On-board MRI for Treatment Verification

O. L. Green, Ph.D.

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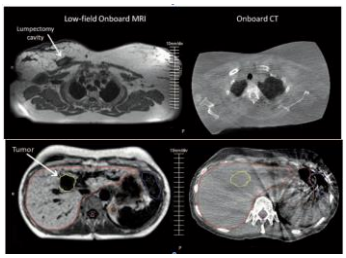
MRI (0.35T) vs CBCT

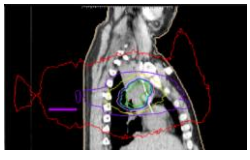


Noel, C.E., Parikh, P.J., Spencer, C.R., Green, O.L., Hu, Y., Mutic, S. and Olsen, J.R., 2015. Comparison of onboard low-field magnetic resonance imaging versus onboard computed tomography for anatomy visualization in radiotherapy. Acta Oncologica, 54(9), pp.1474-1482.

Challenges of MRI – Linac Integration

- Dosimetry:
  - Magnetic field influences path of electrons, affecting dose distribution (especially at heterogeneous tissue boundaries)
- Image Quality:
  - Linac components may influence both field homogeneity (spatial integrity) and signal-to-noise ratios
- Additional patient concerns:
  - Presence of ferromagnetic materials in the body
  - Claustrophobia
  - Duration of treatment session
  - Patient heating (SAR)

Raaijmakers, A. J. E., Bas W. Raaymakers, and Jan JW Lagendijk. "Magnetic-field-induced dose effects in MR-guided radiotherapy systems: dependence on the magnetic field strength." Physics in Medicine & Biology 53.4 (2008): 909.



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Current Commercially-Available MRgRT Systems

1.5T (Elekta Unity)

0.35 T (ViewRay MRIdian)

On-board Volumetric MRI imaging
Real-time cine imaging during treatment

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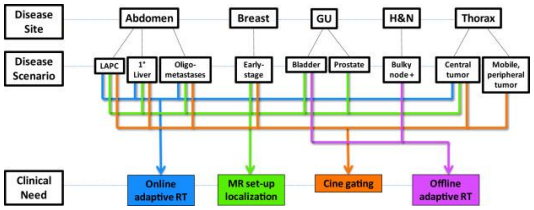
0.35T MRgRT Utilization at Washington University



Fischer-Valuck, Benjamin W., et al. "Two-and-a-half-year clinical experience with the world's first magnetic resonance image guided radiation therapy system." Advances in radiation oncology 2.3 (2017): 485-493.

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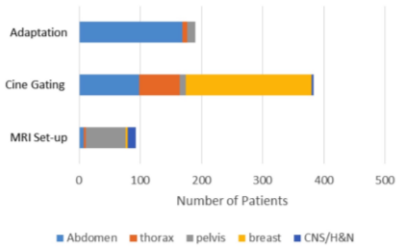
0.35T MRgRT Utilization at Washington University



Henke, L.E., Contreras, J.A., *et al.* Magnetic Resonance Image-Guided Radiotherapy (MRIgRT): A 4.5-Year Clinical Experience. Clinical Oncology, 30(11), pp.720-727.

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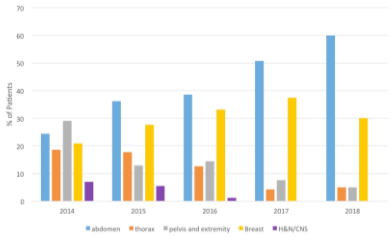
0.35T MRgRT Utilization at Washington University



Henke, L.E., Contreras, J.A., *et al.* Magnetic Resonance Image-Guided Radiotherapy (MRIgRT): A 4.5-Year Clinical Experience. Clinical Oncology, 30(11), pp.720-727.

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Outline

- Localization
- Adaptation
- Response prediction

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Outline

- Localization
- Adaptation
- Response prediction via functional imaging

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Accelerated Partial Breast Irradiation with 0.35T MRgRT:

Acharya, S., Fischer-Valuck, B.W., Mazur, T.R., Curcuru, A., Sona, K., Kashani, R., Green, O., Ochoa, L., Mutic, S., Zoberi, I. and Li, H.H., 2016. Magnetic resonance image guided radiation therapy for external beam accelerated partial-breast irradiation: Evaluation of delivered dose and intrafractional cavity motion. *International Journal of Radiation Oncology* Biology* Physics*, *96*(4), pp.785-792.

- Treated breast volume has been shown to correlate with adverse cosmetic outcomes in APBI
  - Jagsi et al, *IJROBP*, 2010
- MRgRT allows for accurate setup and gating – therefore, why not reduce the treated volume?

