Developments in Directional Brachytherapy

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Disclosure

- Research collaboration with Elekta Brachytherapy

Cervical Cancer

After long dormancy, there is a wonderful renaissance of clinical and technological innovations spurring in cervical cancer brachytherapy, motivated by use of 3D imaging, especially the MRI (and US, CT, PET)

DCE-MRI, DWI, FDG-PET for GTV_B

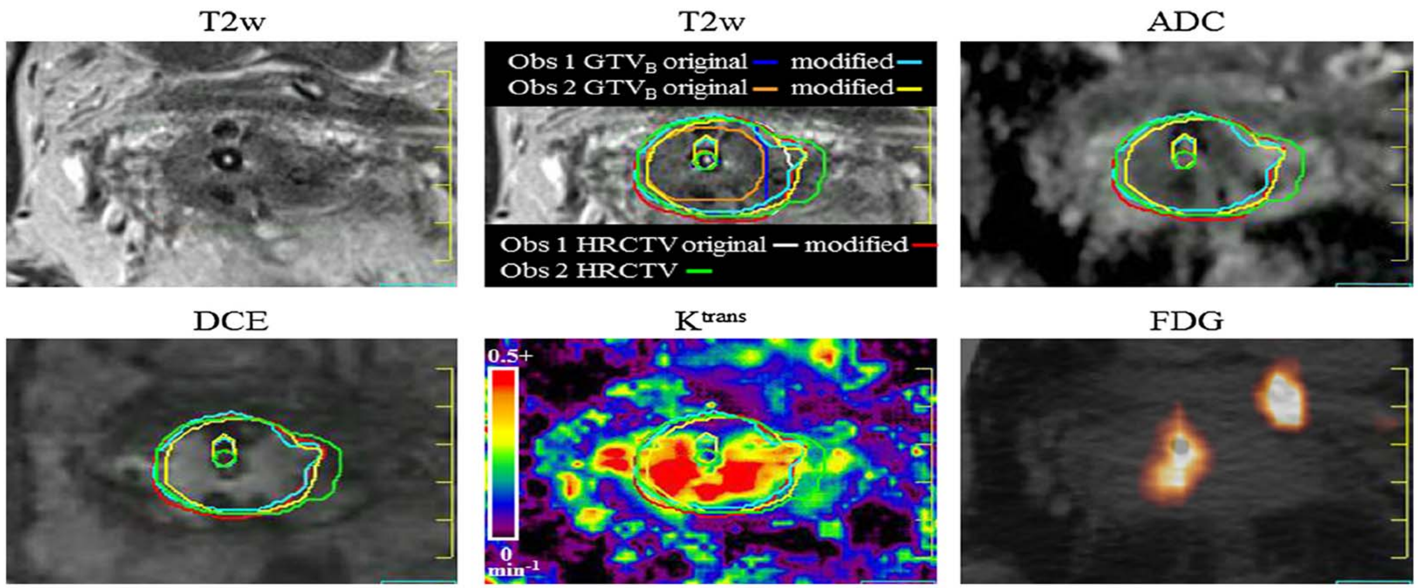
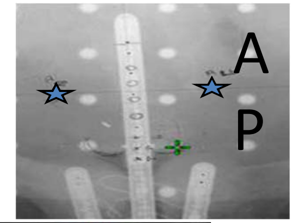


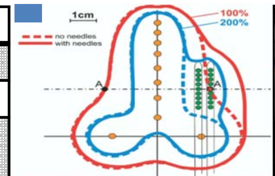
Fig. 2. Axial T2w MR and functional images of a patient with stage IIA cervical cancer at the time of brachytherapy. Both observers modified their T2w-derived GTV_B based on clearer demarcation of the left lateral extent of the tumor via restricted diffusion and early DCE-MRI enhancement. Observer 1 also modified the HRCTV to incorporate the left lateral extent of GTV_B that was not appreciated on T2w MR.

