MR Simulation and MR-only planning

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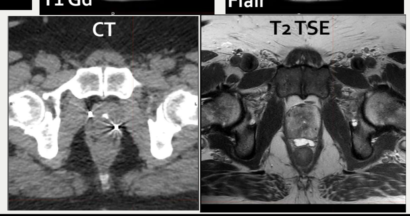
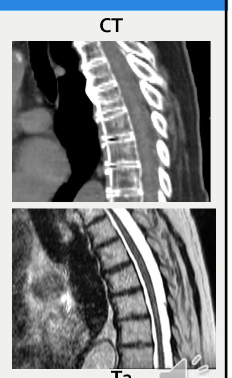
Disclosure

- Collaborative research agreement with Philips Healthcare

Advantages of MR in RT





- Superior soft tissue contrast
- Wealth of additional anatomy and pathology information

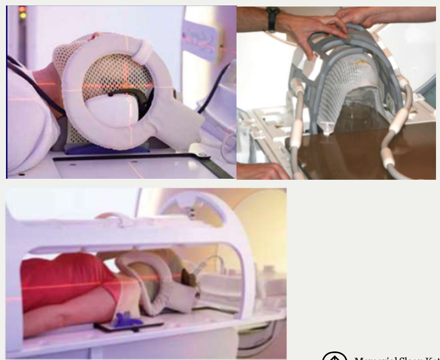
Major differences from Diagnostic MR

	Diagnostic MRI	Rad Onc MR simulation
Purpose	Detection, characterization and staging of disease	Determining geometrically the true disease extent relative to adjacent OARs
Acquisition parameters	Reduced FOV	Large FOV
	Slice thickness 4-5mm, interslice gaps, Non-axial/Oblique	Thin, non-oblique axial slices
	Readout bandwidth (RBW): tradeoff between SNR and fat/water shift	High RBW: reduce water/fat shift and susceptibility artifacts, and distortion
	Image distortion and artifacts not as crucial	Distortion and image artifacts need to be quantified and corrected
Hardware	Curved couch	Flat couch for immobilization devices
	Optimized receiver coils for each imaging site	Non-ideal coil configurations to mimic RT setup
	No external lasers	External lasers for marking/leveling

Coil configurations

Diagnostic MR

Dedicated Rad Onc MR simulation



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Coil configurations

Diagnostic MR

Dedicated Rad Onc MR simulation

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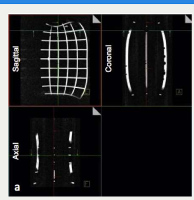
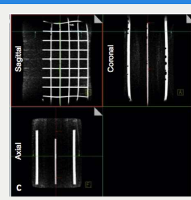
Geometric Distortion mitigation

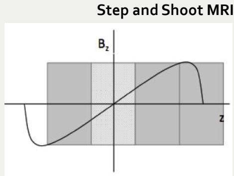
No distortion correction

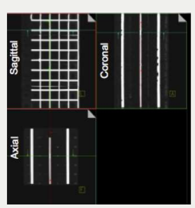


Vendor 3D distortion correction



Step and Shoot MRI





Major contributor: Gradient non-linearity

Paulson et al., Medical Physics 42(1) 2015:28-39

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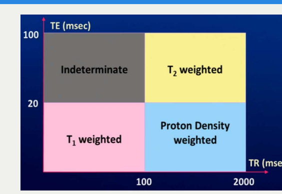
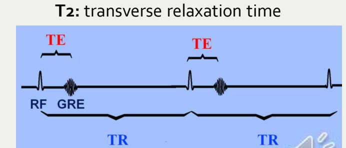
General Sequence overview

- **T1-weighted**: gross structural information. tumor volume, lymph node involvement and OAR
- **T2-weighted:** pathological information. fat/fluid infiltration
- **Post contrast T1-weighted**: differentiate between tumor enhancement and fat/edema
- **Diffusion weighted imaging**



