Intensity Modulated Brachytherapy Using Directional Sources

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pxAlpha

Conflict of Interest Disclosure

- Founder of pxAlpha, LLC, which is developing rotating shield brachytherapy technology

What is IMBT?

INSTITUTE OF PHYSICS PUBLISHING PHYSICS IN MEDICINE AND BIOLOGY

Phys. Med. Biol. **47** (2002) 2495–2509 PII: S0031-9155(02)35423-X

Possibilities for intensity-modulated brachytherapy: technical limitations on the use of non-isotropic sources

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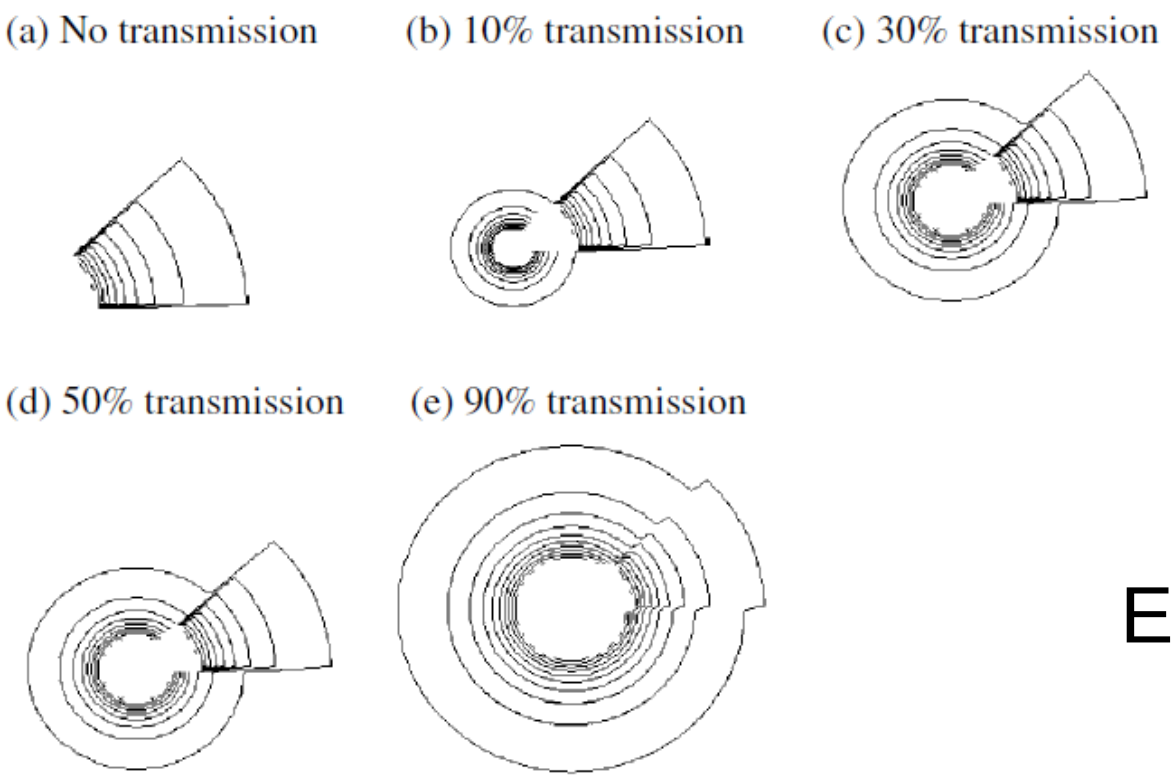
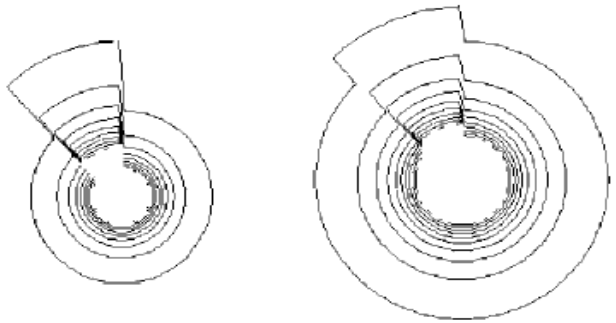
Partially-Shielded Sources

- ^{192}Ir dose distributions
- Ignore scatter
- 45° emission at various shield transmission levels



Effects of transmission on dose distribution:



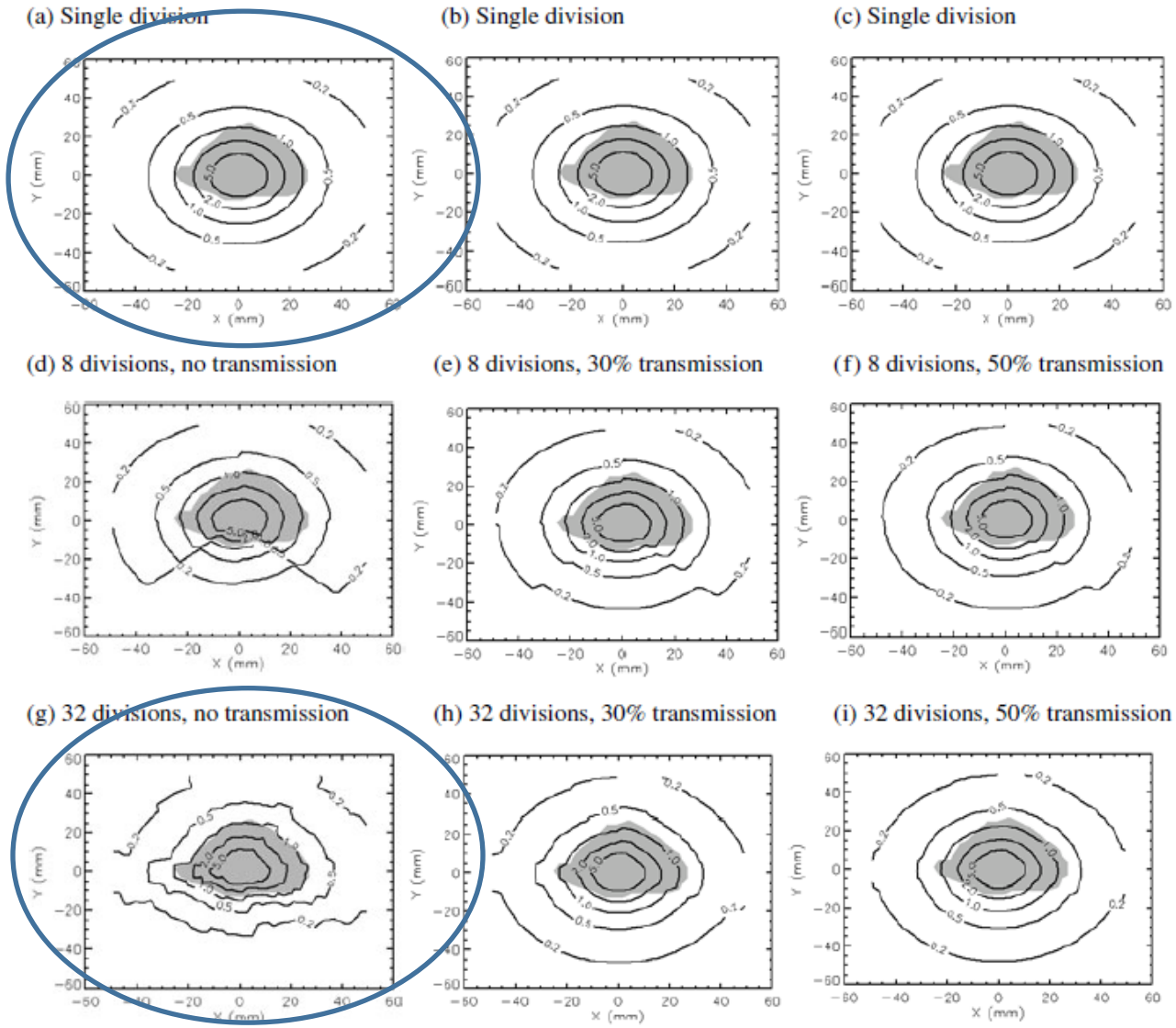
Emission: 45° x 1 11.25° x 4

Ebert MA, Phys Med Biol 47, 2495-2509 (2002)

IMBT Improves Tumor Dose Conformity Relative to HDR

Conventional

Better

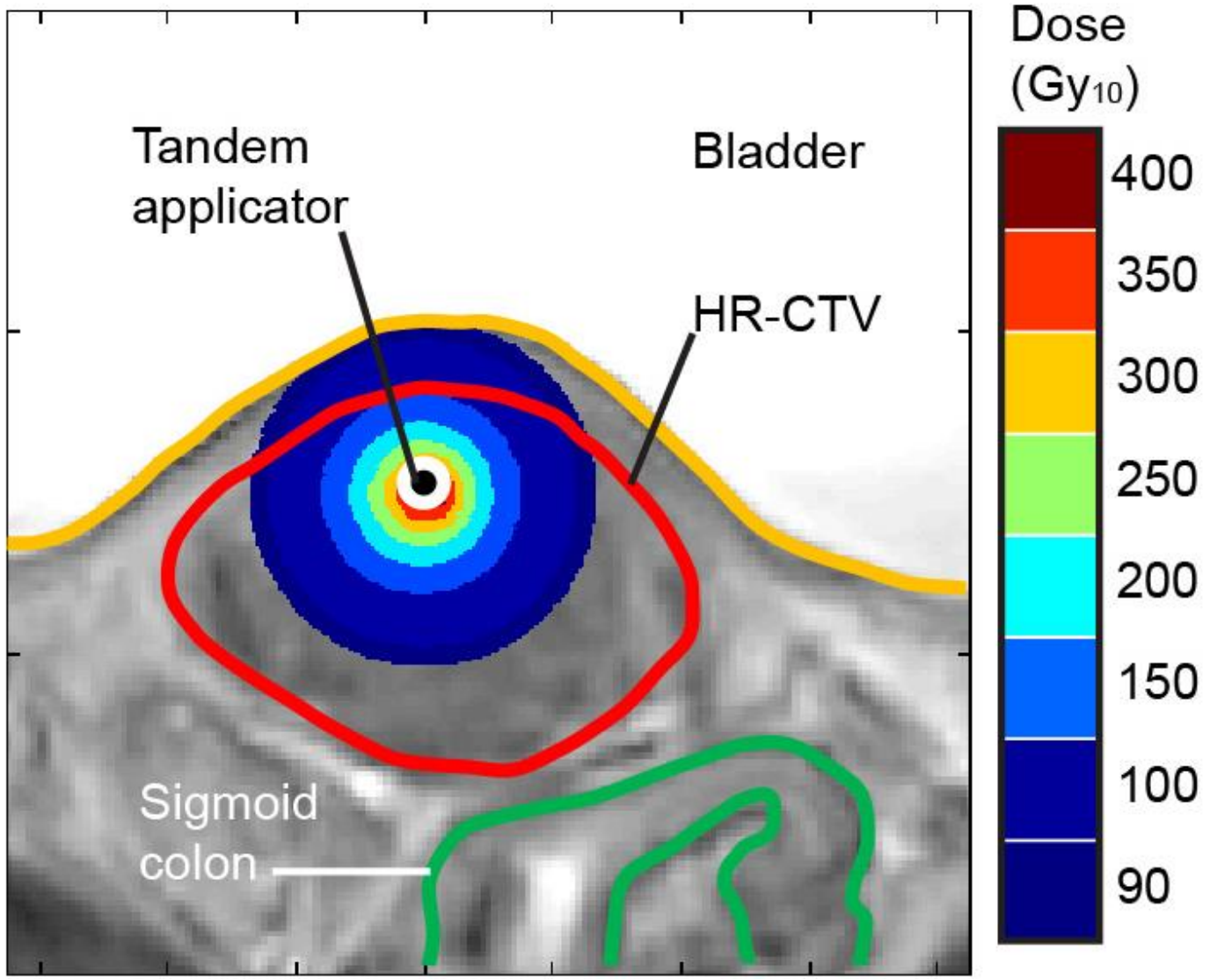


Ebert, Phys Med Biol 47, 2495-2509 (2002)

