Real-time adaptation: Rationale, system overview and clinical experience

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AUSTRALIAN CANCER RESEARCH FOUNDATION

THE UNIVERSITY OF SYDNEY

Disclosures

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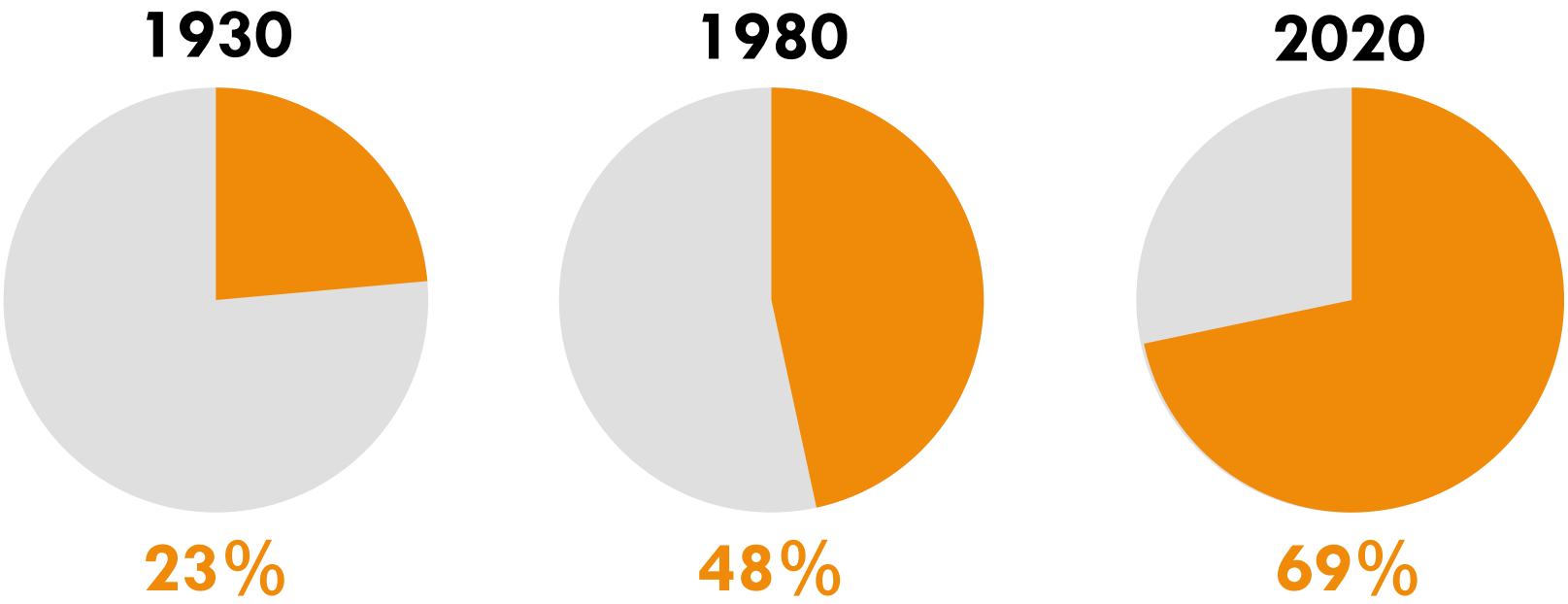
- **Patents:** Several awarded patents and pending applications
- **Licenses:** Leo, Opus, Standard Imaging, Varian
- **Industry research grants:** Siemens (PI), Varian (CI)
- **New entities:** Cancer Research Innovations (Partner), Leo (Founder), Opus (Founder), SeeTreat (Founder)

Real-time adaptation: Rationale, system overview and clinical experience

5-year cancer survival is increasing with time



Cancer Australia

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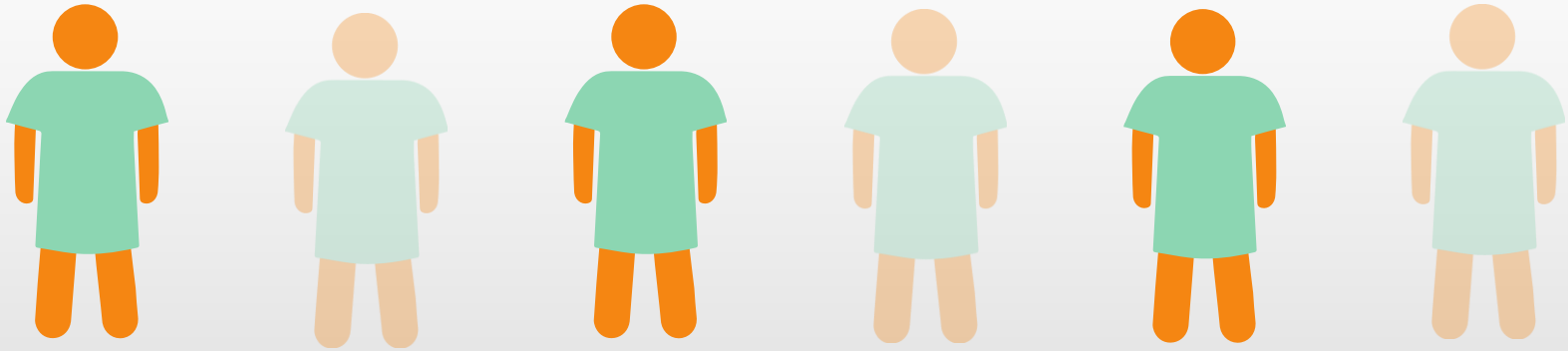
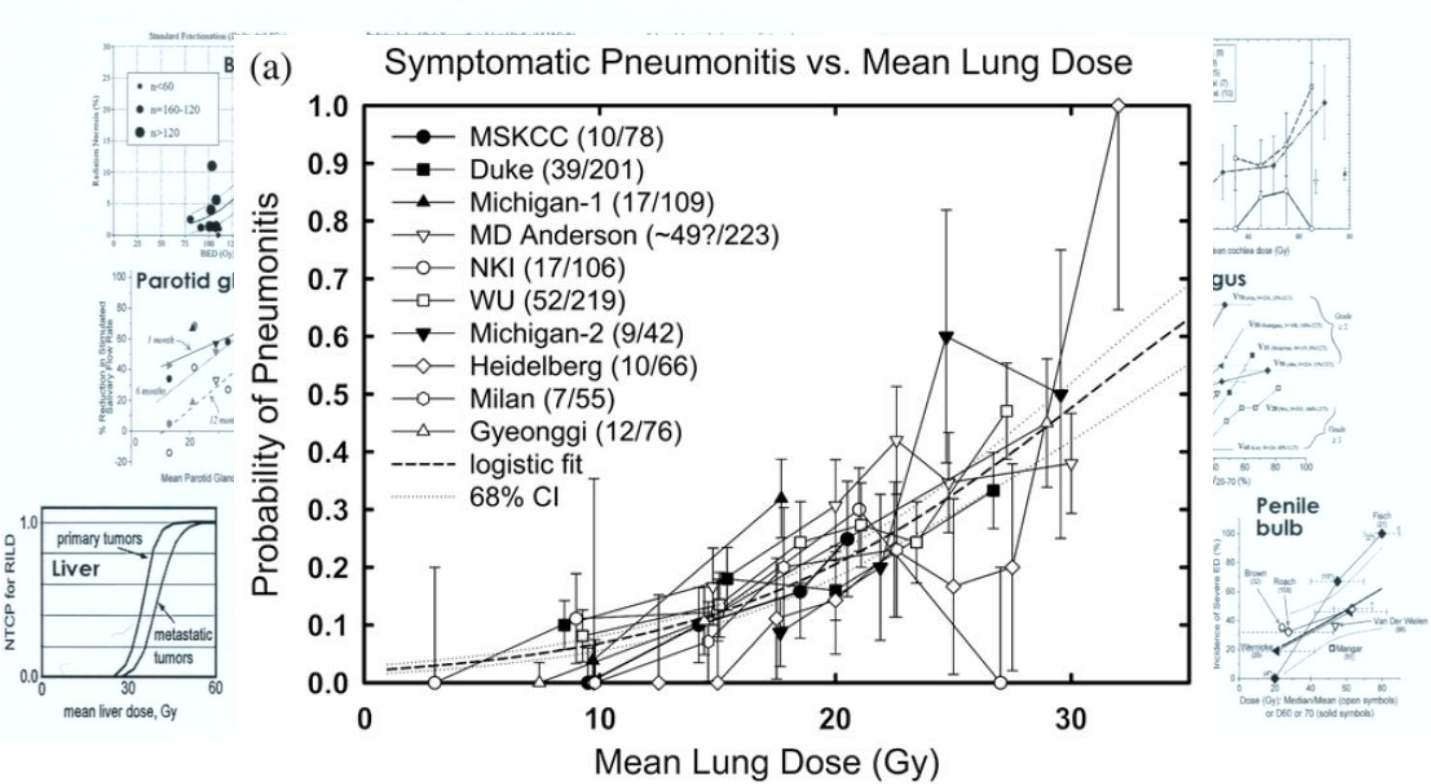
1 in 2