T1: longitudinal relaxation time
T2: transverse relaxation time



Metcalfe et al., Tech Can Res & Treatment, 2013

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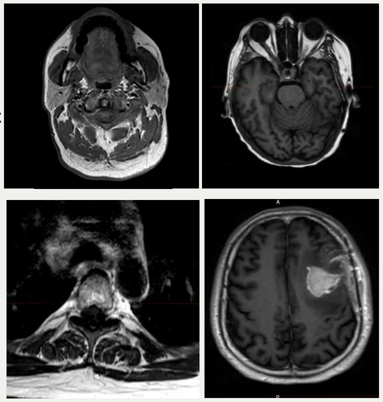
T1 pre and post Gd contrast

T1 Pre-contrast

T1 Post contrast



- Tumor
  - Gd contrast serves as T1 shortening agent, enhancing the tumor volume
- Organs-at-risk (OAR):
  - Nerves
  - axillary lymph nodes
- Prostate post biopsy hemorrhage
- Post operative blood products

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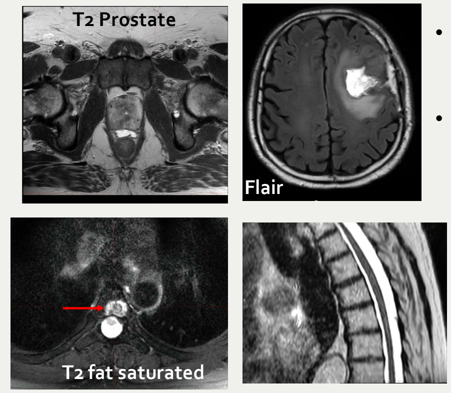
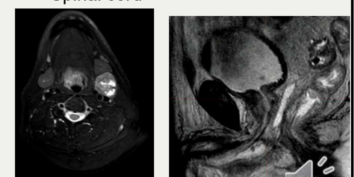
T2 and T2 Fat-Saturated



- Tumor:
  - Edema and infiltration
- Organs-at-risk (OAR):
  - rectum, bladder, urethra
  - Spinal cord



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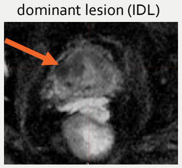
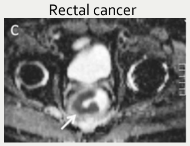
Diffusion weighted imaging

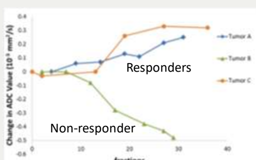
Intraprostatic dominant lesion (IDL)

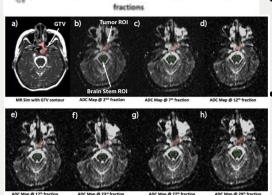


Rectal cancer



Lambrecht et al., IJROBP 2012





Yang et al., Medical Physics 2016

Tissue cellularity

- Apparent diffusion coefficient (ADC)
  - Assessed with multiple b-values
- Tumors
  - high cellular density → low ADC values
  - Change in ADC can be monitored for treatment response assessment
- Challenges
  - Severe distortion with standard EPI method
  - Methods with less distortion (TSE) suffer from low SNR

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- ***Comprehensive summary specific to radiation oncology applications***

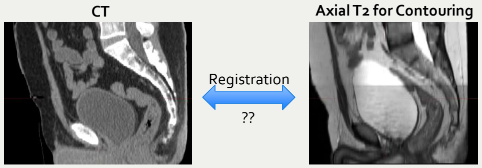
  Paulson et al., Medical Physics 42(1) 2015:28-39
- **MR sim for RT AAPM guidance**
  - TG 284:Magnetic Resonance Imaging - Simulation in Radiotherapy: Considerations for Clinical Implementation, Optimization, and Quality Assurance (in progress)

TABLE II. Site-specific MRI simulation reference guide for external beam radiation treatment planning.

