normal organs due to reduction of irradiated volume potentially.

- Integration of MRI into Treatment Planning

    - Dose discrepancy in MR based treatment planning could shows good agreement with less than 1%.

    - MR simulation should be established carefully: geometrical distortion due to magnetic field strength, RF coil etc

- Near future, MR-Only RT process including in-room image-guidance and real-time imaging could be established.

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