people with cancer need radiation therapy

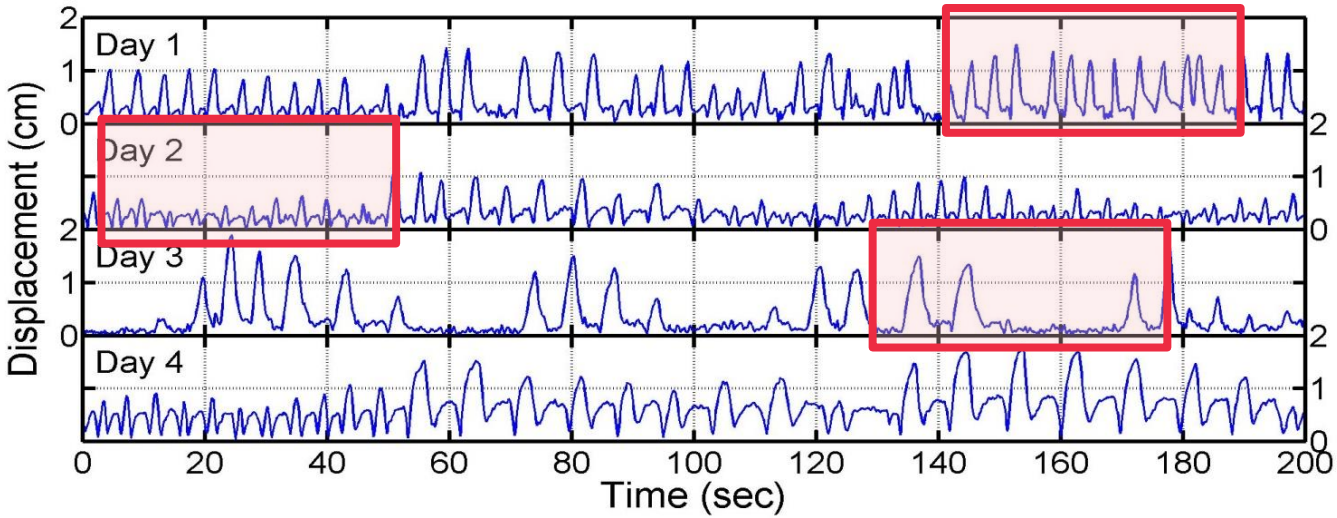
Barton *et al.* Rad Onc 2014

Clinical benefit of improved IGRT



Marks IJROBP 2010

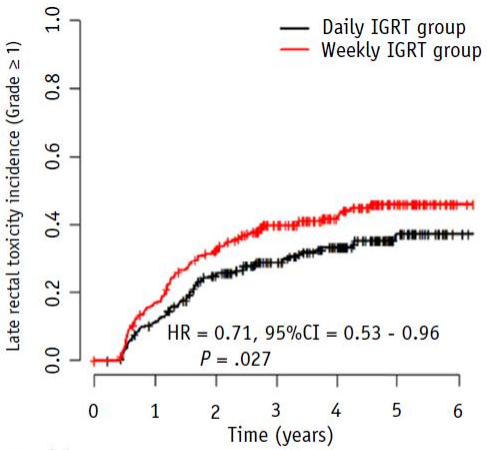
Tumor motion varies from breath to breath and day to day



Shah IJROBP 2013

Daily IGRT improves outcomes vs weekly IGRT

- 470 pts randomized between daily and weekly IGRT
- Biochemical progression-free interval significantly longer HR=0.45
- Late grade ≥1 rectal toxicity significantly lower HR=0.71
- Daily IGRT significantly improves local control and reduces rectal toxicity



No. At Risk							
Daily IGRT group	236	206	161	123	84	31	5
Weekly IGRT group	234	191	150	108	73	39	5