Site	Sequence/contrast	Suggested uses for RTP	Issues/confounds
Brain	Axial T2 FLAIR	Delineation of vasogenic edema/infiltrative glioma (bright)	CSF pulsation artifacts
	Axial ADC	Differentiation of hypercellularity (dark) from coagulation necrosis	
	Axial postcontrast T1	Delineation of BBB disruption and neovascularization (bright)	Postoperative blood products
	Axial ΔT1 (Post T1–Pre T1)	Same as postcontrast T1, but without confounding blood products	
Breast	Axial T1	Delineation of axillary lymph nodes (dark) and brachial plexus	Postoperative blood products
	Axial T2 STIR	Delineation of lumpectomy cavity seroma; IMC, axillary nodes (bright)	
	Sagittal fat-suppressed T2	Delineation of lumpectomy cavity seroma; IMC, axillary nodes (bright)	
Cervix	Sagittal T2	Delineation of rectum and bladder	
	Axial T2	Delineation of tumor (bright)	
	Axial ADC	Delineation of tumor (dark)	Geometric distortion
	Axial fat-suppressed postcontrast T1	Delineation of tumor (bright)	
Head and neck	Axial T2 STIR	Differentiation of edema (bright; mostly on edges of tumor)	Swallowing motion, flow artifacts
	Axial T1	Delineation of nerves, teeth	
	Axial ADC	Delineation of hypercellularity (dark)	
	Axial fat-suppressed postcontrast T1	Delineation of disrupted, leaky tissue (bright)	Swallowing motion, flow artifacts
Liver	Axial fat-suppressed T2	Differentiation of hepatocytes from tumor (bright)	Triggered (50% phase)
	Axial fat-suppressed T1	Differentiation of hepatocytes from tumor (dark)	Breath held
	Axial fat-suppressed, postcontrast T1 arterial phase	Delineation of hypervascular hepatocellular carcinoma, melanoma, renal cell, carcinoid, or thyroid tumors (bright)	Breath held
	Axial fat-suppressed, postcontrast T1 5 min delay	Delineation of hypovascular metastases (dark)	Breath held
Pancreas	Axial T2	Delineation of duodenal wall (dark)	Triggered (50% phase)
	Axial fat-suppressed T1	Delineation of normal pancreas gland (isointense)	Breath held
	Axial fat-suppressed, postcontrast T1 late arterial phase	Delineation of tumor (dark regions within gland); lymph nodes (bright)	Breath held
Prostate	Sagittal T2	Delineation of rectum and bladder	
	Axial T2	Delineation of prostate gland and extracapsular disease (dark)	Postbiopsy hemorrhage
	Axial fat-suppressed T2	Delineation of intracapsular disease (dark); lymph nodes (bright)	Postbiopsy hemorrhage
	Axial T1	Detection of postbiopsy hemorrhage (bright)	
	Axial ADC	Delineation of tumor (dark)	Geometric distortion
Rectum	Sagittal T2	Delineation of rectum and bladder	
	Axial fat-suppressed T2	Delineation of tumor (bright)	
	Axial ADC	Delineation of tumor (dark)	Geometric distortion
	Axial fat-suppressed postcontrast T1	Delineation of tumor (bright)	
Sarcoma	Axial T2 STIR	Differentiation of edema (bright; mostly on edges of tumor)	
	Axial ADC	Delineation of tumor (dark)	Geometric distortion
	Axial fat-suppressed postcontrast T1	Delineation of disrupted, leaky tissue (bright)	
Spine	Sagittal T2 STIR	Differentiation of edema (bright)	
	Sagittal T1	Delineation of tumor (dark)	
	Axial fat-suppressed postcontrast T1	Delineation of disrupted, leaky tissue (bright)	

Why MR-only treatment planning

CT based planning



Propagated and will persist throughout treatment

- Different patient position, organ filling, respiration

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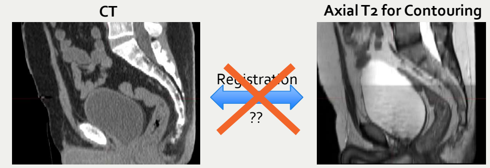
MR-only treatment planning