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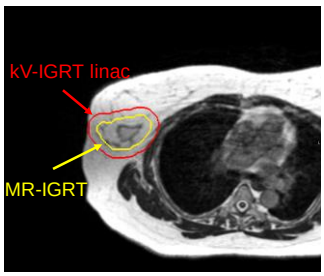
Accelerated Partial Breast Irradiation with 0.35T MRgRT:



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Accelerated Partial Breast Irradiation with 0.35T MRgRT:

Kennedy, W.R., Thomas, M.A., DeBroeck, K.R., Ochoa, L.L., Atkinson, A.R., Green, O.L. and Zoberi, I., 2018. Postoperative Single-Fraction Partial Breast Irradiation for Low-Risk Stage 0 and I Breast Carcinomas: Results of a Prospective Clinical Trial. *International Journal of Radiation Oncology* Biology* Physics*, *102*(3), pp.S227-S228.

- Prospective trial:
  - Single Fraction APBI for Low-risk Stage 0 and I Breast Carcinoma
    - PI: I. Zoberi, MD
  - Primary objective:
    - Incidence of acute and late Grade 3+ CTCAE toxicity
  - Inclusion:
    - 50 women with low-risk, stage 0-1 breast carcinoma with negative margins after lumpectomy
  - Prescription
    - 20 Gy to cavity surface; 7Gy to 1cm margin around cavity (replicate brachytherapy dose distribution)

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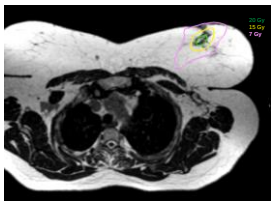
Accelerated Partial Breast Irradiation with 0.35T MRgRT:

Kennedy, W.R., Thomas, M.A., DeBroeck, K.R., Ochoa, L.L., Atkinson, A.R., Green, O.L. and Zoberi, I., 2018. Postoperative Single-Fraction Partial Breast Irradiation for Low-Risk Stage 0 and I Breast Carcinomas: Results of a Prospective Clinical Trial. *International Journal of Radiation Oncology• Biology• Physics*, *102*(3), pp.S227-S228.

- Accrual completed in early 2018
- 1 patient with grade-2 chestwall pain
- No reduction in patient-reported QOL
- Excellent-to-good cosmesis:
  - 97% and 100% pretreatment
  - 97% and 100% at 8 weeks
  - 100% and 100% at 6 months
    - radiation oncologist vs. patient



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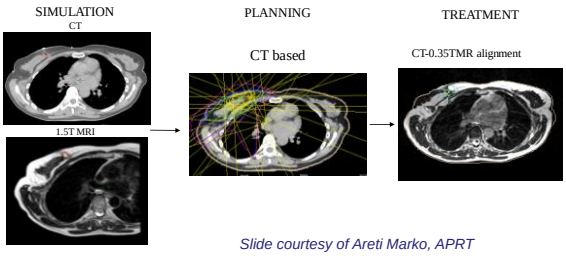
MRI-only APBI: Current Process



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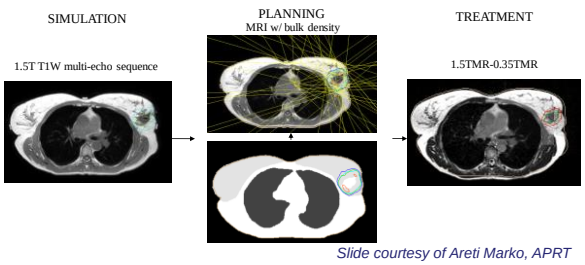
MRI-only APBI: New Process



Slide courtesy of Areti Marko, APRT

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MRI-only APBI – Dosimetric Analysis

- 18 patients from Jan 2019 through June 2019
- Open FOV 1.5T MRI rather than previously used half scan, used as primary
- CT performed as a secondary scan
- Two plans generated
  - Bulk- density overrides
  - CT fused as secondary and calculated on
- D95 and Max doses

STRUCTURE	TYPE	DENSITY (WATER=1.0)
CAVITY_MRI	WATER	1
AIR	AIR	0.0012
BREAST_R	FAT	0.89
BREAST_L	FAT	0.89
LUNG_R	LUNG	0.26
LUNG_L	LUNG	0.26
HEART	WATER	1
SKIN	WATER	1

Slide courtesy of Areti Marko, APRT

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MRI-only APBI – Dosimetric Analysis