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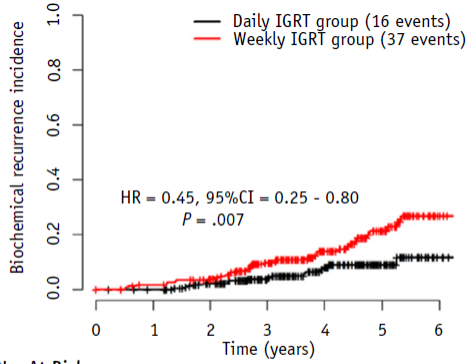


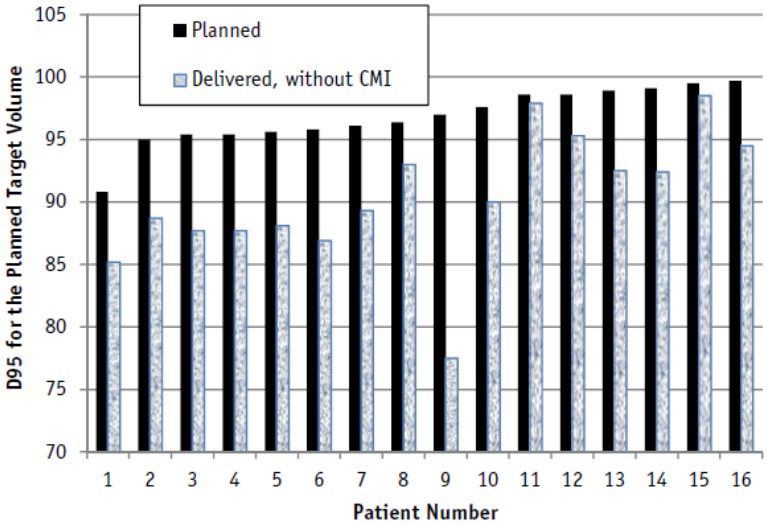
No. At Risk							
Daily IGRT group (16 events)	236	232	207	164	108	46	8
Weekly IGRT group (37 events)	234	226	213	164	108	54	8

De Crovisier IJROBP 2018

Continuous Monitoring and Intrafraction Target Position Correction During Treatment Improves Target Coverage for Patients Undergoing SBRT Prostate Therapy

D. Michael Lovelock, PhD,* Alessandra P. Messineo, BS,* Brett W. Cox, MD,† Marisa A. Kollmeier, MD,* and Michael J. Zelefsky, MD*

Results: After the initial setup, 1.7 interventions per fraction were required, with a concomitant increase in time for dose delivery of approximately 65 seconds. Small systematic drifts in prostate position in the posterior and inferior directions were observed in the study patients. Without CMI, intrafractional motion would have resulted in approximately 10% of patients having a delivered dose that did not meet our clinical coverage requirement, that is, a PTV D95 of >90%. The posterior PTV margin required for 95% of the dose to be delivered with the target positioned within the PTV was computed as a function of time. The margin necessary was found to increase by 2 mm every 5 minutes, starting from the time of the imaging procedure.

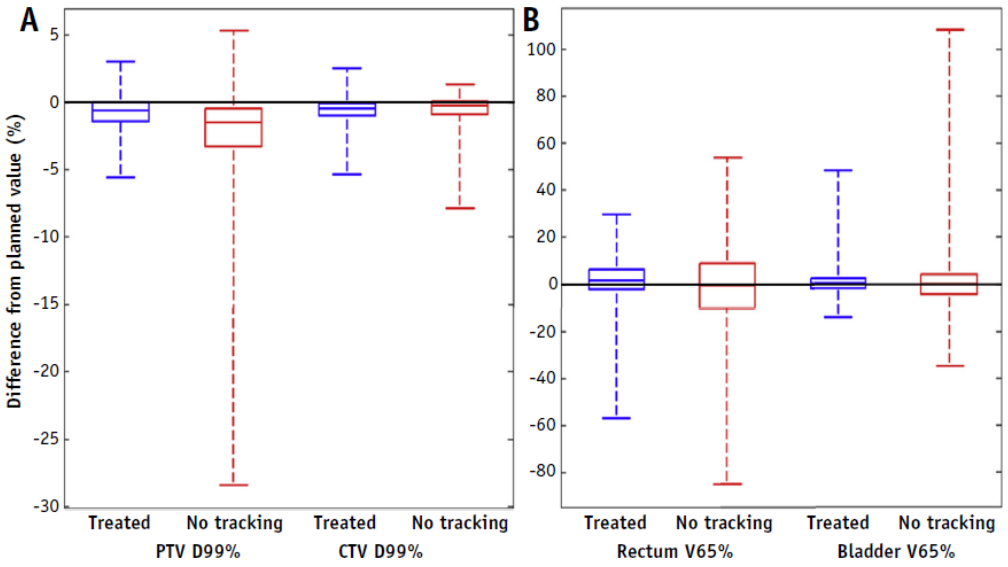


Lovelock, IJROBP 2015

Multileaf Collimator Tracking Improves Dose Delivery for Prostate Cancer Radiation Therapy: Results of the First Clinical Trial

Emma Colvill, MSc,*,† Jeremy T. Booth, PhD,†,‡ Ricky T. O'Brien, PhD,* Thomas N. Eade, MBBS,† Andrew B. Kneebone, MBBS,† Per R. Poulsen, PhD,§ and Paul J. Keall, PhD*

*Radiation Physics Laboratory and ‡School of Physics, University of Sydney, Sydney, NSW, Australia; †Northern Sydney Cancer Centre, Royal North Shore Hospital, St. Leonards, NSW, Australia; and §Aarhus University Hospital, Aarhus, Denmark



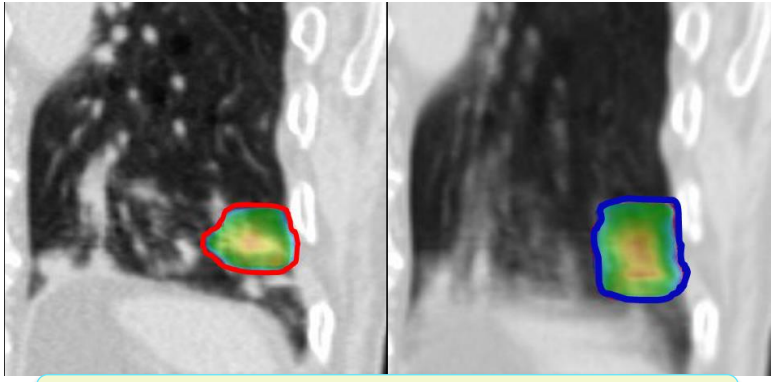
Conclusion: This study shows that MLC tracking improves the consistency between the planned and delivered doses compared with the modeled doses without MLC tracking. The implications of this finding are potentially improved patient outcomes, as well as more reliable dose-volume data for radiobiological parameter determination.