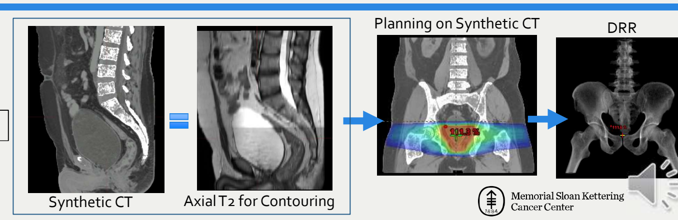
CT based planning



- ~~Different patient position, organ filling, respiration~~

~~*Propagated and will persist throughout treatment*~~

MR simulation



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Synthetic CT generation methods

- Image source: T1, T2, mDixon fat water separation, UTE
- Voxel-based
  - Uses voxel intensities in the MR to assign electron density
    - Standard or non-standard sequences, often requires information from multiple sequences
- Atlas-based
  - Single or multiple generalized MR atlas → deformed to CT atlas→
  - Often have trouble handling atypical anatomy due to reliance on atlas
- Hybrid methods
- **Deep learning methods**

Johnstone et al., IJROBP 2017
Edmund and Nyholm, Radiation Oncology 2017

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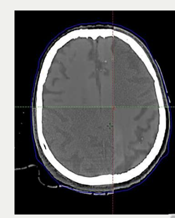
Deep learning methods

- Brain:
  - T1 image as input
  - U-net[1] and Generative adversarial network (GAN)[2]
  - Generative adversarial network (GAN) with mutual information as loss function [3]
    - Retrospective n=77, multi vendor 1.5T
    - Significant improvements in Mean absolute error (MAE):
      - 184 HU (multiatlas methods) → ***47.2 HU***
      - Average PTV and OAR dose difference <1%
  - Soft tissue preserving U-net architecture [4]
    - Soft-tissue MAE 17.6 HU
    - CBCT alignment difference <0.2 mm



[1] Ronneberger et al., MICCAI 2015
[2] Goodfellow et al., General Adversarial Networks 2014
[3] Kazemifar et al., Radiotherapy and Oncology 2019
[4] Gupta et al., Fronteriors in Oncology 2019

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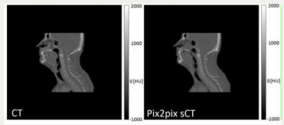
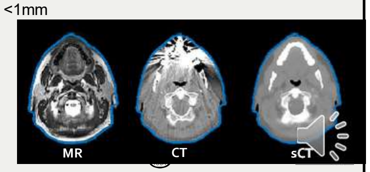
Deep learning methods

- Head and Neck:
  - Dental artifacts present a larger challenge than other investigated disease sites
  - Larger deformation uncertainties between MR and CT
  - Patch-based deep learning methods:
    - Improve robustness caused by abnormal anatomies
  - Pix2pix and CycleGAN [1]
    - Cross validated MAE 66.9 HU, non-ideal cases: MAE 122.1 HU
    - PTV, OAR dose difference < 2%, DRR alignment <1mm
  - 3D Convolutional Neural network (CNN) [2]
    - MAE 75 HU
    - Dental artifact mitigated with in combination with Turbo Spin Echo MRI

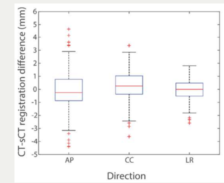




[1] Klages et al., Medical Physics 2019
[2] Dinkla et al., Medical Physics 2019

Current Clinical Status

- Most widely utilized in pelvis anatomy [1]
  - Primarily in prostate [2-3]
    - OAR and PTV dose differences < 1%
    - Bony match DRR difference <0.5 mm (AP largest)
    - Fiducial match <0.6 mm
  - Gyn, rectum, pelvic lymph nodes also implemented [4]
    - OAR and PTV dose differences < 0.5%
    - DRR positioning difference 0.3mm
- Clinical adoption in brain and head and neck treatments remain limited