Cervical Cancer

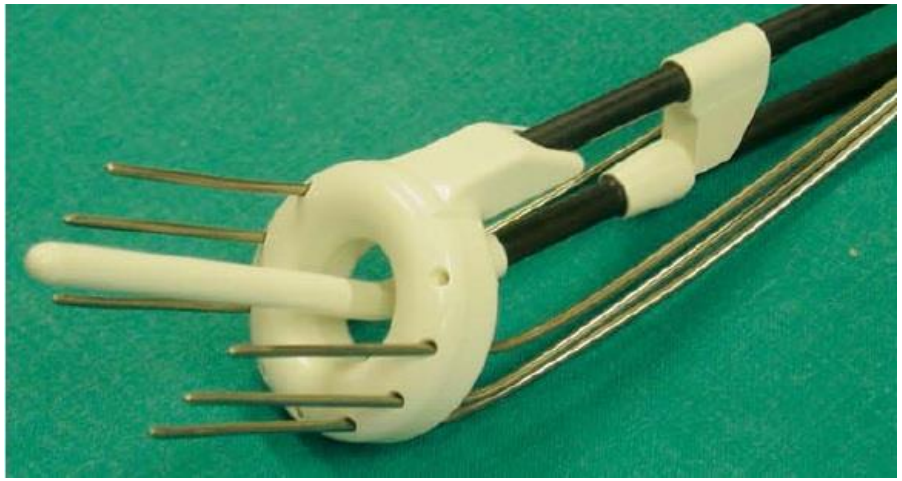
- 13,240 women estimated to be diagnosed with cervical cancer in the U.S. alone in 2018 (Siegel et al, 2018)
- For stage IB and higher tumors, standard treatment is Chemo + External Beam RT + Brachytherapy
- Brachytherapy boost is critical for tumor control
- Tumors are often irregularly-shaped, laterally-extended, and BT applicator not centered

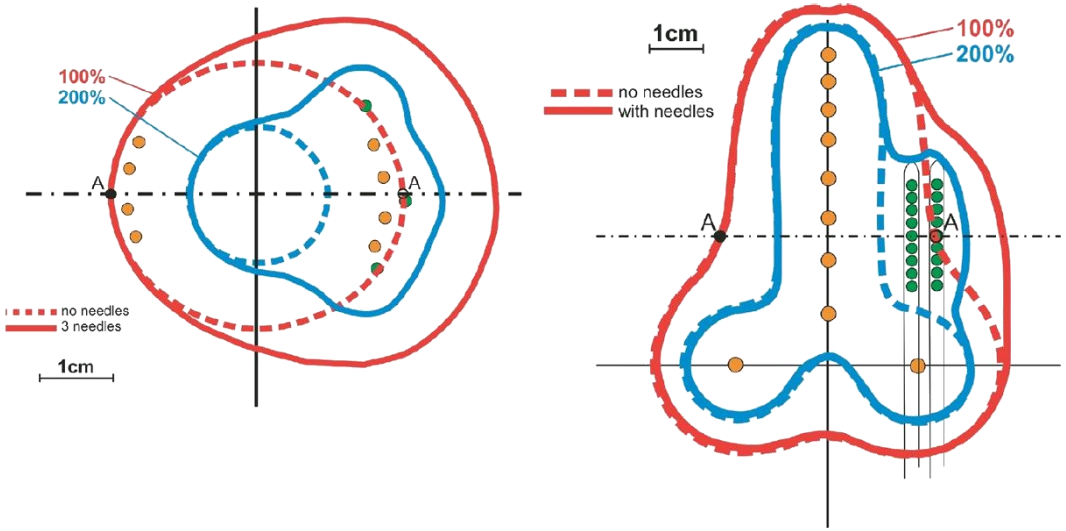
How can IMBT Benefit Cervical Cancer Patients?

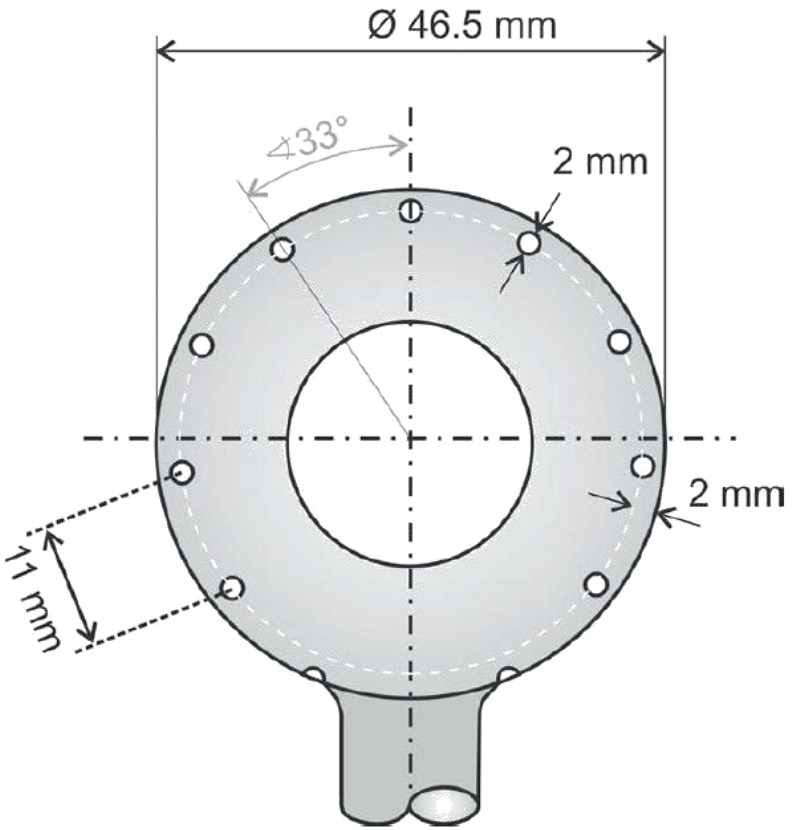


(including EBRT)

Intracavitary/Interstitial Approach to Improve Dose Distributions

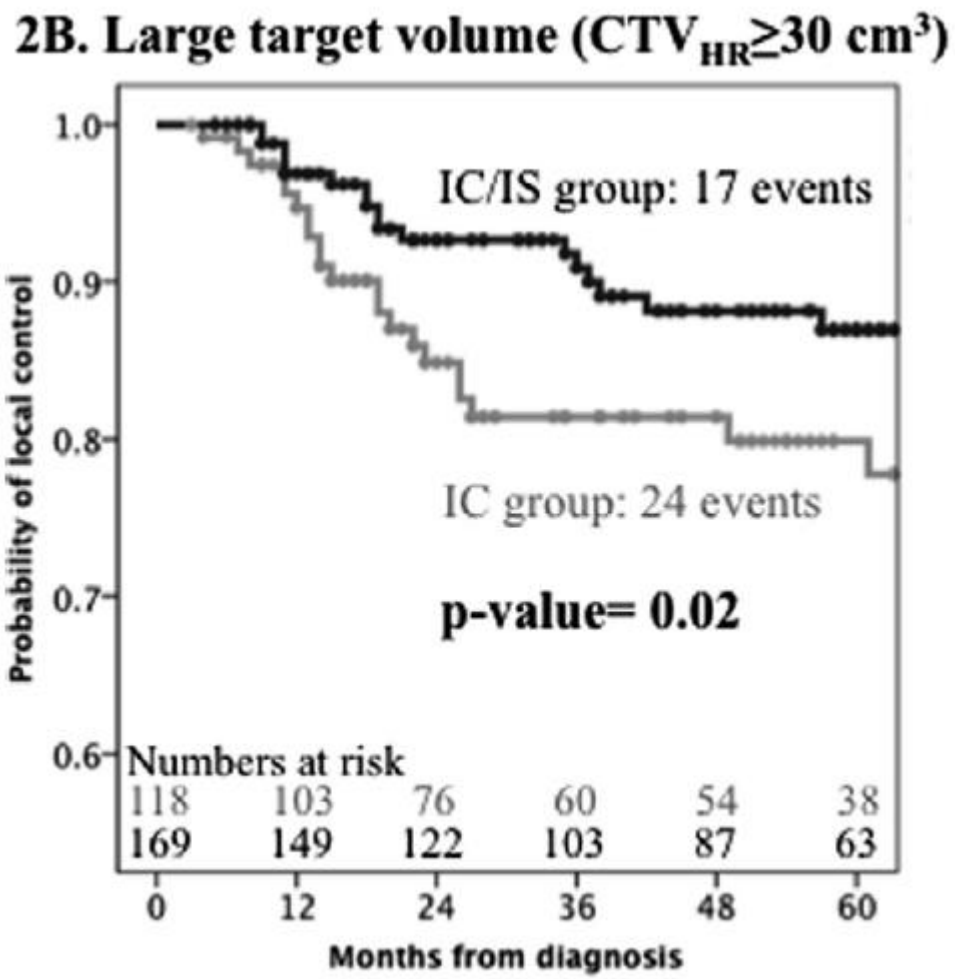






Images from Kirisits et al, IJROBP 65, 624-30 (2006)

The Intracavitary/Interstitial Approach Works



- RetroEMBRACE: Retrospective study completed prior to EMBRACE I (2008)
- Local control at 3 years for HR-CTVs ≥30 cm^3
  - 92% at centers with IC/IS (n=169)
  - 82% at centers with IC only (n=118)
- Local control at 5 years:
  - 87% at centers with IC/IS (n=124)
  - 80% at centers with IC only (n=163)
- EMBRACE II: Launched in 2016
  - ≥20% of patients at a participating center must receive IC/IS

L. Fokdal et al, Radiother Oncol **120**, 434-440 (2016)
Pötter et al, "The EMBRACE II study..." Clin Transl Radiat Oncol **9**, 48-60 (2018)

Logistical Benefits of an Intracavitary Only Approach

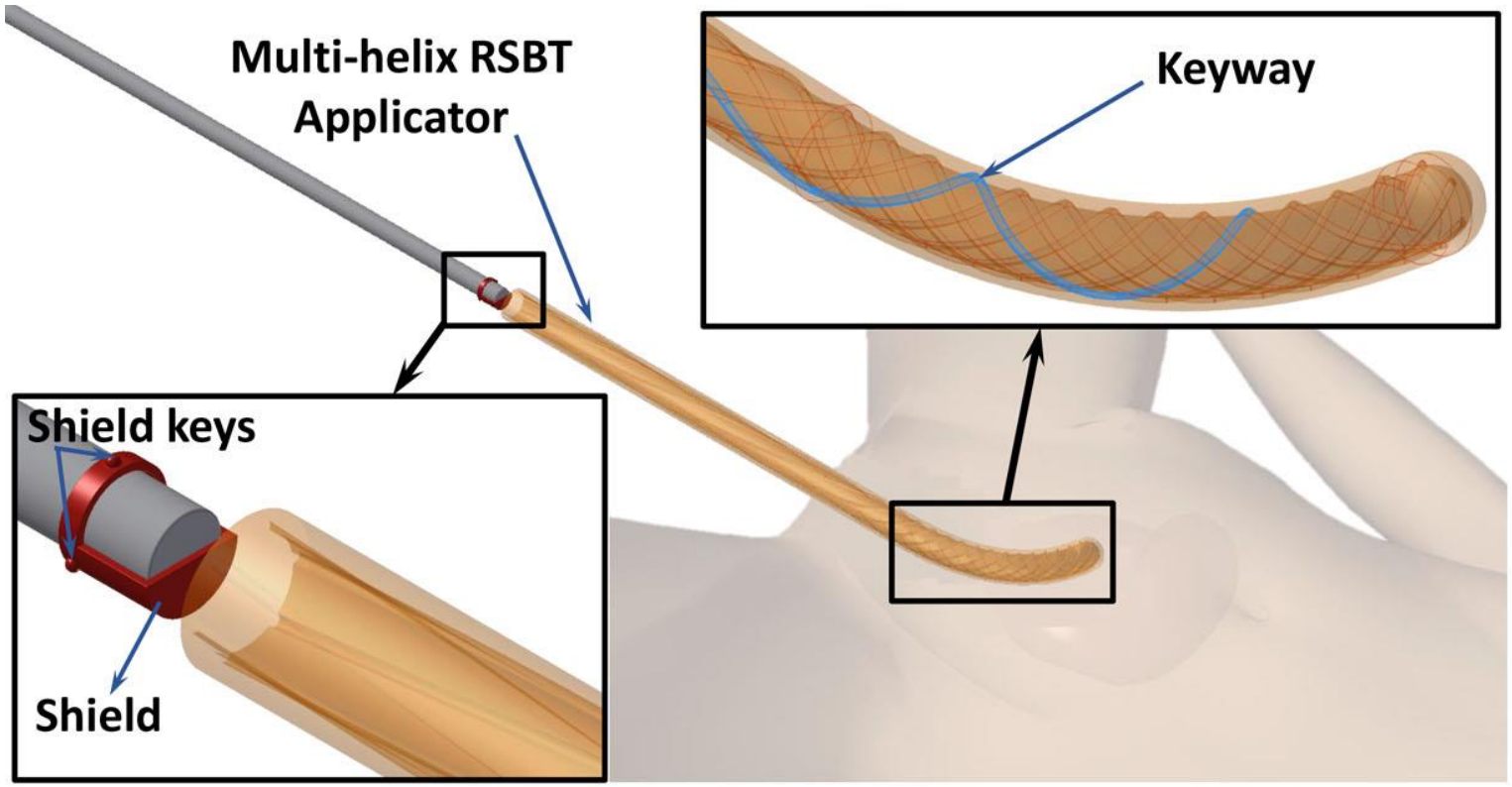
- 25% decline in average number of residency-based IS brachytherapy procedures reported between 2006-2007 and 2010-2011 (Compton et al)