Colvill, IJROBP 2015

Real-time adaptive rationale

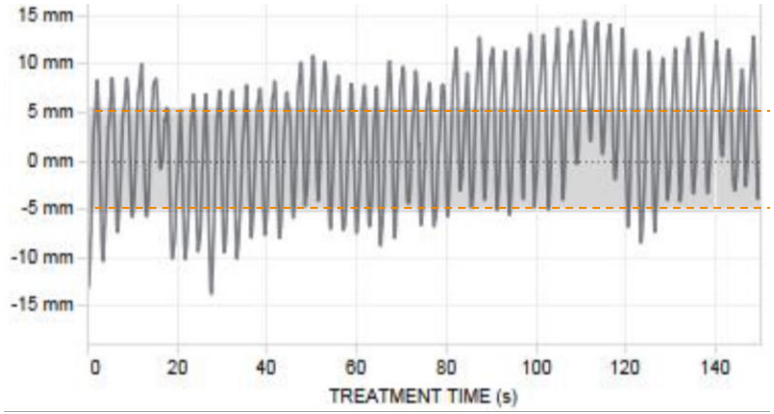
Planning

Real-time | Standard



Average 40% reduction in PTV

Delivery



4D CT motion

Courtesy Jeremy Booth

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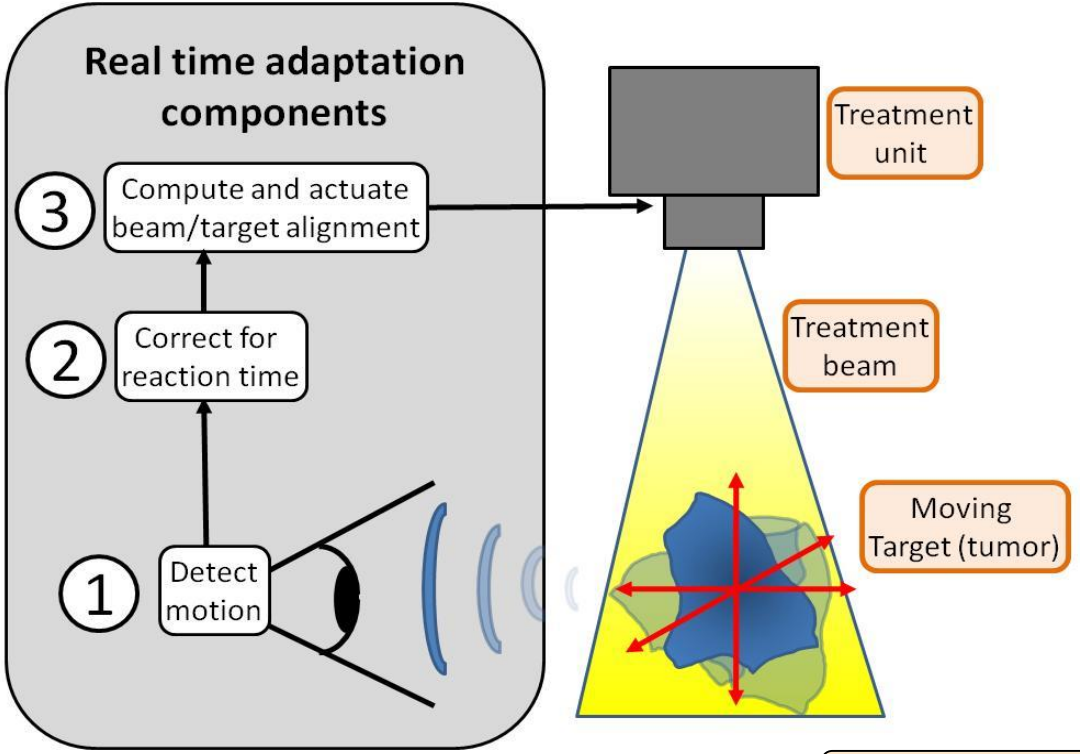
Real-time adaptation: Rationale, system overview and clinical experience

Real-time adaptive radiation therapy components



Dieterich Med Phys 2008

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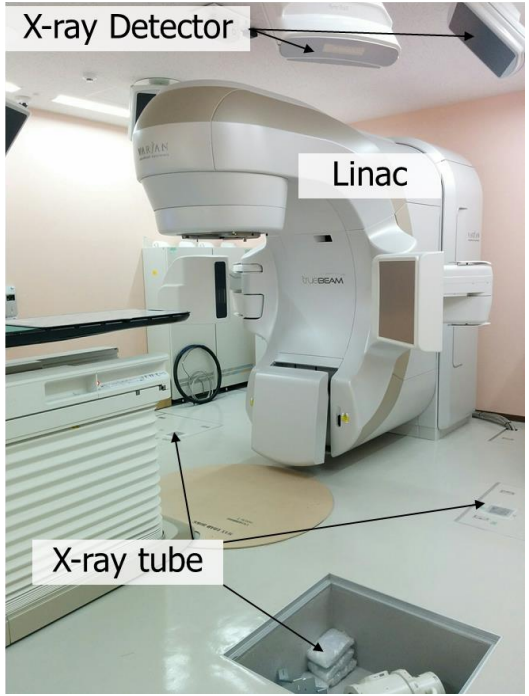
Real-time tracking: The Pioneers in 1998

Real-time tumour-tracking radiotherapy THE LANCET • Vol 353 • April 17, 1999

Hiroki Shirato, Shinichi Shimizu, Tadashi Shimizu, Takeshi Nishioka, Kazuo Miyasaka

- Real-time fluoro imaging of gold markers with gating
- Markers inserted into/near the tumour in 10 patients
- No complications or local relapses within a 6 month follow-up
- *"A real-time tumour-tracking system can improve the accuracy of radiotherapy and reduce the volume of normal tissue irradiated"*
- 2014 applied technology to proton therapy



Courtesy Prof Hiroki Shirato

Real-time adaptive radiation therapy systems

Robotic linac
CyberKnife
Synchrony
Clinical 2004

Gimbaled linac
Vero/
Mitsubishi
Clinical 2011

MLC
Clinical 2013
Widely available
Smallest, lightest
6 DoF
Deformation

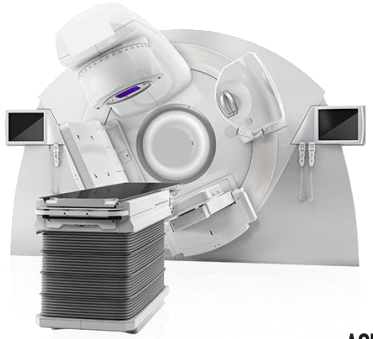
Robotic couch
Clinical 20??
Widely
available

Real-time adaptive radiation therapy

Tipping point

Introduction of real-time 3D IGRT systems

Integration with standard linacs



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What tools are available on standard linacs today?