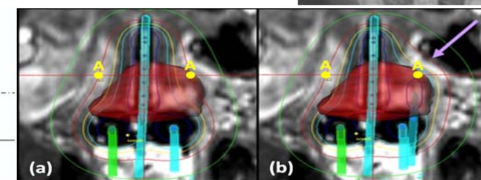
Han *et al*., Radiother Oncol 2016;120:519-525.



Cervical Cancer

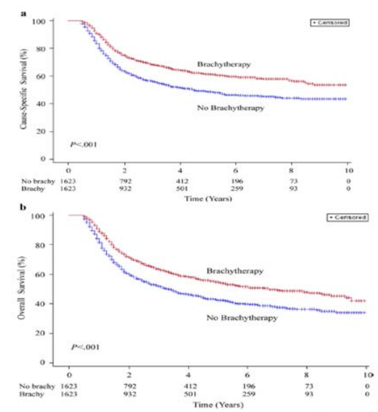
		Conventional BT	IGBT
Imaging method		2D (X-ray)	3D (CT/MRI)
CTV	Size	Same	Different a), b)
	Invasion (shape)	Circle (cylinder)	Biased invasion b)
	Position	Same	Different c) (endophytic-/exophytic growth pattern)
OARs consideration		No	Yes a), b), c)



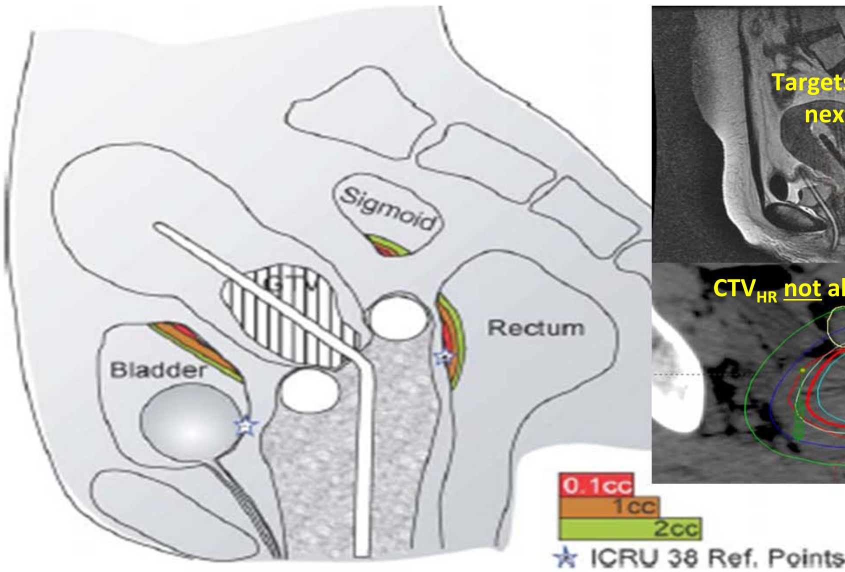


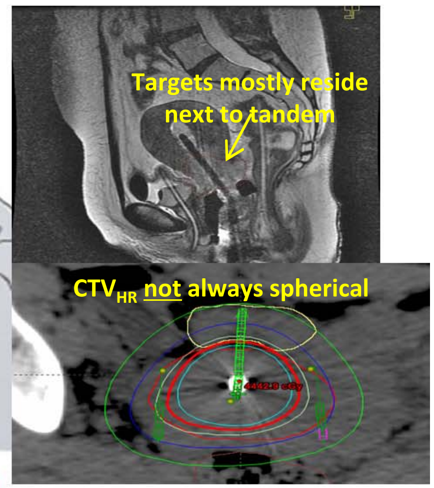
Vienna Applicator

- Pre-defined isodose shape (i.e., “pear”)
- Symmetric dose distribution, loading patterns w/ T&O, T&R, needles
- For delivering dose to an asymmetric cancers:
  - Extra needles are required, causes pain/trauma, **AND** <u>additional</u> physician training
- Patterns of RT for intact cervical cancer in USA; **Eifel *et al.*, *Red J* 2014;89(2):249-**
  - >65% of patients get treatment in a facility that treats ≤3 eligible patients/yr
  - **Thus, <u>difficult</u> to maintain “needle-insertion” skills**
- Analysis of the SEER Report; **Han et al., *Red J* 2013;87(1):111-**
  - BT utilization rate has dropped to 58% in 2008, from 83% in 1988 (p<0.001)
  - BT use is independently associated with <u>significantly higher CSS and OS</u>
  - BT use is associated with significant resources & training!
  - Advances in technology, including ease-of-use ↑, could boost users?? (e.g., IMRT)