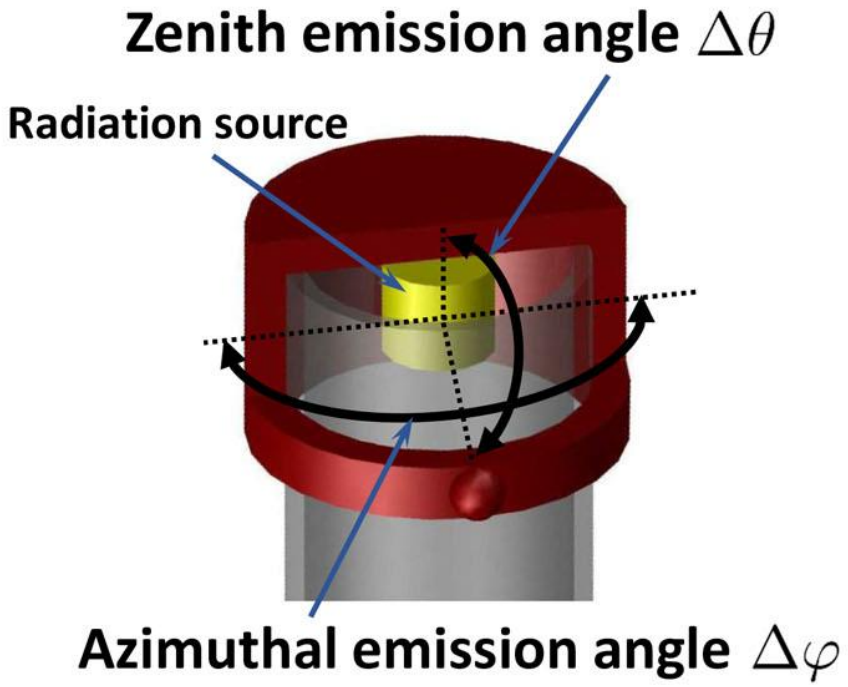
- 50% of Canadian centers with the capability to treat gynecological cancer patients with HDR-BT also have IC/IS capability (Gaudet et al)
  - Even so, <10% of residents and fellows reported being satisfied with the IC/IS training they received (Gaudet et al)
  - Opposite case for IC-only training: 70% satisfied (Gaudet et al)

- Numbers in US not available but unlikely more in favor of IC/IS than for Canada since U.S. centers tend to be less consolidated and more widely dispersed

J. J. Compton et al, Brachytherapy **12**, 622-627 (2013).
M. Gaudet et al, Brachytherapy **14**, 197-201 (2015).

Helical Rotating Shield Brachytherapy Using Axxent



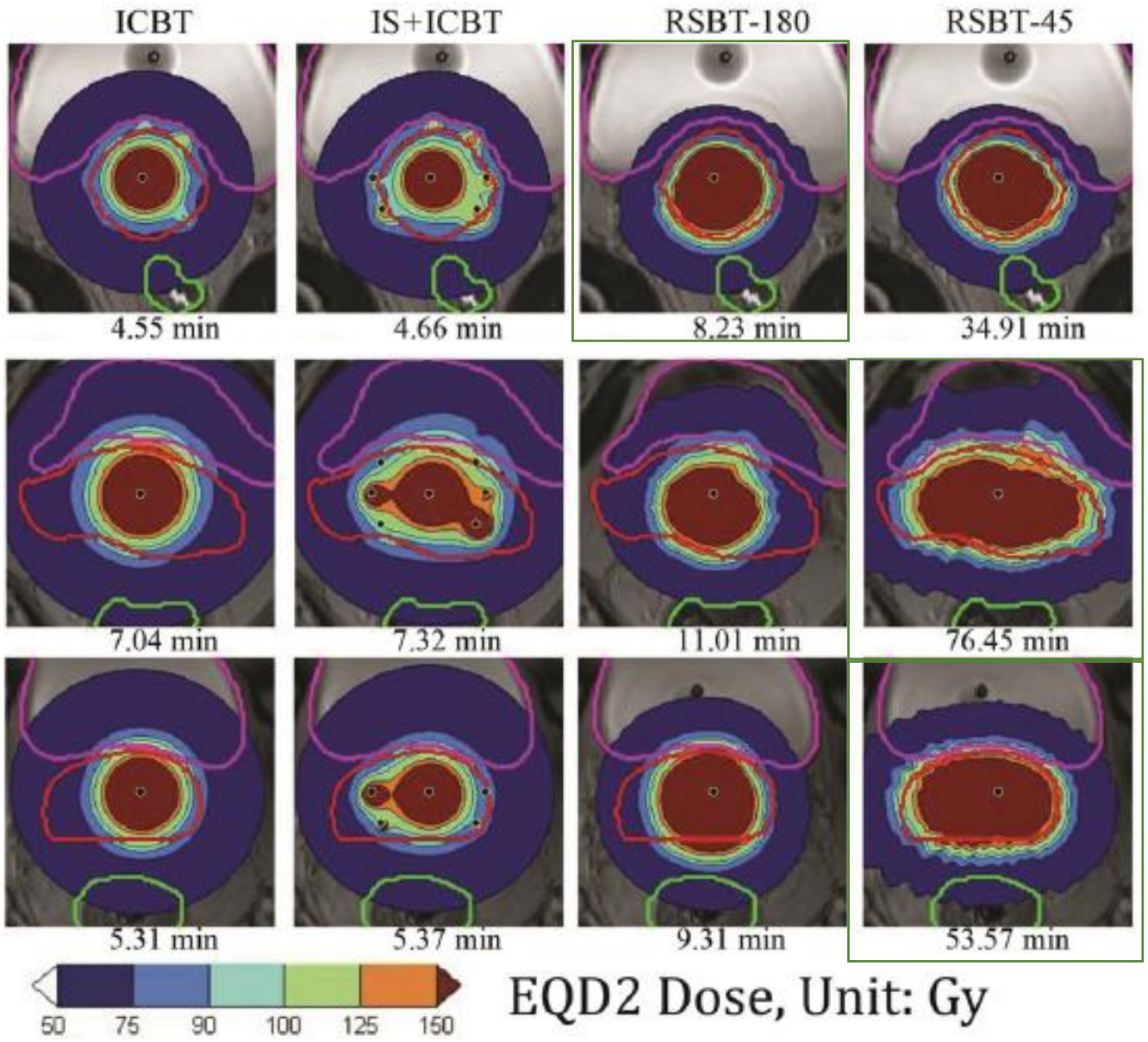


Dadkhah et al, Med Phys 42, 6579-6588 (2015)

Cho et al, Med Phys 44, 5384-5392 (2017)