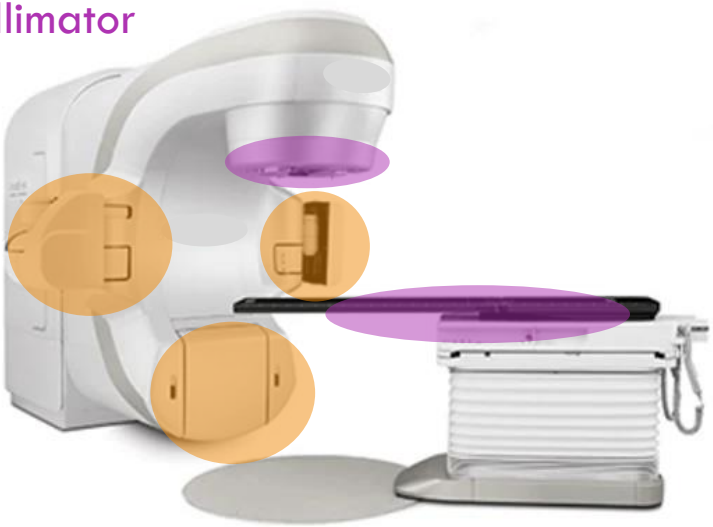
Find the target

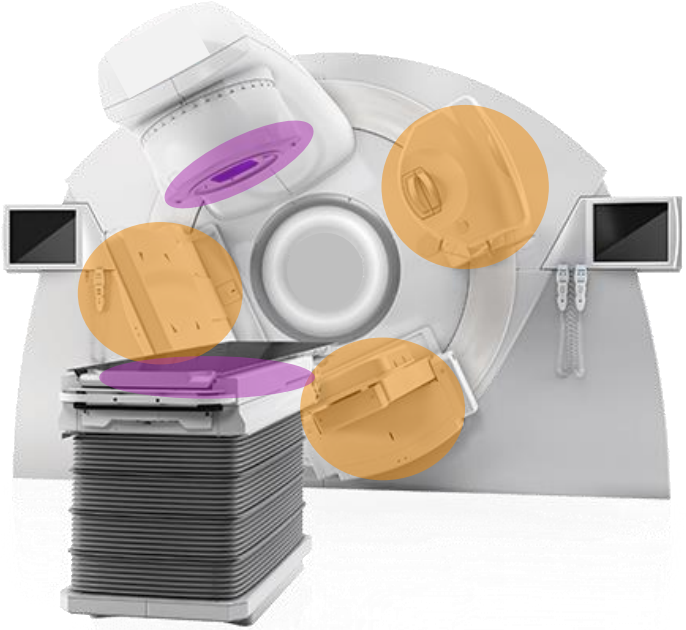
kV and MV X-ray imaging systems

Respiratory monitoring

Hit the target

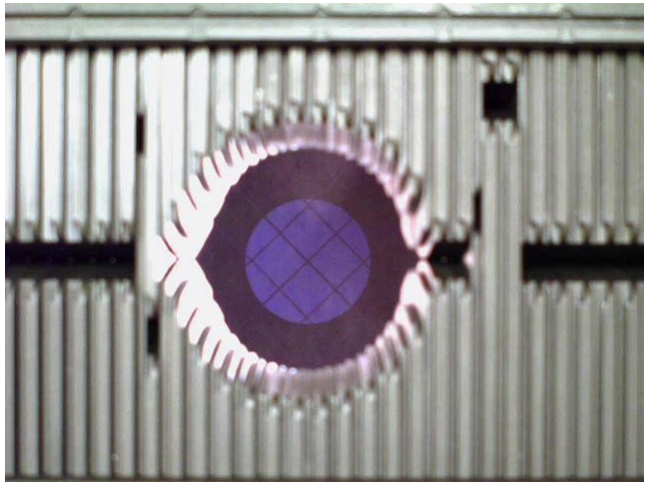
Multileaf collimator



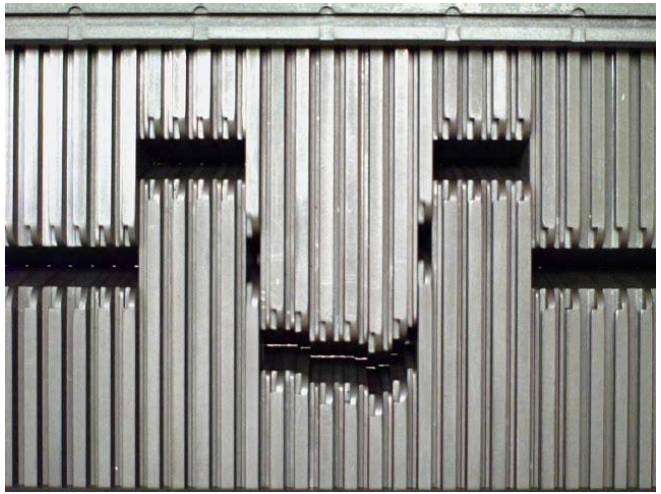


MLC tracking real-time adaptive therapy options

Conformal

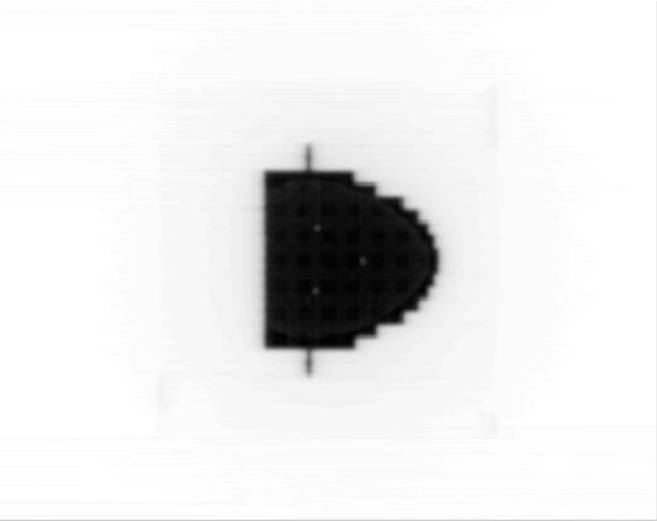


IMRT

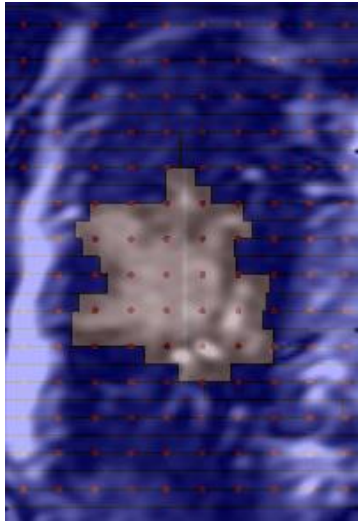


MLC tracking real-time adaptive therapy future options

Rotation + Translation

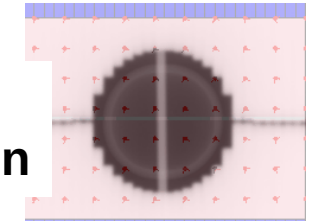


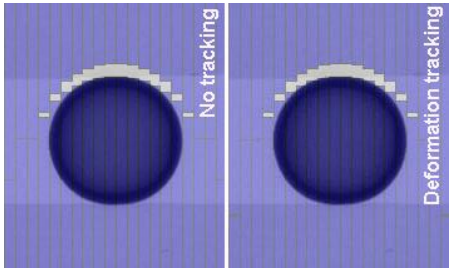
Deformation



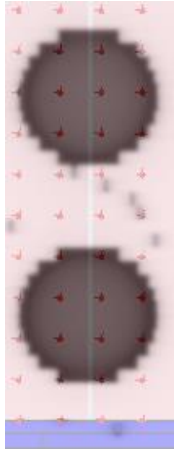
MLC tracking real-time adaptive therapy future options

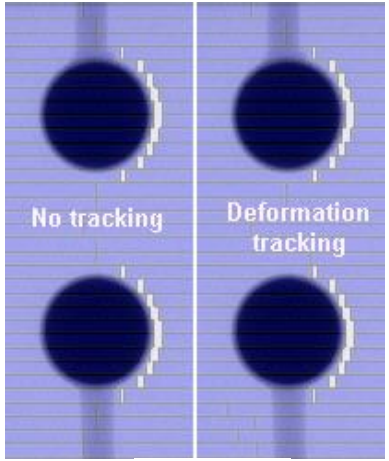
Single Deformation





System Deformation





Conformal RT

IMRT

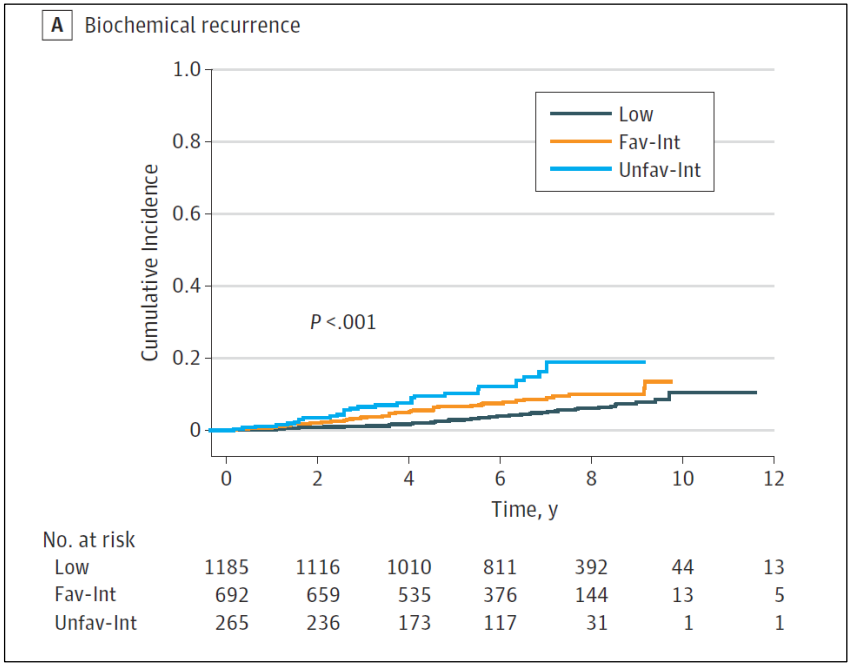
Real-time adaptation: Rationale, system overview and clinical experience

Original Investigation | Oncology

Long-term Outcomes of Stereotactic Body Radiotherapy for Low-Risk and Intermediate-Risk Prostate Cancer

JAMA Network Open

Amar U. Kishan, MD; Audrey Dang, MD; Alan J. Katz, MD, JD; Constantine A. Mantz, MD; Sean P. Collins, MD, PhD; Nima Aghdam, MD; Fang-I Chu, PhD; Irving D. Kaplan, MD; Limor Appelbaum, MD; Donald B. Fuller, MD; Robert M. Meier, MD; D. Andrew Loblaw, MD; Patrick Cheung, MD; Huong T. Pham, MD; Narek Shaverdian, MD; Naomi Jiang, MD; Ye Yuan, MD, PhD; Hilary Bagshaw, MD; Nicolas Prionas, MD, PhD; Mark K. Buyyounouski, MD, MS; Daniel E. Spratt, MD; Patrick W. Linson, MD; Robert L. Hong, MD; Nicholas G. Nickols, MD, PhD; Michael L. Steinberg, MD; Patrick A. Kupelian, MD; Christopher R. King, MD, PhD



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JAMA Network Open. 2019;2(2):e188006.