CONVENTIONAL (CT) PLANNING				MRI-ONLY PLANNING				ABSOLUTE DIFFERENCE FROM CT STANDARD			
PTV	Ipsilateral Breast	Ipsilateral Lung	Heart	PTV	Ipsilateral Breast	Ipsilateral Lung	Heart	PTV	Ipsilateral Breast	Ipsilateral Lung	Heart
D95 (%)	MAX	MAX	MAX	D95 (%)	MAX	MAX	MAX	D95 (%)	MAX	MAX	MAX
97.75	40.17	28.02	20.73	98	40.48	27.77	20.67	0.25	0.31	0.25	0.06
100	42.36	29.56	2.5	100	42.43	28.82	3.23	0	0.07	0.74	0.73
99.63	43.92	30.42	5.25	99.61	43.98	31.07	5.33	0.02	0.06	0.65	0.08
99.51	42.56	26.65	5.21	99.43	42.51	26.78	5.36	0.08	0.05	0.13	0.15
99.5	42.29	22.3	3.93	99.79	43.12	22.62	3.84	0.29	0.83	0.32	0.09
99.53	42.62	22.08	3.37	99.66	42.79	21.47	3.45	0.13	0.17	0.61	0.08
94.74	43.01	25.41	15.44	95.72	43.17	25.02	15.56	0.98	0.16	0.39	0.12
98.66	43.18	11.32	10.38	98.4	43.11	11.11	10.45	0.26	0.07	0.21	0.07
94.73	42.83	35.59	12.04	95.99	43.89	36.04	12.02	1.26	1.06	0.45	0.02
94.3	44.04	25.6	10.07	95	44.19	26.28	9.64	0.7	0.15	0.68	0.43
97.72	41.93	34.65	18.28	98.65	42.24	34.54	18.14	0.93	0.31	0.11	0.14
98.92	44.56	31.08	5.99	99.23	44.28	31.42	5.61	0.31	0.28	0.34	0.38
94.4	44.58	11.13	5.78	95.01	44.64	11.39	5.59	0.61	0.06	0.26	0.19
95.61	43.12	21.89	3.4	95.27	43.36	21.87	3.55	0.34	0.24	0.02	0.15
95.07	42.13	34.06	3.83	95.77	42.93	34.52	3.88	0.7	0.8	0.46	0.05
98.83	44.21	12.44	5.25	99	43.97	12.64	5.12	0.17	0.24	0.2	0.13
99.9	42.18	26.07	9.52	99.88	42.73	26.21	9.71	0.02	0.55	0.14	0.19
98.69	44.75	28.94	9.95	99.37	44.28	29.35	10.45	0.68	0.47	0.41	0.5

Slide courtesy of Areti Marko, APRT

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Oligometastatic lymph nodes with 1.5T MRgRT

Winkel, Dennis, *et al.* "Individual lymph nodes:"See it and Zap it"." Clinical and Translational Radiation Oncology (2019).

- 10 patients: 7 pelvic, 3 para-aortic
- median short-axis diameter: 7.5 mm [5.3–21.3 mm]
- Rx 35 Gy

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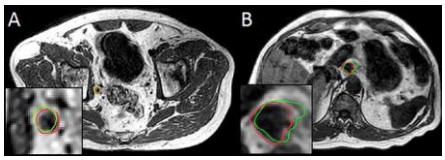
Oligometastatic lymph nodes with 1.5T MRgRT

- Results:
  - All lesions were well-visualized on MRI
  - For 45 of the 50 fractions (90%) the GTV V35Gy on the post-delivery MRI remained 100%



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Outline

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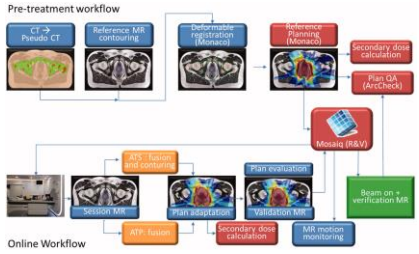
Adaptive Workflow – Elekta Unity



Bertelsen, Anders S., et al. "First clinical experiences with a high field 1.5 T MR linac." *Acta Oncologica* (2019): 1-6.

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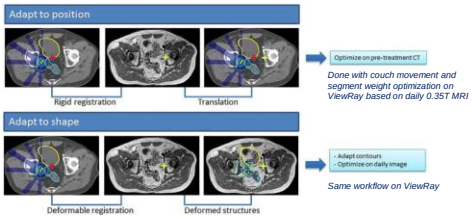
Adaptive Workflow - Elekta Unity



Winkel, Dennis, et al. "Adaptive radiotherapy: The Elekta Unity MR-linac concept." Clinical and Translational Radiation Oncology (2019).

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First Prospective Online Adaptive Radiotherapy Trial 0.35T:

Henke, L., …& Olsen, J., 2018. Phase I trial of stereotactic MR-guided online adaptive radiation therapy (SMART) for the treatment of oligometastatic or unresectable primary malignancies of the abdomen. *Radiotherapy and Oncology*, *126*(3), pp.519-526.