Patent pending

RSBT Provides Excellent HR-CTV Dose Conformity

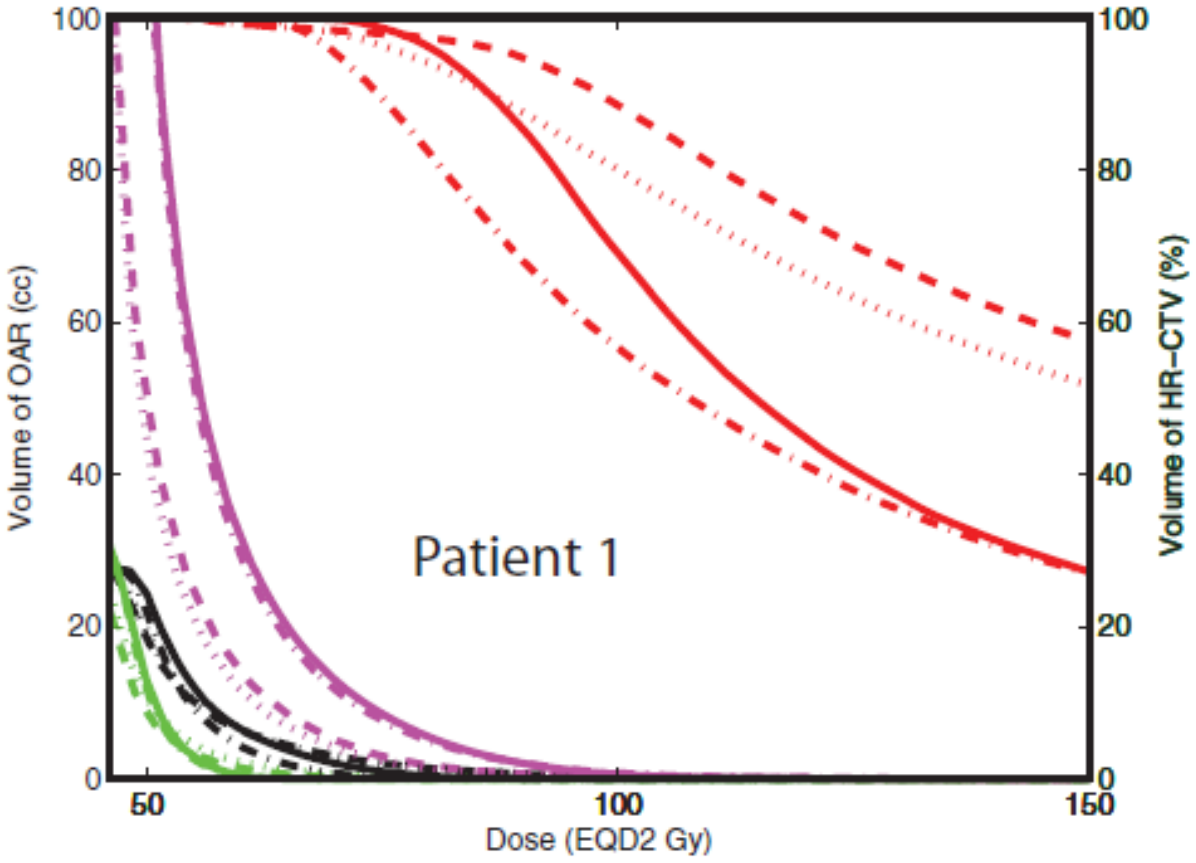


"Best" plan

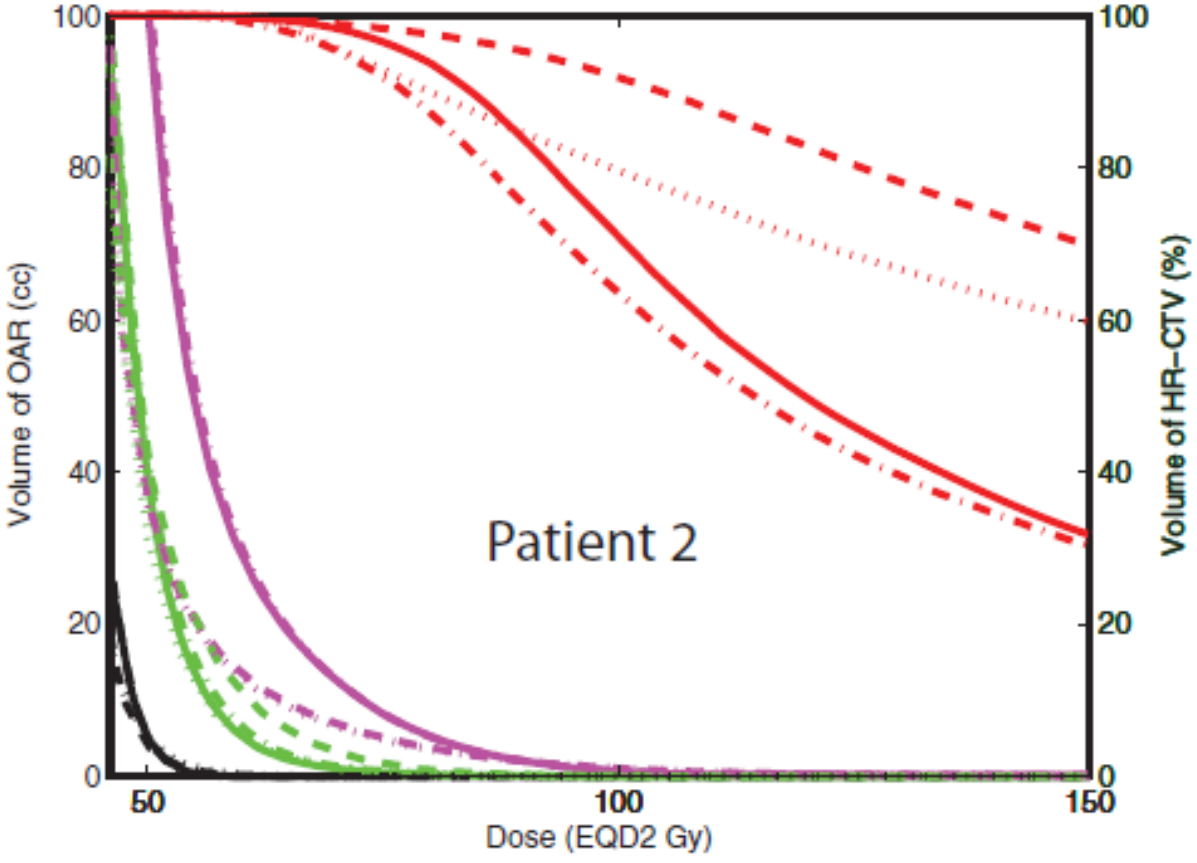
Yang et al, PMB 58, 3931-41 (2013)

Dadkhah et al, Med Phys 42, 6579-6588 (2015)

RSBT Provides Excellent HR-CTV Dose Conformity



Yang et al, PMB 58, 3931-41 (2013)



Dadkhah et al, Med Phys 42, 6579-6588 (2015)

Physics Contribution

Direction-Modulated Brachytherapy for High-Dose-Rate Treatment of Cervical Cancer. I: Theoretical Design

Dae Yup Han, MSc,[*,†] Matthew J. Webster, MSc,[*,‡] Daniel J. Scanderbeg, PhD,[*] Catheryn Yashar, MD,[*] Dongju Choi, PhD,[*] Bongyong Song, PhD,[*] Slobodan Devic, PhD,[§,‖] Ananth Ravi, PhD,[¶] and William Y. Song, PhD[*,¶]

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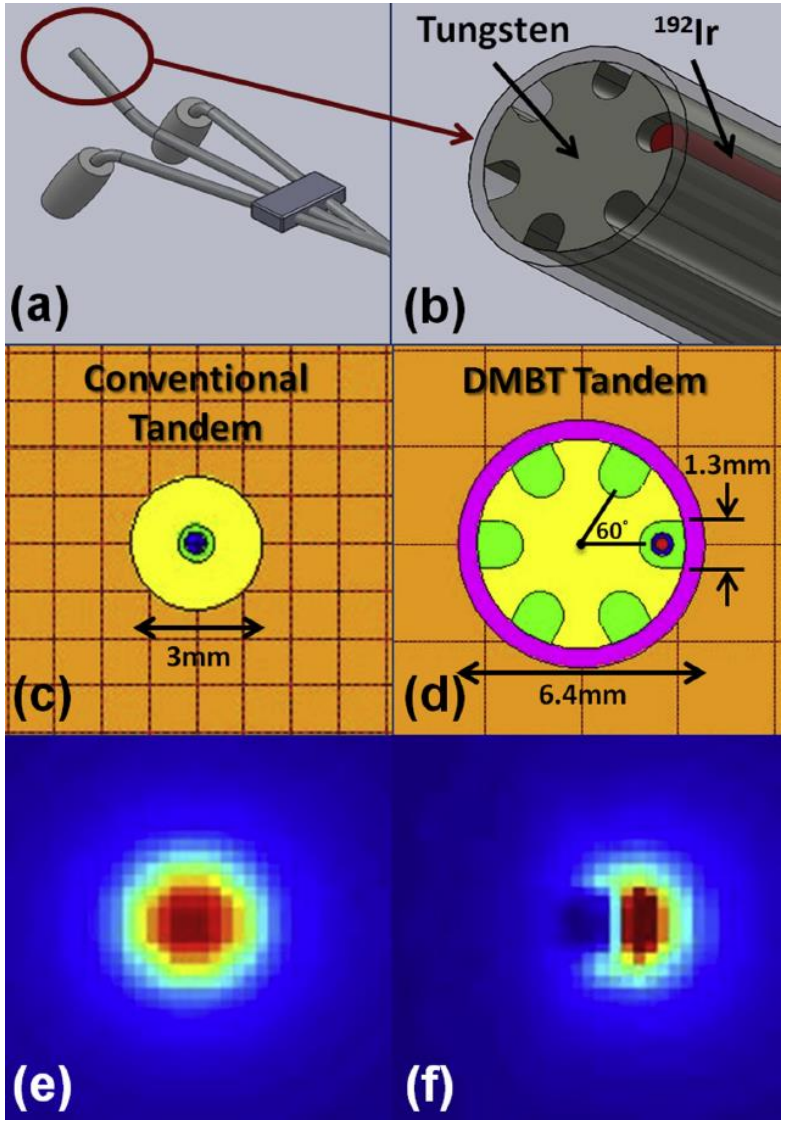
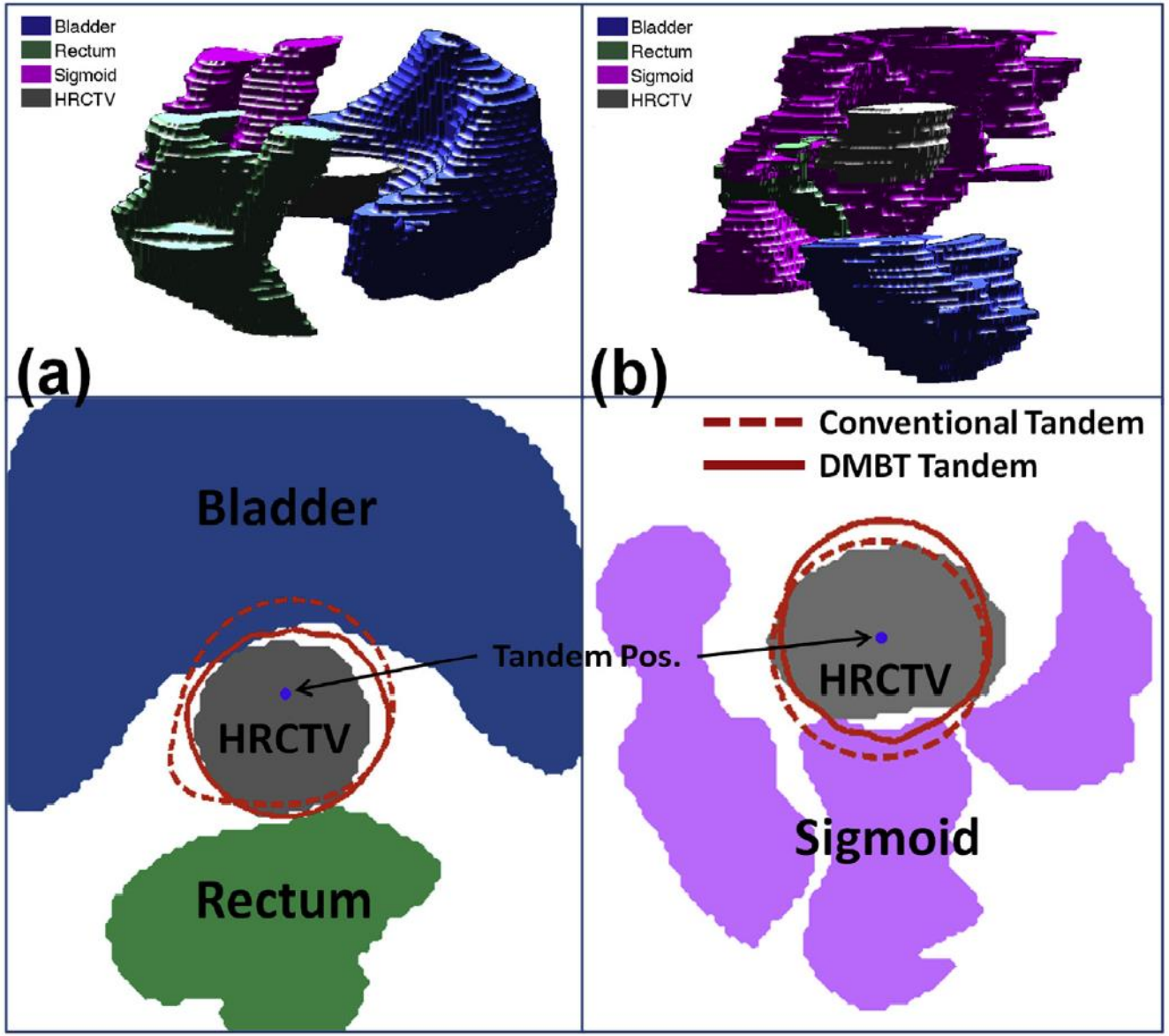
^{192}Ir based Direction-Modulated Brachytherapy



Han DY, …., Song WY, Int J Radiat Oncol Biol Phys 89(3), 666-673 (2014)

^{192}Ir DMBT for Cervical Cancer



Han DY, …., Song WY, Int J Radiat Oncol Biol Phys 89(3), 666-673 (2014)