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Toxic Event	Crude Incidence, No. (%)[b]	Cumulative Incidence Estimate (95% CI)	
		5 y	7 y
Grade 2			
Acute GU	153 (9.0)	NA	NA
Acute GI	56 (3.3)	NA	NA
Late GU	163 (9.6)	11.2 (9.7-12.8)	12.3 (10.8-14.0)
Late GI	67 (3.9)	4.5 (3.6-5.6)	4.5 (3.6-5.6)
Grade ≥3			
Acute GU	13 (0.6)	NA	NA
Acute GI	2 (0.09)	NA	NA
Late GU	46 (2.1)	1.8 (1.3-2.5)	2.4 (1.8-3.2)
Late GI	7 (0.3)	0.4 (0.2-0.8)	0.4 (0.2-0.8)

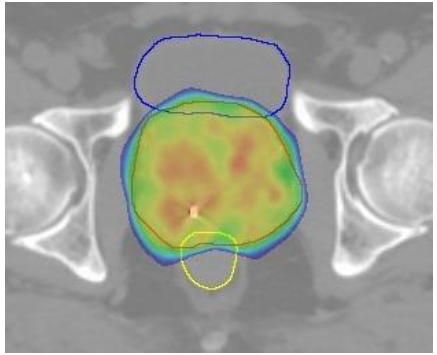
IMAGE X INSTITUTE

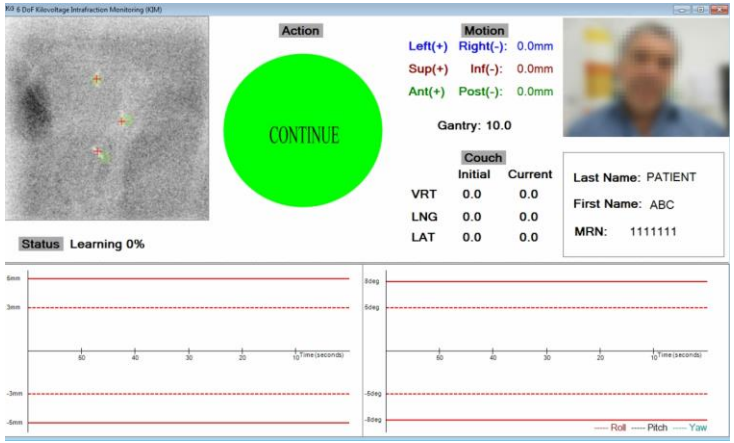
JAMA Network Open. 2019;2(2):e188006.

Dose with and without MLC tracking

Colvill IJROBP 2015

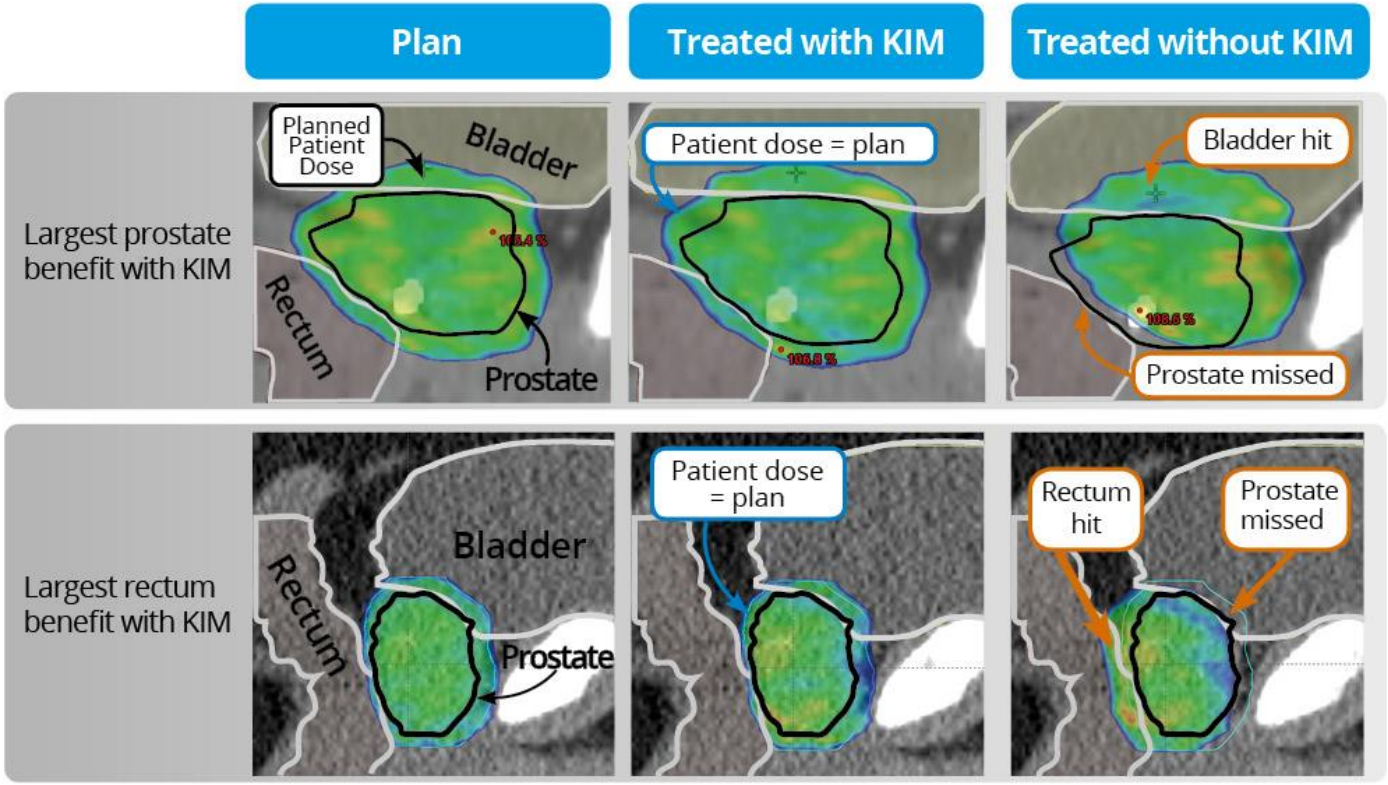
The TROG 15.01 Stereotactic Prostate Ablative Radiotherapy With KIM (SPARK) Trial