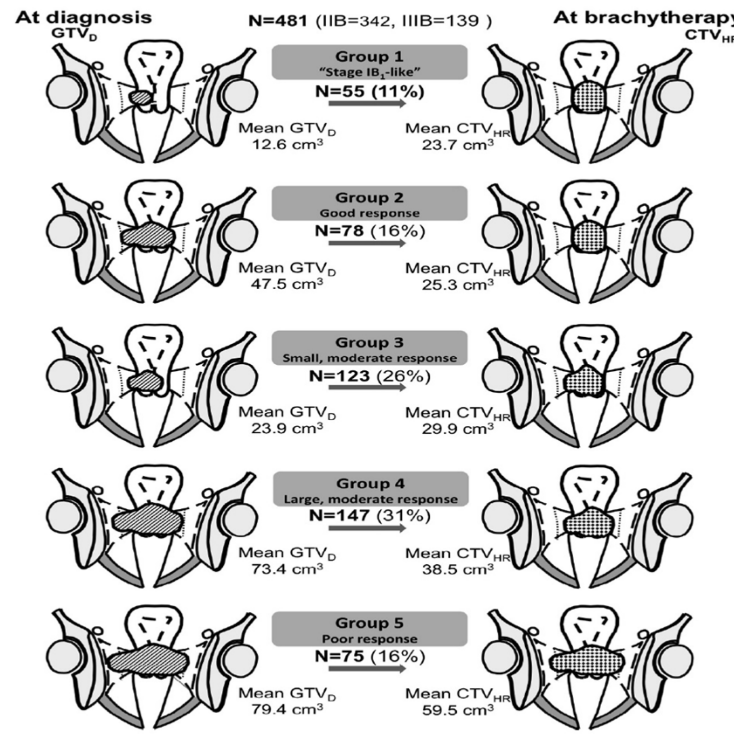


Problem & Opportunity





Potter *et al*., Radiother Oncol 2006;78:67-77.



Jastaniyah *et al*., Radiother Oncol 2016;120:404-411.