Potential Benefits of IMBT for Prostate Cancer

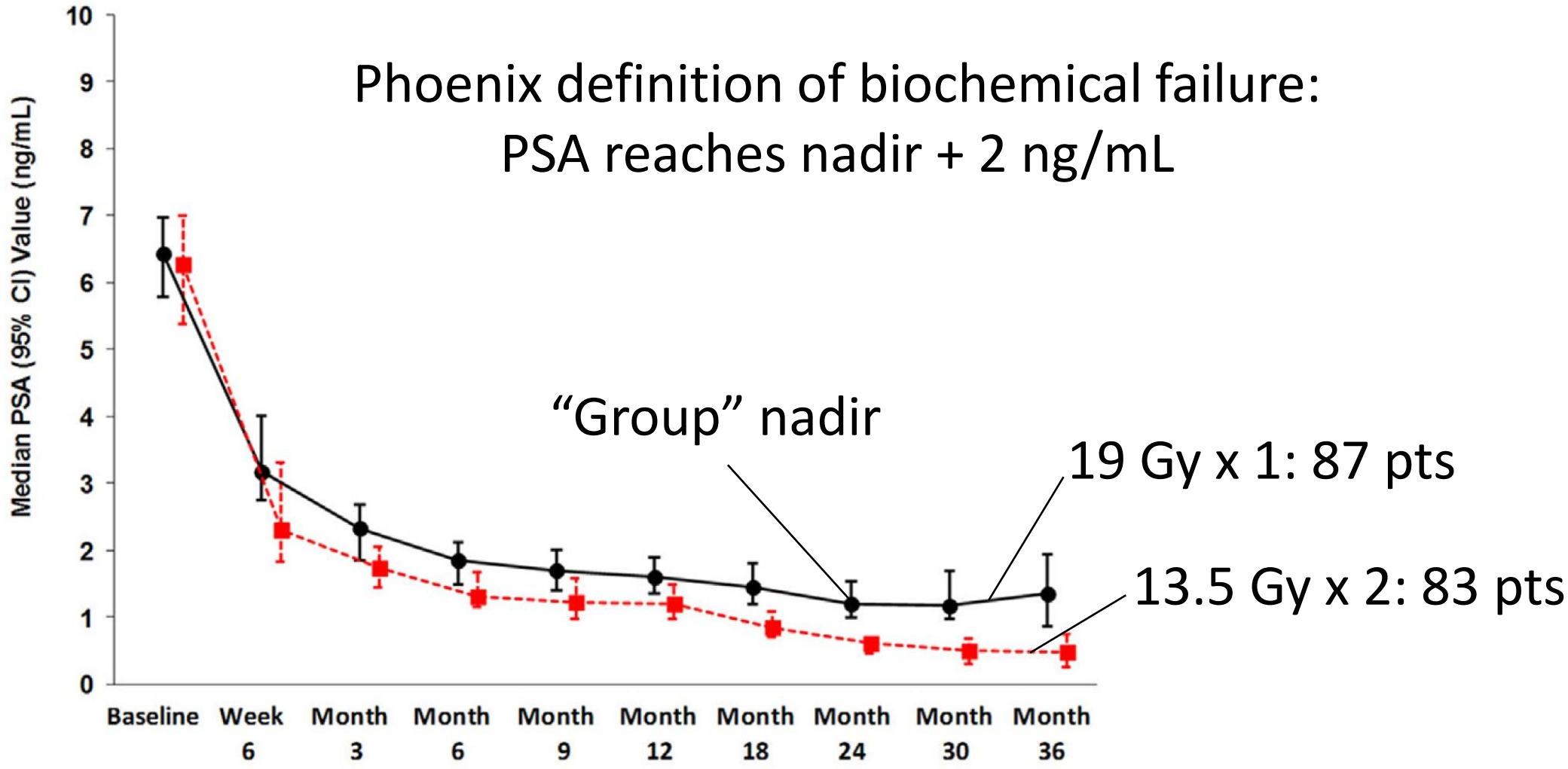
- 160,000 new diagnoses expected in 2018
- 5-year relative survival rates for localized prostate cancer are >99%
- 30,000 deaths expected in 2018, 2nd highest for cancer death in men
- Treatments that improve convenience for the patient and maintain low toxicity without compromising effectiveness are attractive:
  - SBRT
  - Low-dose-rate brachytherapy
  - One-shot prostate cancer HDR

Siegel et al, “Cancer Statistics, 2018,” CA Cancer J Clin 68,7-30 (2018)

One-Shot Prostate HDR-BT Clinical Results Summary

Series (Last update)	Dose	# Patients	Disease Risk	Median Follow-up	Biochemical Control @ Median F/U	Grade ≥ 3 Toxicity (%)			
						Acute		Late	
						GU	GI	GU	GI
Mt. Vernon Hospital, UK (2017)	19 Gy x 1 20 Gy x 1	23 26	Int, High Int, High	4.1 4.1	94% 94%	0 9	0 0	2.6	0
Santander, Spain (2016)	19 Gy x 1	60	Low, Int	6.0 y	66%	0	0	0	0
Toronto Sunnybrook (2017)	19 Gy x 1	87	Low, Int	2.25 y	92%	1.1	0	1.1	0
Oakland U., Michigan (2017)	19 Gy x 1	58	Low, Int	2.9 y	93%	0	0	0	1.7

Single Fraction HDR – Toronto Sunnybrook



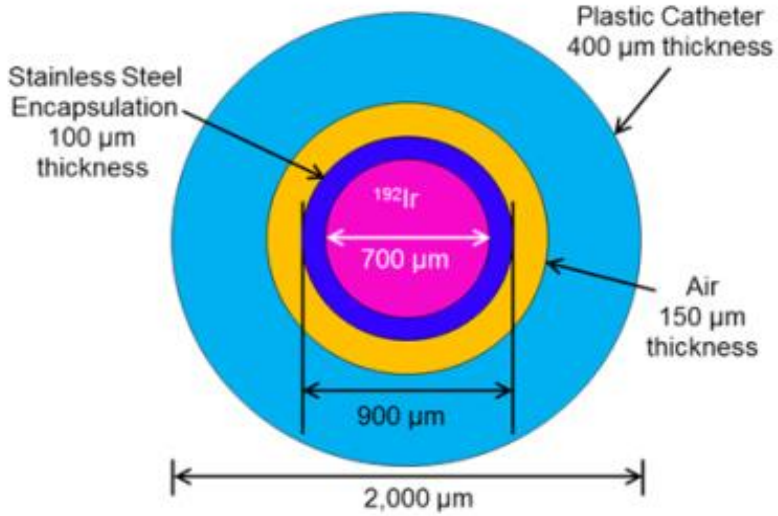
Morton et al, Brachytherapy 16, S19-S20 (2017)
Morton et al, Radiother Oncol 122, 87-92 (2017)

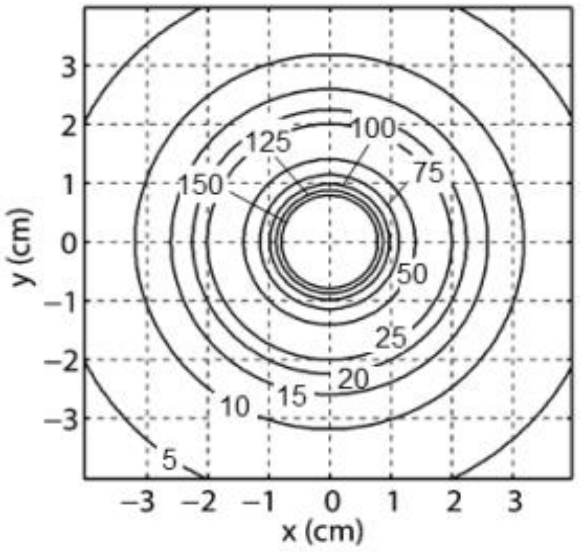
Technology

Radiation Source Cross Section

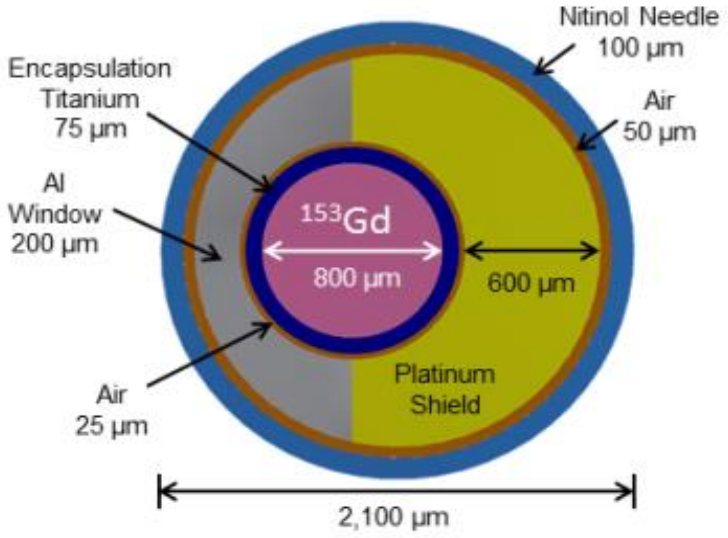
Dose from Each Source

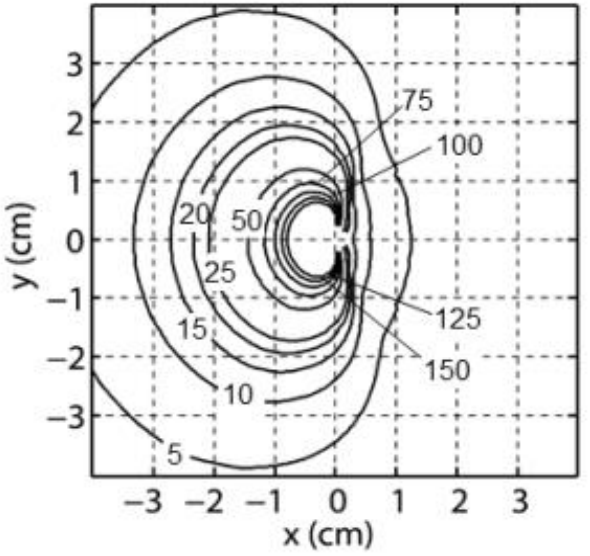
Conventional High-dose-rate Brachytherapy





Rotating Shield Brachytherapy (RSBT)