Prostate SABR + KIM

SPARK: Primary outcome – dosimetric improvement



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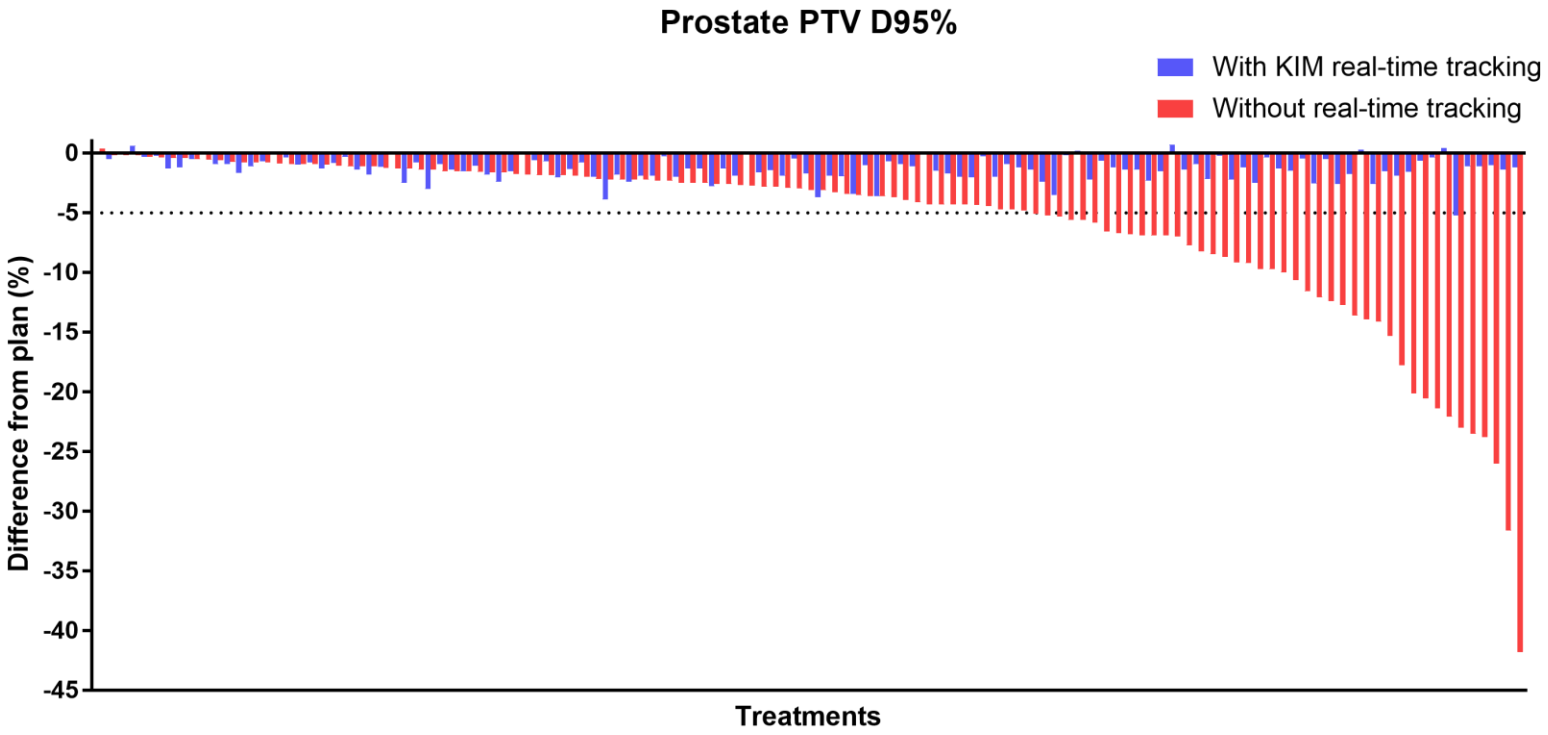

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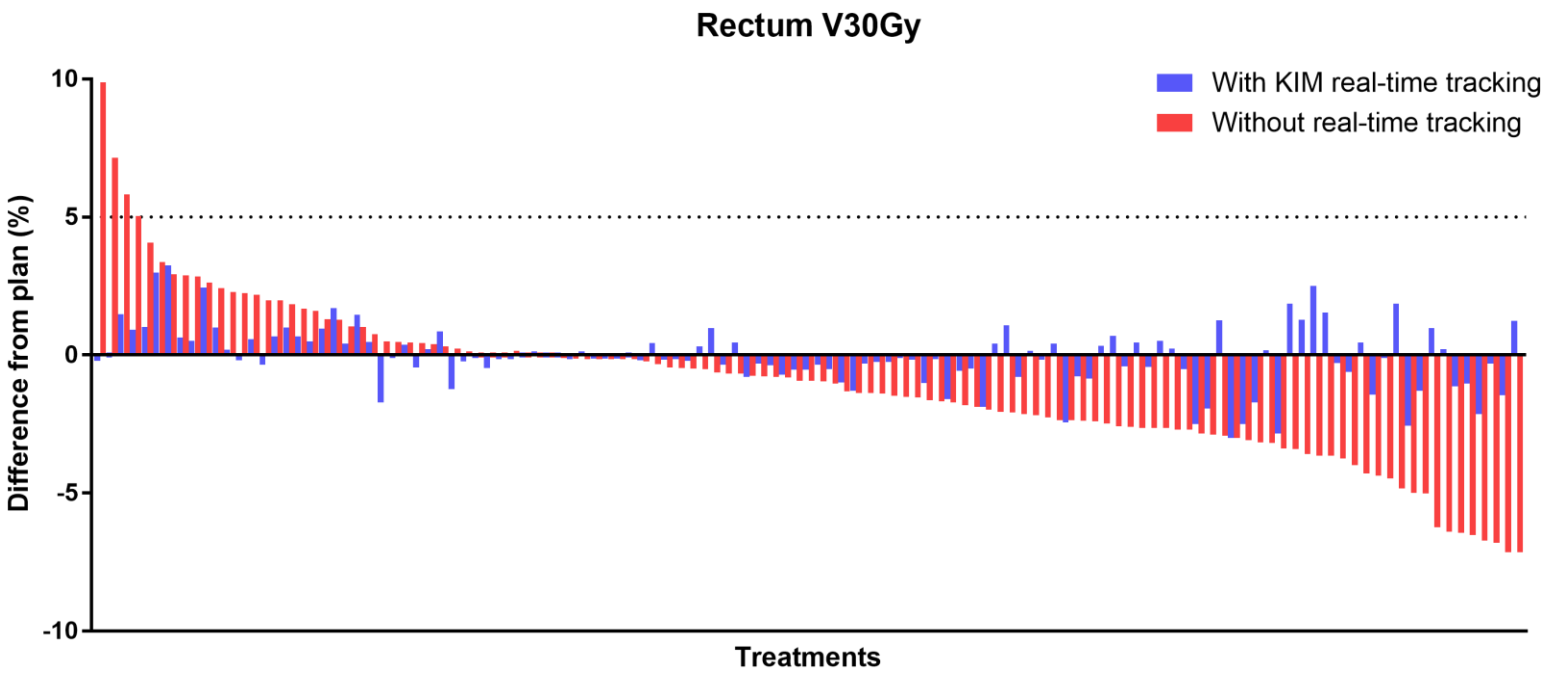

Keall IJROBP 2020

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Real-time adaptation: Rationale, system overview and clinical experience

Summary

Summary: Real-time adaptive radiation therapy …

… has fast-growing clinical uptake

… has compelling clinical drivers and clinical results

… has demonstrated the combined benefit of increased accuracy and increased efficiency