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Problem & Opportunity

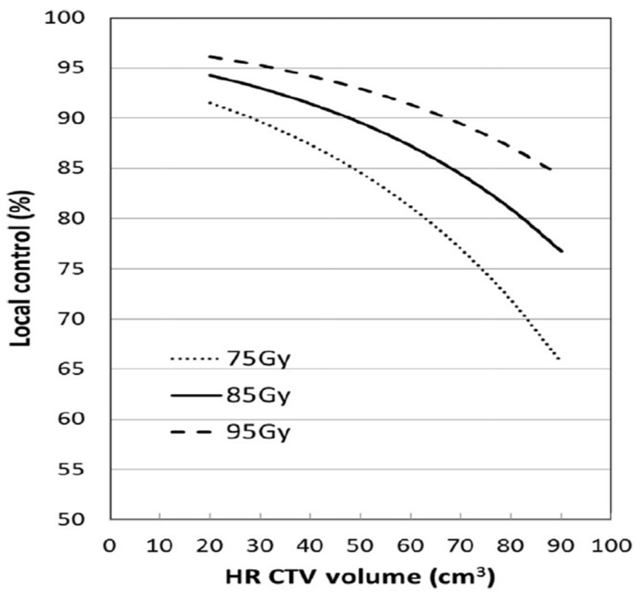
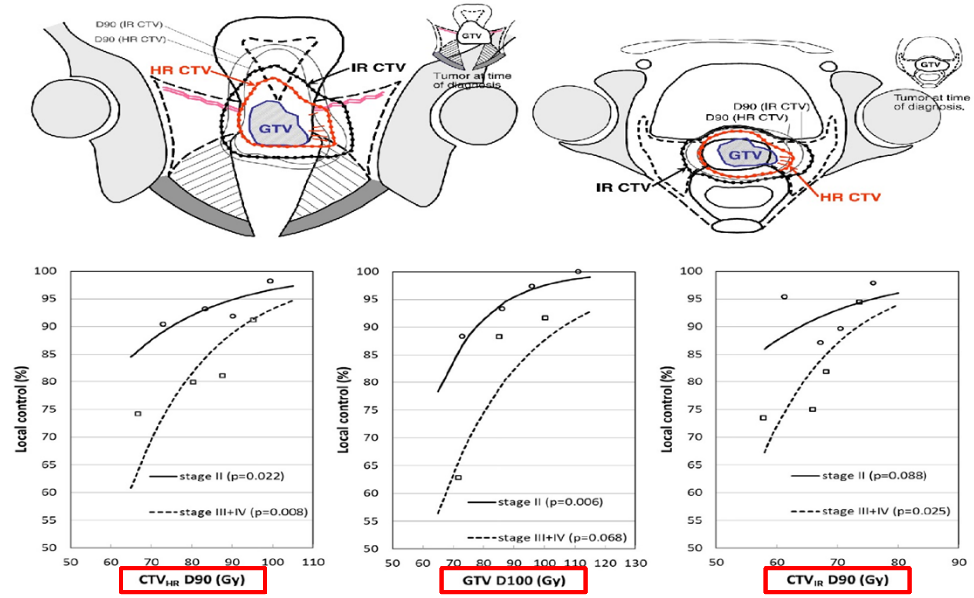


Fig. 2. Local control as depending on CTV_{HR} dose and volume according to the multivariate Cox regression model. The figure shows predicted 3-year actuarial local control as a function of CTV_{HR} volume for three different dose levels: 75 Gy, 85 Gy and 95 Gy and for the median OTT of 49 days.



D90≥85Gy **D98≥95Gy** **D98≥60Gy**

Tanderup *et al.*, Radiother Oncol 2016;120:441-446.