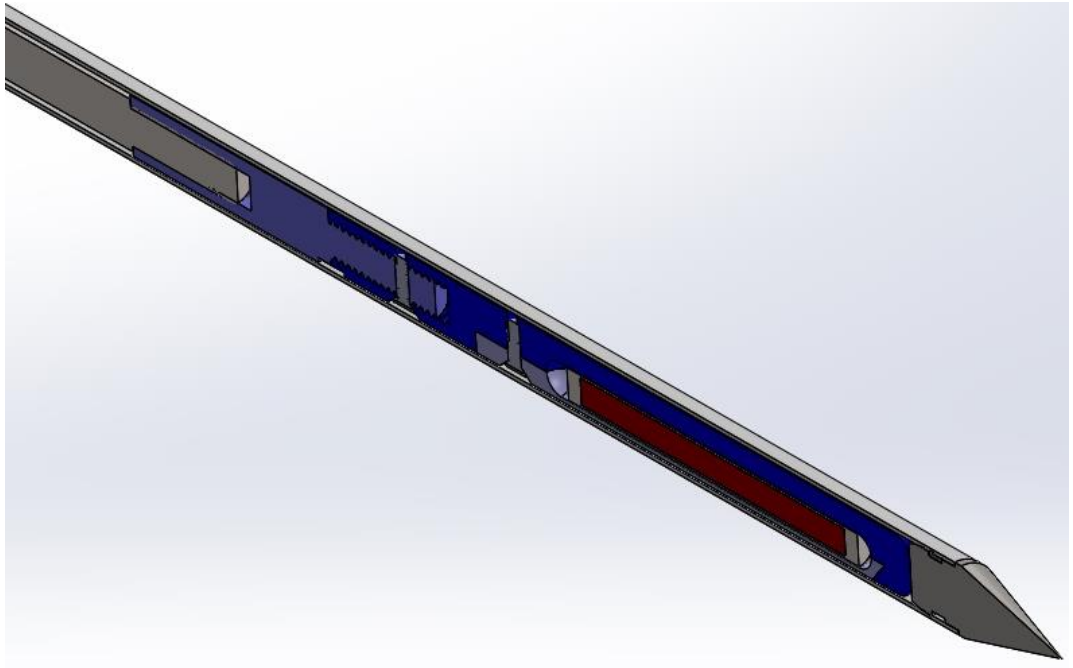




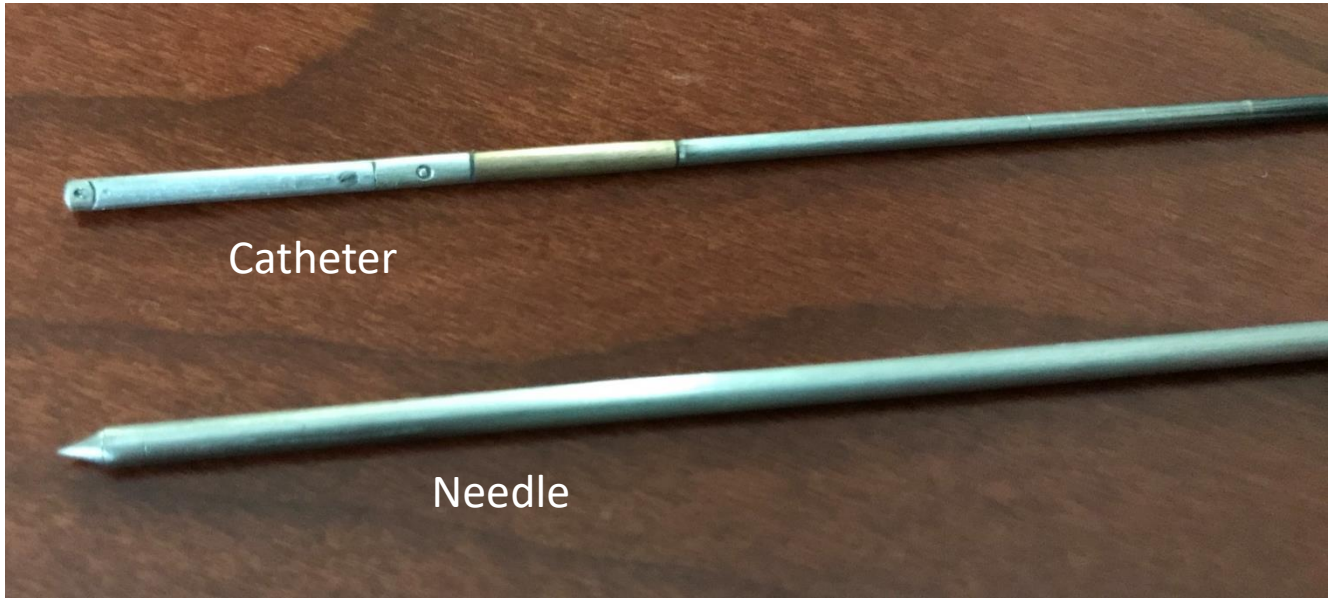
Adams et al, Med Phys 41, 051703 (2014)