- 20 patients, unresectable primary or oligometastatic disease
  - liver (n = 10) & non-liver (n=10) abdomen
- Prescription: 50Gy/5fx (BED=100) with SMART approach
  - using real-time cine MR gating with end-exhale breathhold for volumetric imaging
- Isotoxicity approach
  - dose escalation (or de-escalation) based on strict OAR constraints

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- 83% (79/95) fractions adapted
  - all patients had at least one adaptation during course of treatment
- Plans adapted for 64% of liver & 98% of non-liver abdomen fx
- Initial plans would have violated OAR constraints in 70/95 fx
- 100% of OAR violations resolved with adaptive planning

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- No Grade 3+ toxicity at median 11.8 mo f/u
  - Expected up to 30% based on prior reports accounting for motion (Hoyer, et al. 2005)
- No change in patient-reported quality-of-life scores (P=0.29)
- 95% and 90% control of treated lesions at 3 and 6 months by RECIST criteria

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- Evaluated overall on-table time to establish feasibility
  - Median time 79 min
- 2018: Introduced Advanced Practice Radiation Therapist Position
  - Responsible for contouring of organs-at-risk
  - Aids in workflow and process improvement
  - Significantly reduced physician time at machine
  - Maintain quality and consistency of contouring

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Pilot/Phase I Trial for Ultra-Central Thorax:

Henke, L.E., Olsen, J.R., *et al.*, 2019. Stereotactic MR-guided online adaptive radiation therapy (SMART) for ultracentral thorax malignancies: Results of a phase 1 trial. *Advances in radiation oncology*, *4*(1), pp.201-209..

- Unresectable primary or oligometastatic disease of the ultra-central thorax
  - 5 patients
- Prescription: 50Gy/5fx with SMART approach
- Isotoxicity approach
  - with dose escalation (or de-escalation) based on hard OAR constraints

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Pilot/Phase I Trial for Ultra-Central Thorax:

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- 10/25 fx adapted
  - 4/5 patients adapted at least once
- Reasons for adaptation:
  - 30% of adaptation performed to improve PTV coverage
  - 70% of adaptation performed to reverse unintended OAR violations
- 100% of OAR violations resolved with adaptive planning

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Pilot/Phase I Trial for Ultra-Central Thorax:

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- Local control by RECIST criteria was 100% at three and six months
- Zero Grade 3+ acute (within 6 months) treatment-related toxicities observed

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Initial Clinical Experience 1.5T:

Treatments	# Patient treatments	Prescribed dose (Gy)	Fx	Planned adaptation	MR seq	Fx delivered	Number of ATS
Prostate							
PROMI protocol	4	60	20	ATP	T2	78	16
Prostate only	2*	60	20	ATP	T2	20	4
Partial prostate irradiation	1	60	20	ATP	T2	20	2
Recurrence	1	42.7	7	ATP	T2	7	1
Ovarie irradiation	3	15	3	ATS	T2	9	9
SBRT treatments							
Bone							
Ilium	2	30	3	ATP	T1	6	0
	2*	30	5	ATP	T1	5	0
Vertebre	3*	30	3	ATP	T1	6	2
	1	30	5	ATP	T2	5	1
Soft tissue							
Pelvis	1	27	3	ATP	T2	3	2
Pelvis	1	45	3	ATS	T2	3	3
Abdomen	1	60	6	ATP	T2	6	3
Uterus boost	1	30	6	ATS	T2	6	6
Total	20					176	49

Bertelsen, Anders S., et al. "First clinical experiences with a high field 1.5 T MR linac." *Acta Oncologica* (2019): 1-6.

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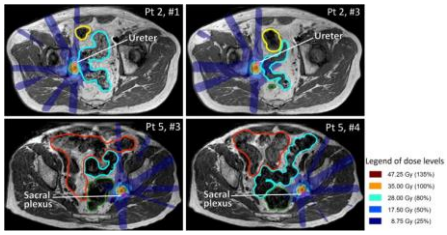
Initial Clinical Experience 1.5T:



Werensteijn-Honingh, Anita M., et al. "Feasibility of stereotactic radiotherapy using a 1.5 T MR-linac: multi-fraction treatment of pelvic lymph node oligometastases." Radiotherapy and Oncology 134 (2019): 50-54.

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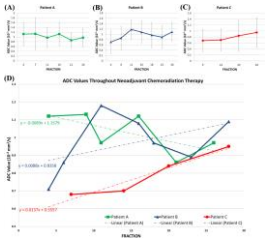
DWI using 0.35T

- Three patients with primary rectal adenocarcinoma
- One of the patients showed little evidence of response via pathological assessment, which corresponded to a high initial ADC value and decreasing ADC values measured over the 1st half of treatment



Shaverdian, Narek, et al. "Feasibility evaluation of diffusion-weighted imaging using an integrated MRI-radiotherapy system for response assessment to neoadjuvant therapy in rectal cancer." The British journal of radiology 90.1071 (2017): 20160739.

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Future Directions

- MRgRT workflow optimization
- Response prediction
- Functional imaging for adaptation
- Real-time dose accumulation

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