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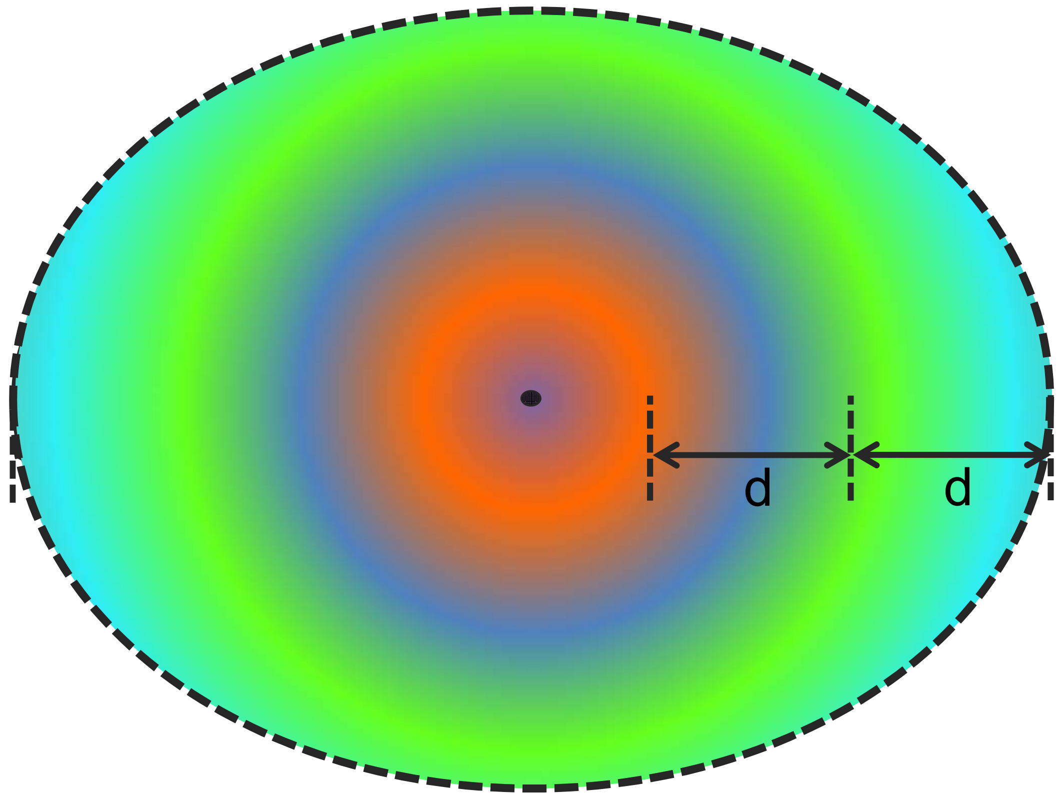
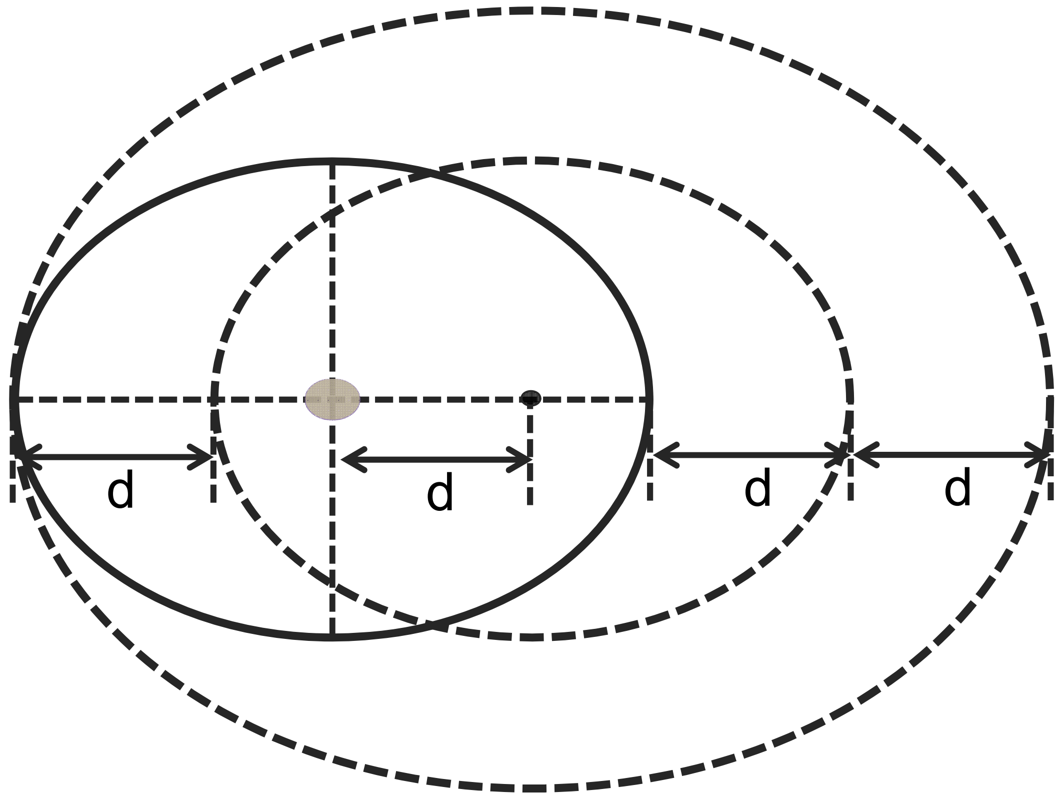
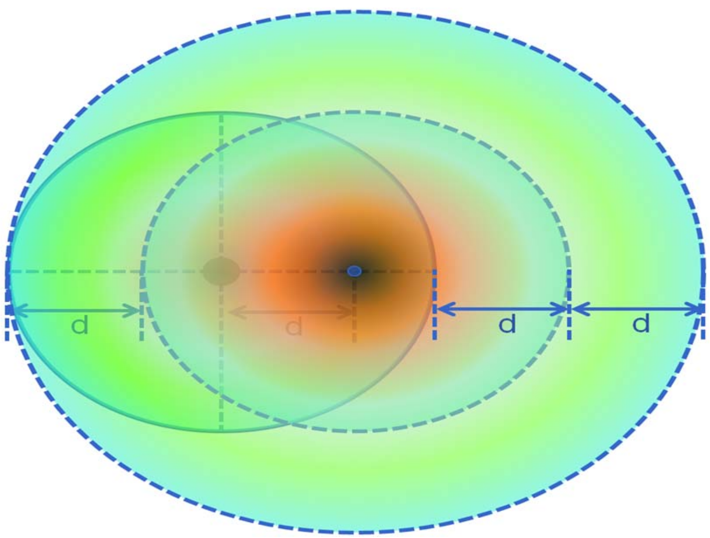
The "Problem"