Needle and Catheter Design and Prototypes

Needle/Catheter/Source Model

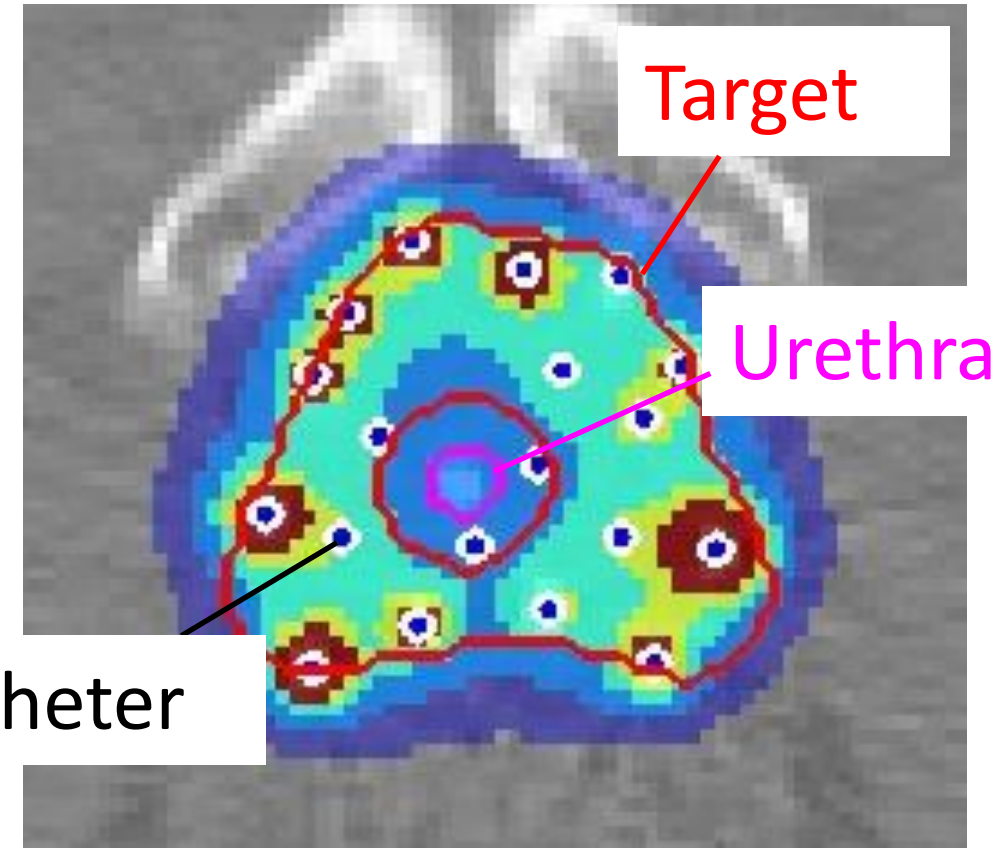


Prototypes



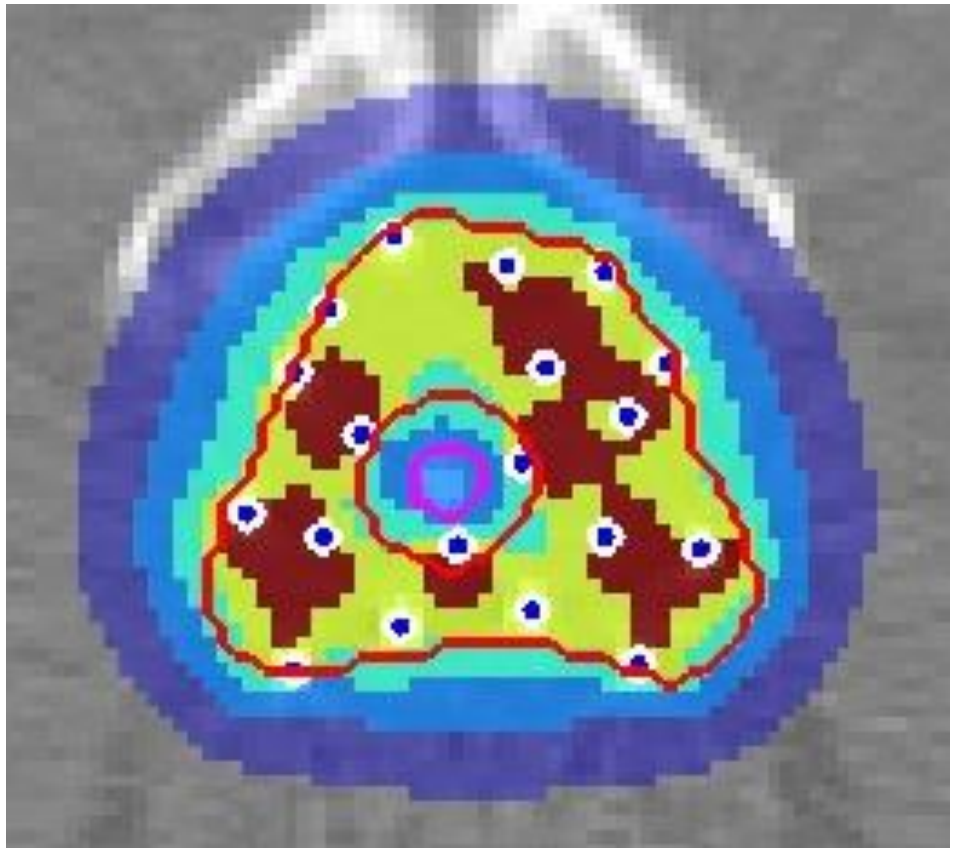
Dose Escalation Achievable with RSBT

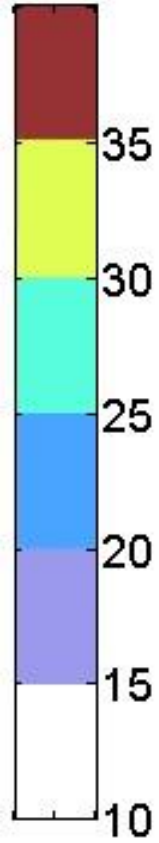
Conventional HDR



One ^{192}Ir source
19 Gy in ~20 minutes

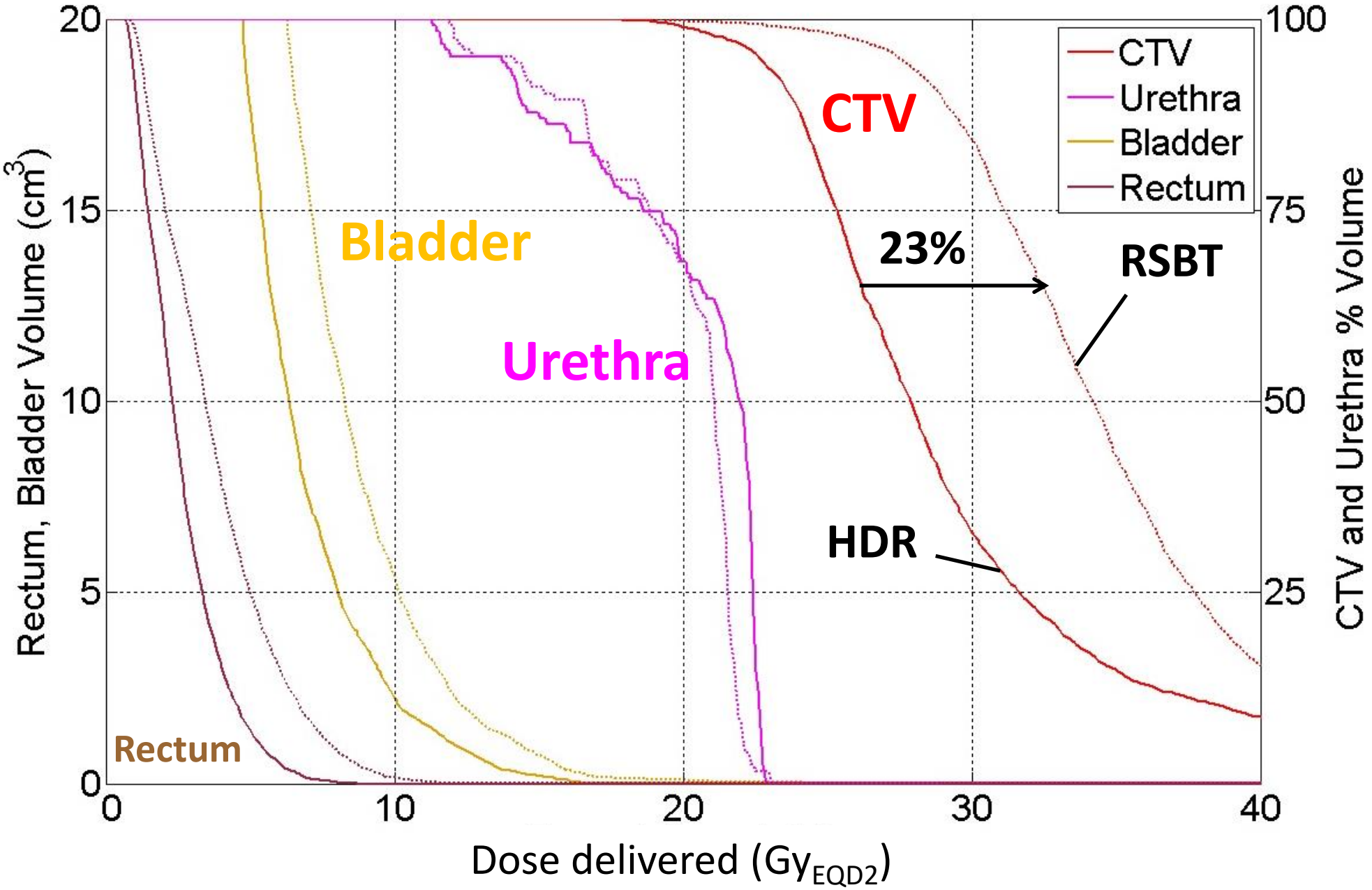
Proposed RSBT



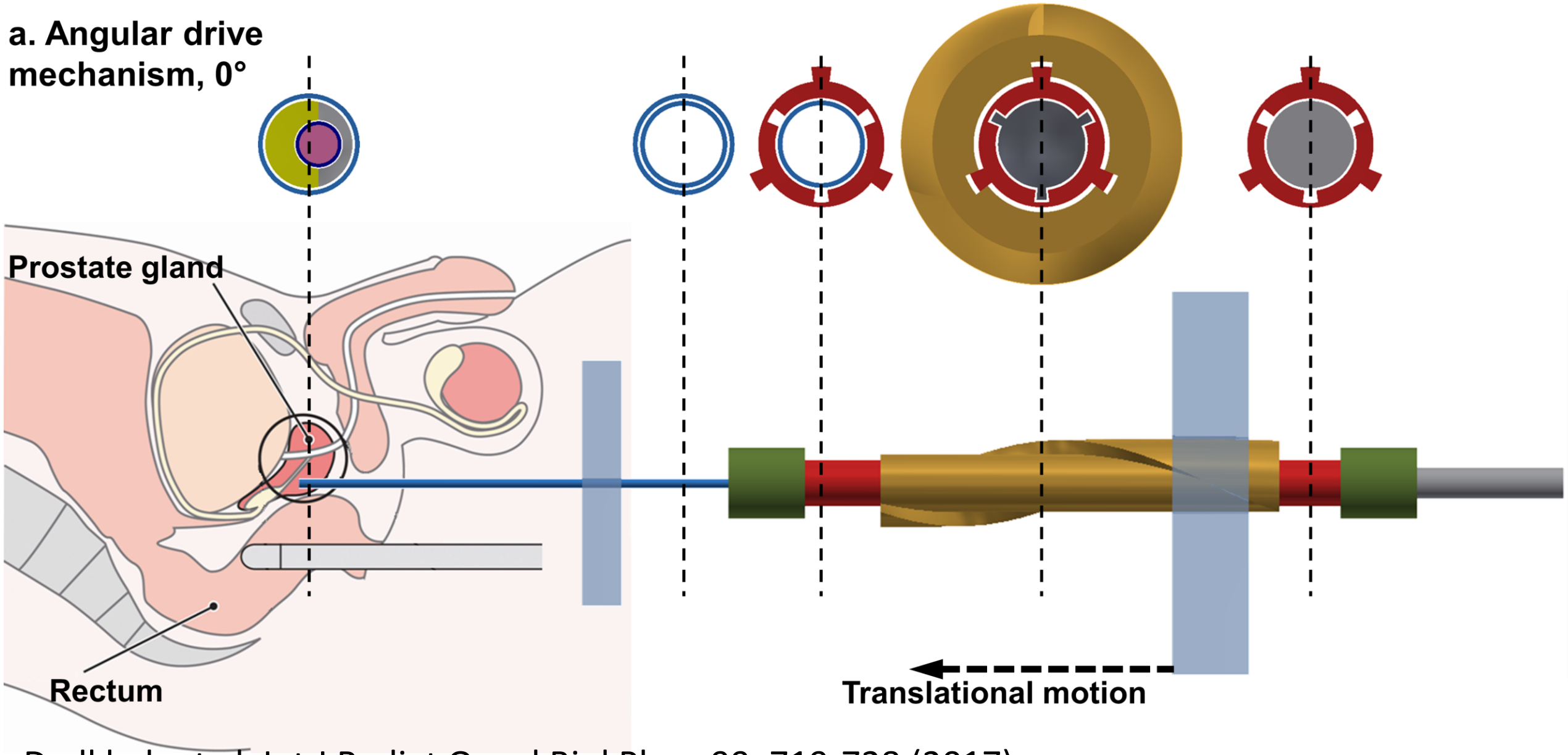


Nineteen ^{153}Gd sources
23 Gy in ~133 minutes
Same Urethral Dose

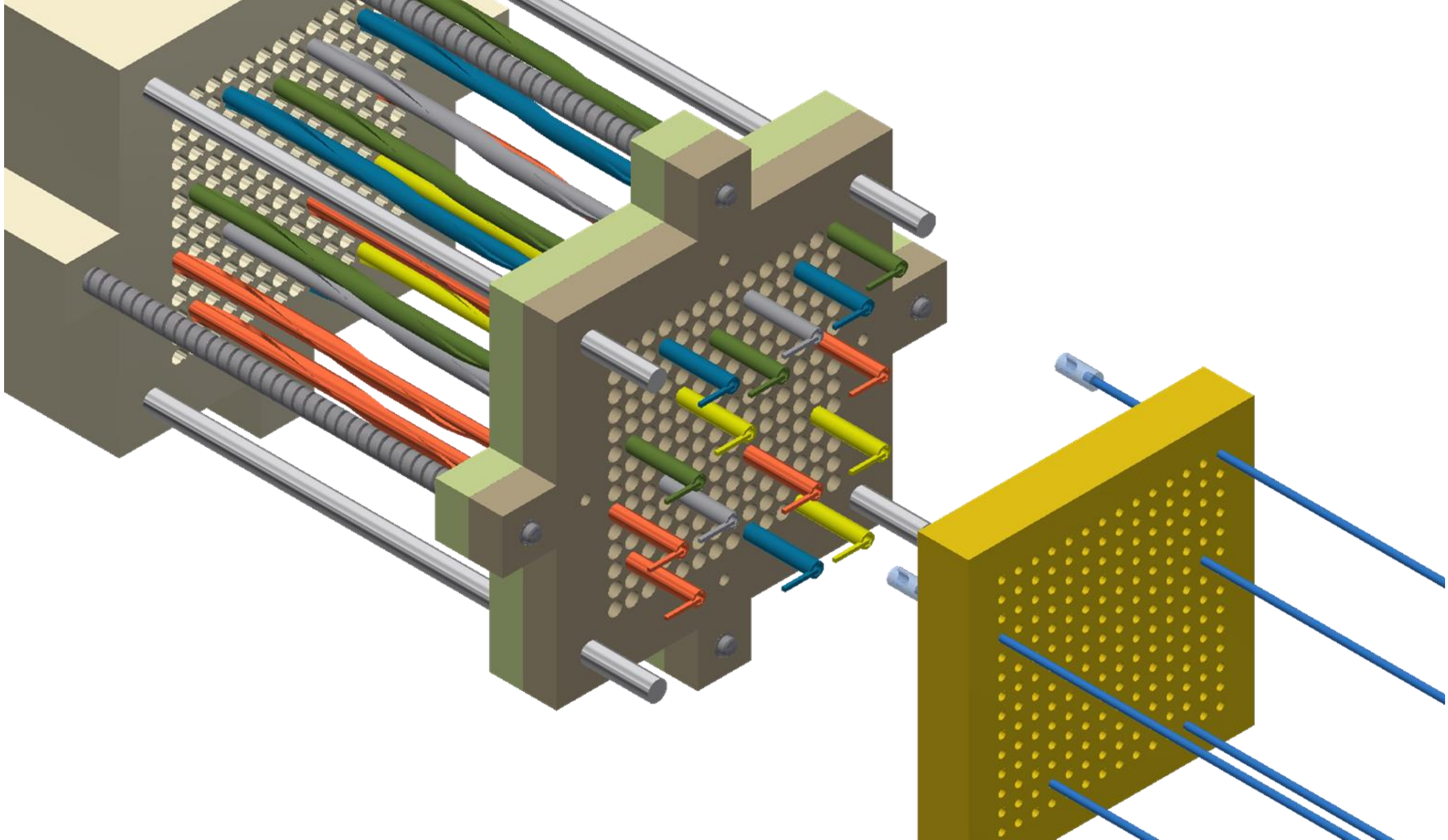
Dose Escalation of 23% Possible with RSBT