[1] Bird et al., IJROBP 2019
[2] Tyagi et al., PMB 2017
[3] Persson et al., IJROBP 2016
[4] Kemppainen et al., Physics and Imaging in Radiation Oncology 2019

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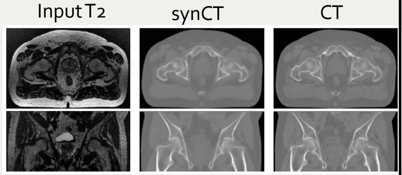
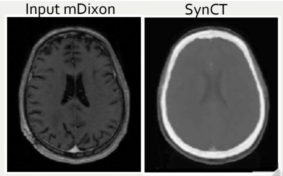
YVYP1

Commercial solutions

SPECTRONIC MEDICAL MRI Planner

- Deep learning transfer function estimation based algorithm
- Scanner and vendor independent
- Input T2-weighted image
- CE marked for prostate, brain and head and neck treatments





Spectronic medical white paper

Persson et al., IJROBP 2017

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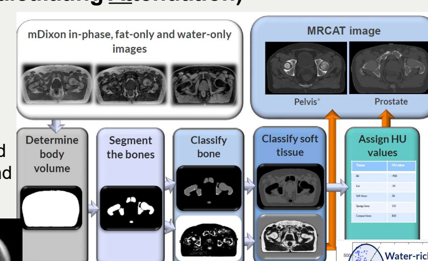
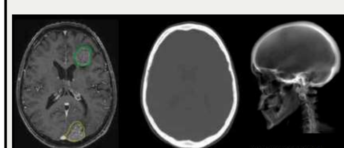
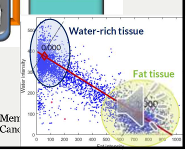
Commercial solutions

Philips MRCAT (MR for Calculating Attenuation)

- Scanner specific
- 3D mDixon FFE scan
- Online reconstruction of synthetic CT directly on scanner after acquisition
- CE-marked and FDA approved for prostate, general pelvis, and brain







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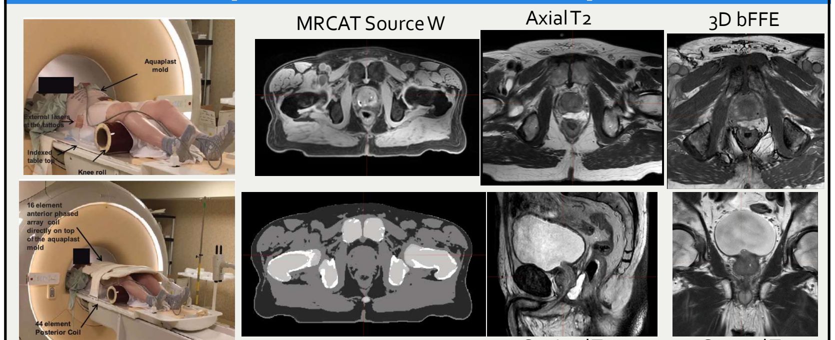
Our Experience: MRCAT in prostate



- Exam time 25 minutes
- 4 years, >1300 patients to date

Tyagi et al., Radiation Oncology 2017

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Main Challenges

- non-ideal bowel and bladder prep or persistent gas
- Patient motion during exam
  - Could result in synthetic CT reconstruction failures or inaccurate external body contour
- Difficulty in gold fiducial seed identification
  - Biopsy artifacts, surgical clips, LDR seeds
- Metal hip implants or spinal hardware
- FOV limits to satisfy vendor model-based reconstruction requirements
  - AP: 36.8cm, LR: 55.2cm

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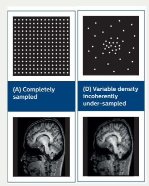
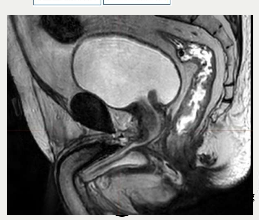
Compress Sensing acceleration in MR sim

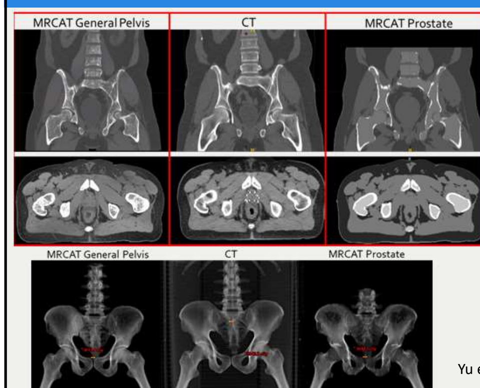
- Signal processing technique
  - Variable density incoherent under-sampling of k-space to incoherently distribute artifacts over the image
- Reduce scan time
- Increase resolution, FOV coverage, and SNR
- Average 30% decrease in scan time
- Notable clinical benefit: enabled high resolution 3D T2 scan for urethra visualization
  - SBRT and post brachy cases had foley catheters placed for urethra contouring before
  - only ~10% of patients needed foley catheter after case-by-case sim/physics team assessment

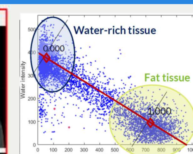


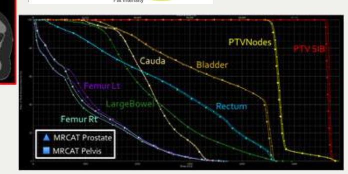


Tyagi et al., MR-in-RT 2019. Zakian et al., ISMRM 2020.

Continuous HU MRCAT general pelvis







- <1% dose difference

Yu et al., AAPM 2020: PO-GeP-M-420

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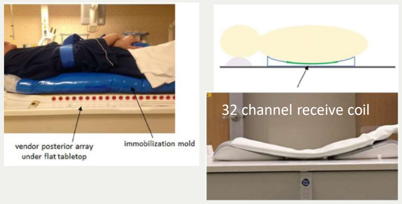
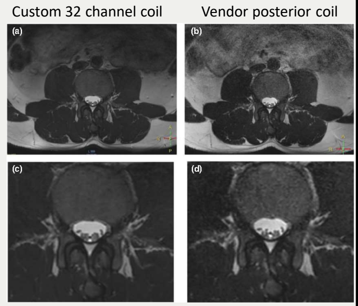
Custom-designed flexible coil for MR sim





- Placed in between patient immobilization alpha cradle
- Significant SNR improvement
- Reproducible setup to treatment position

Tyagi et al., Medical Physics 2020.

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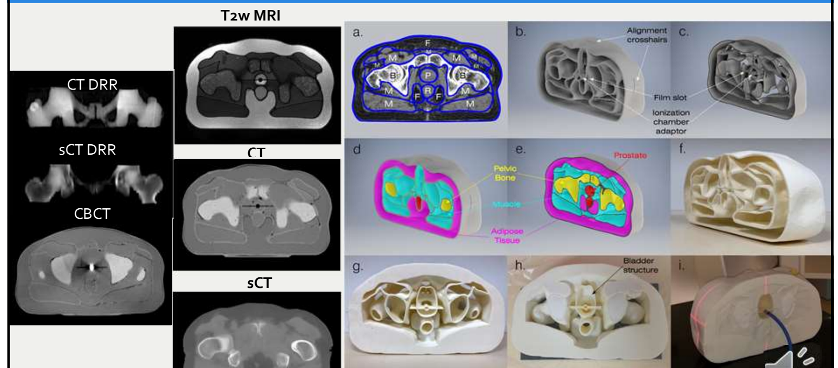
MR-only phantom developments



Singhrao et al., Medical Physics 2020
Singhrao et al., PMB 2020

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Next steps

- **Further developments of RT-specific imaging sequences**
  - **Standardization of additional advanced sequences into routine treatment planning workflow**
  - **Robust MR biomarkers for treatment response assessment**
- **Further image acquisition acceleration**
- **Clinical evaluations, implementations and widespread adoption for MR-only planning in Brain and Head and Neck patients remains to be seen**

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