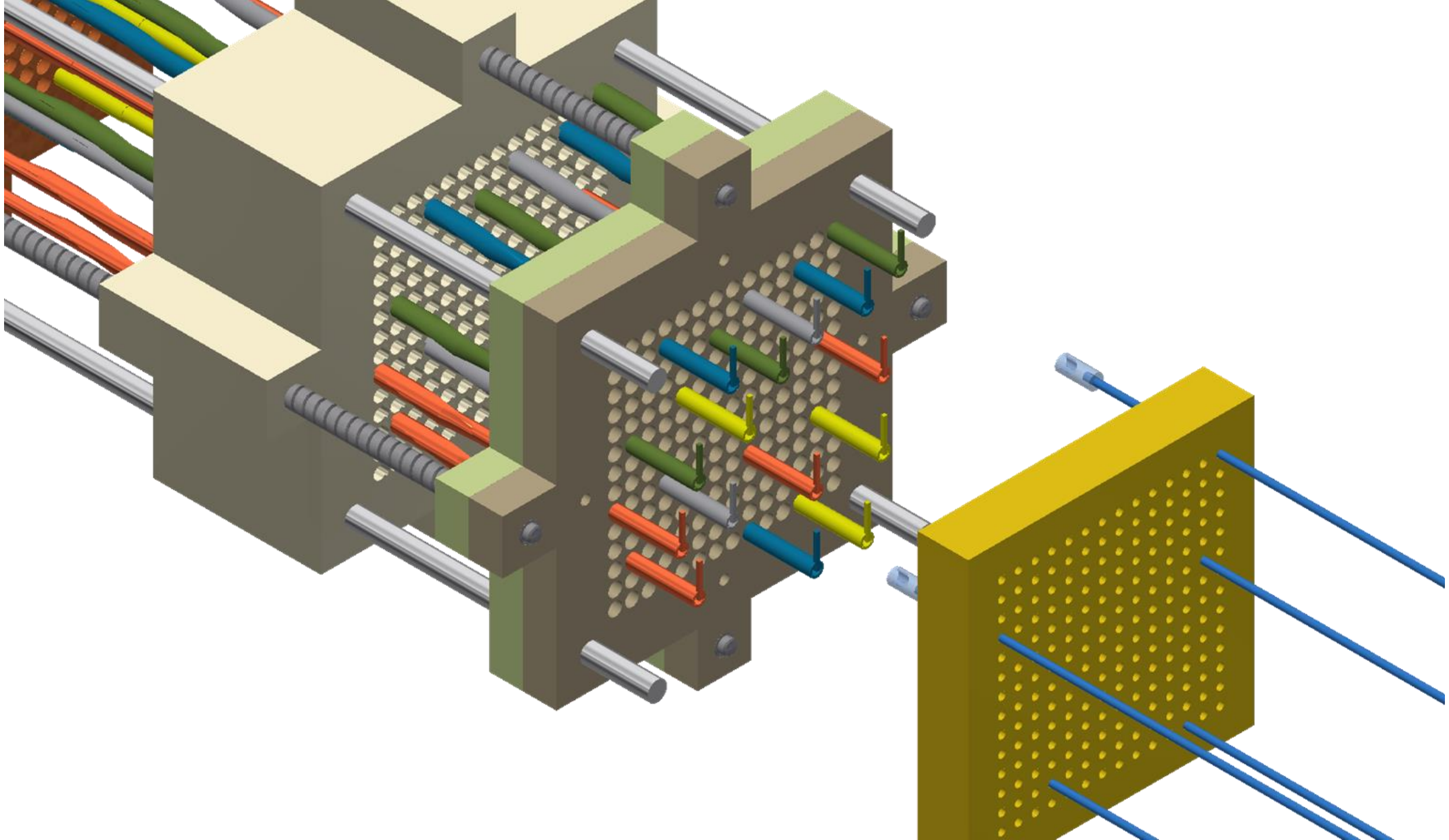


Multisource RSBT Apparatus: Angular Drive Mechanism

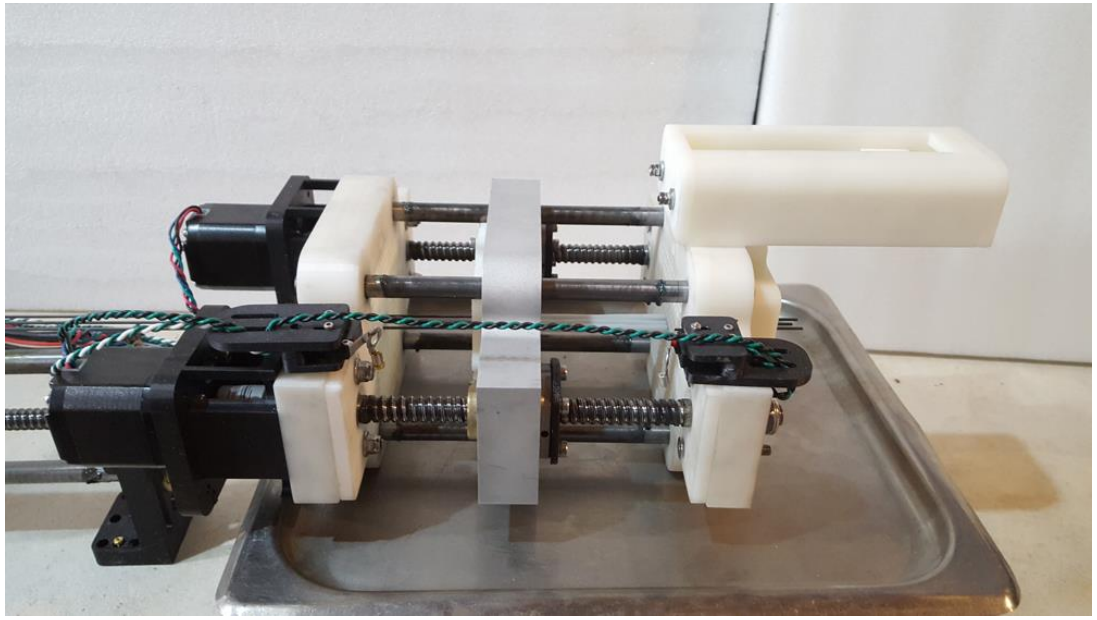


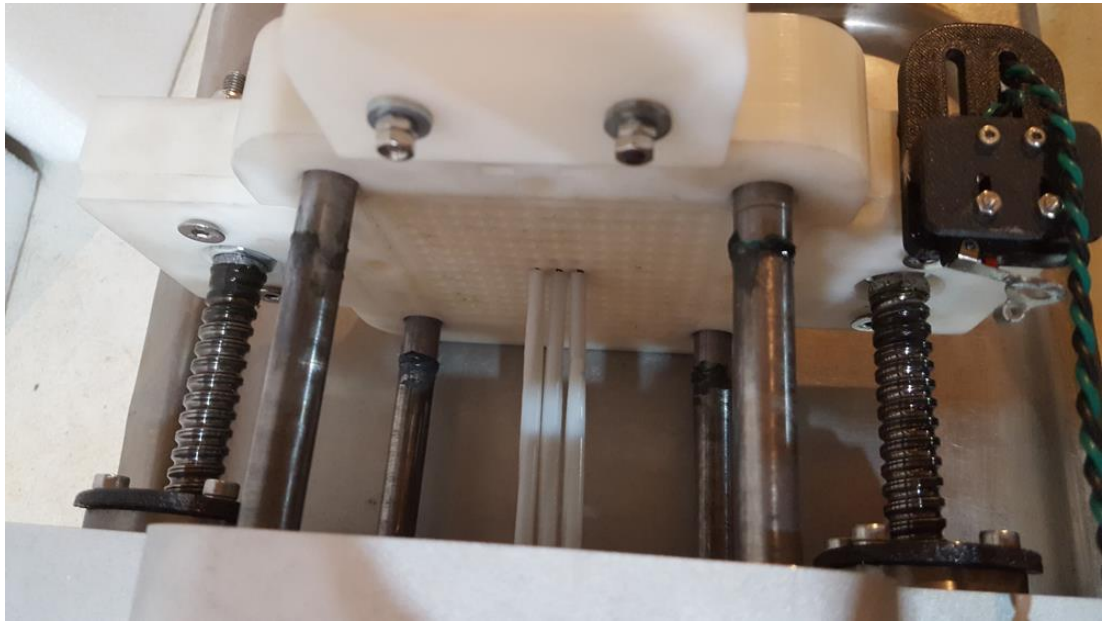
Dadkhah et al, Int J Radiat Oncol Biol Phys, 99, 719-728 (2017)

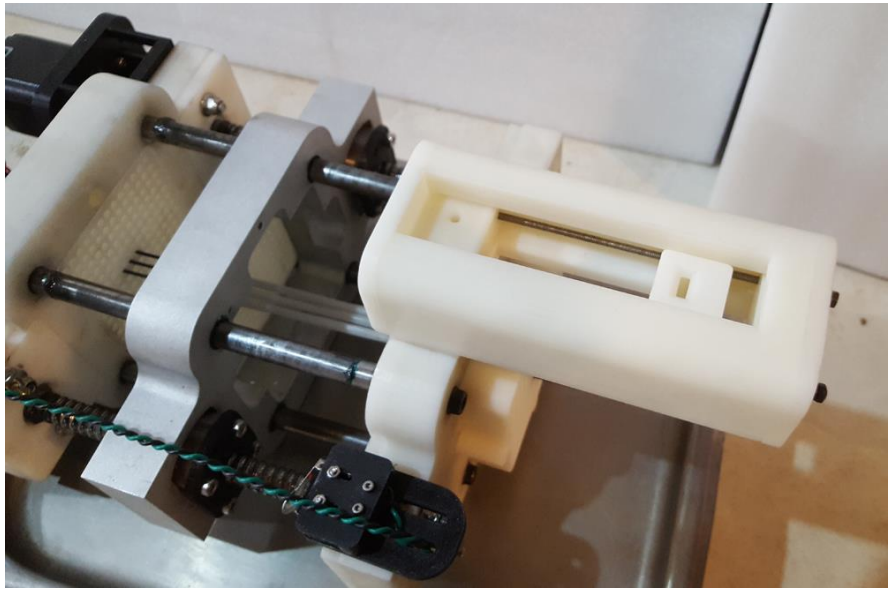




Prototype Construction

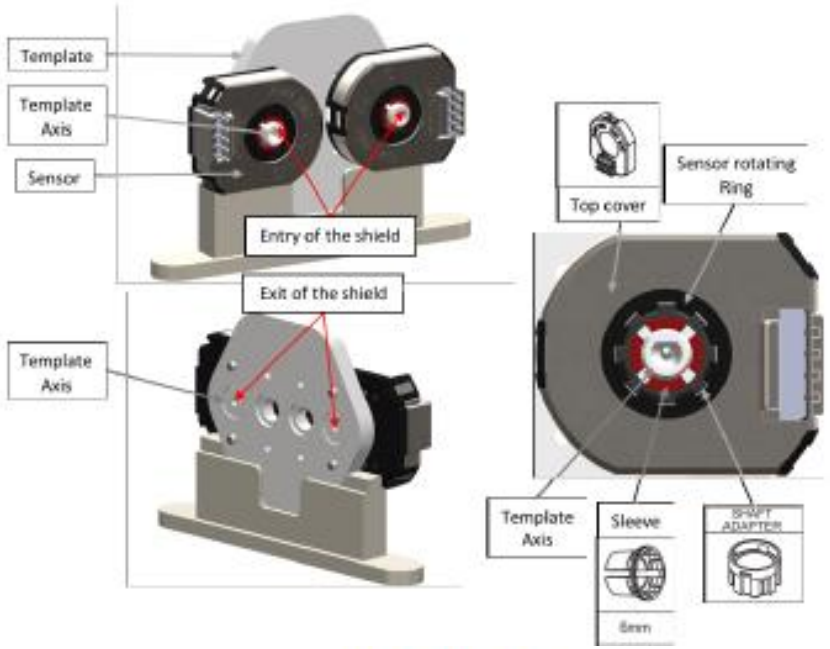


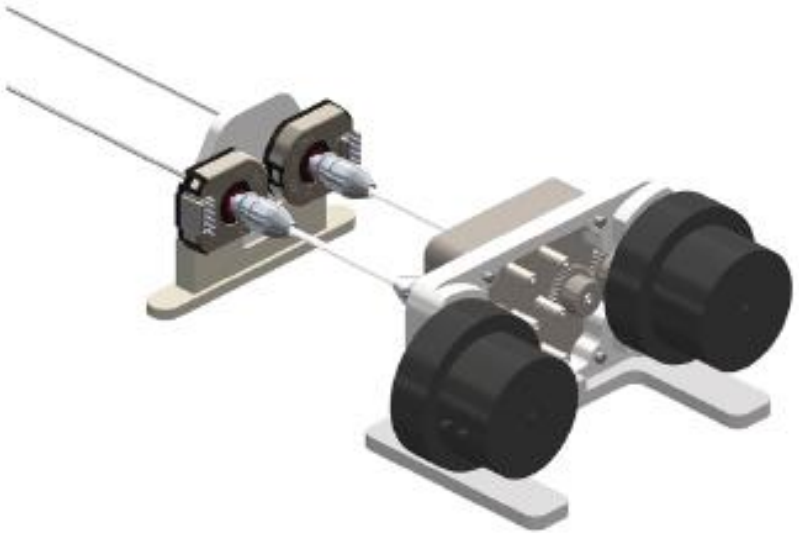




Images from Bounnak Thammavong

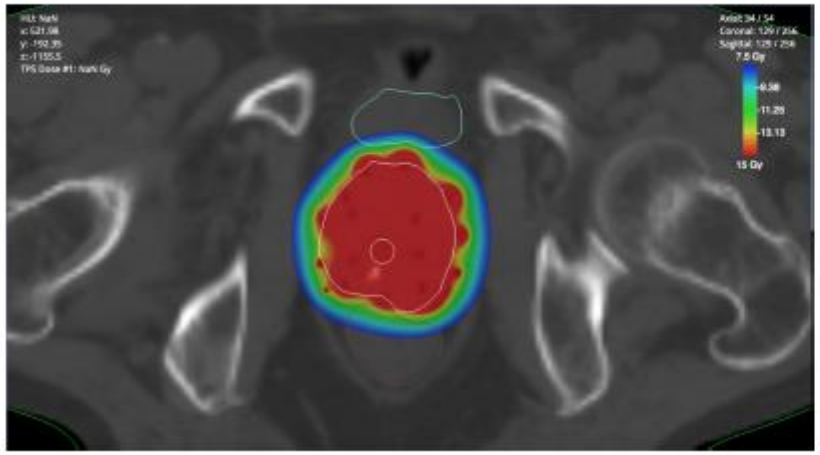
Prostate IMBT System Design from McGill (Enger) Group

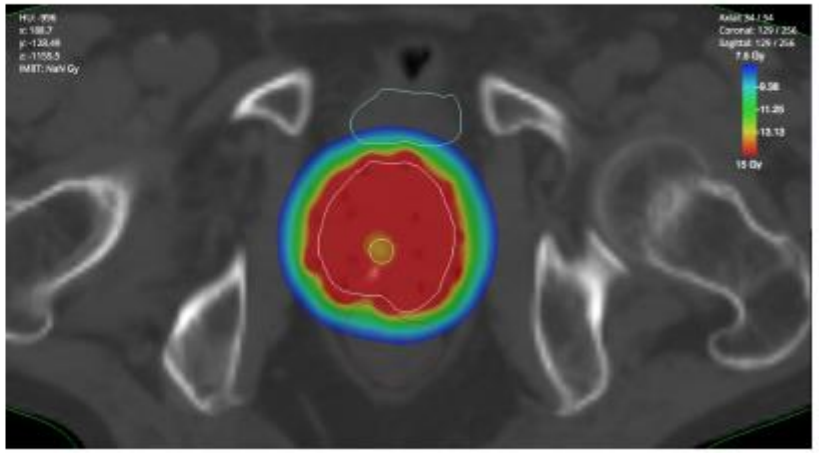




HDR BT

IMBT





Famulari et al (2018)

Conclusions

- IMBT has the potential to significantly improve dose distributions relative to conventional HDR
- For cervical cancer, IMBT could eliminate the need for combined intracavitary and interstitial brachytherapy
- For prostate cancer, IMBT could provide superior one-shot temporary brachytherapy to ^{192}Ir-based HDR
- An isotope other than ^{192}Ir is needed for prostate IMBT

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R01 EB020665

NIH National Cancer Institute

R41 CA210737 (STTR Phase I)

Questions?

Young Corn,
by (Iowan) Grant Wood (1931)