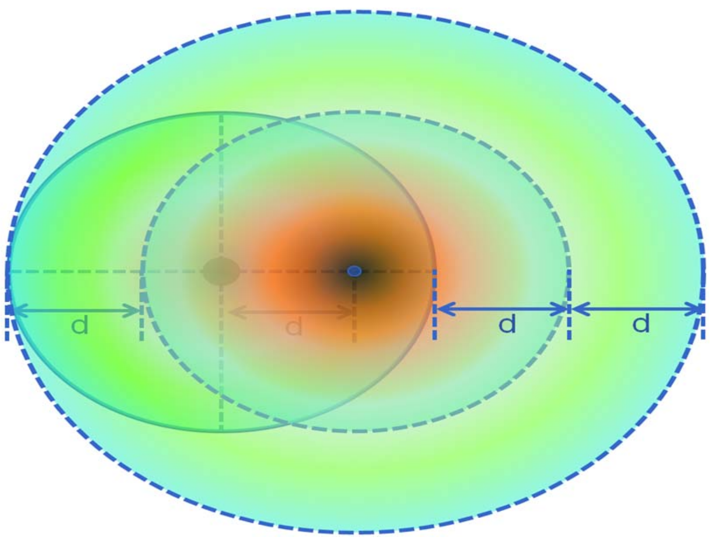
The “Problem” = <u>Geometry!</u>

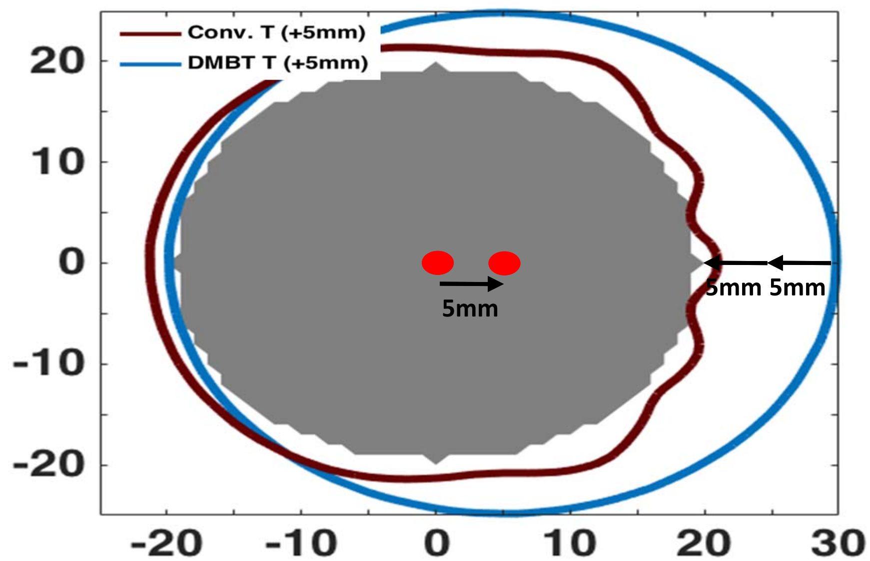


The "Opportunity"



The “Opportunity” - DMBT

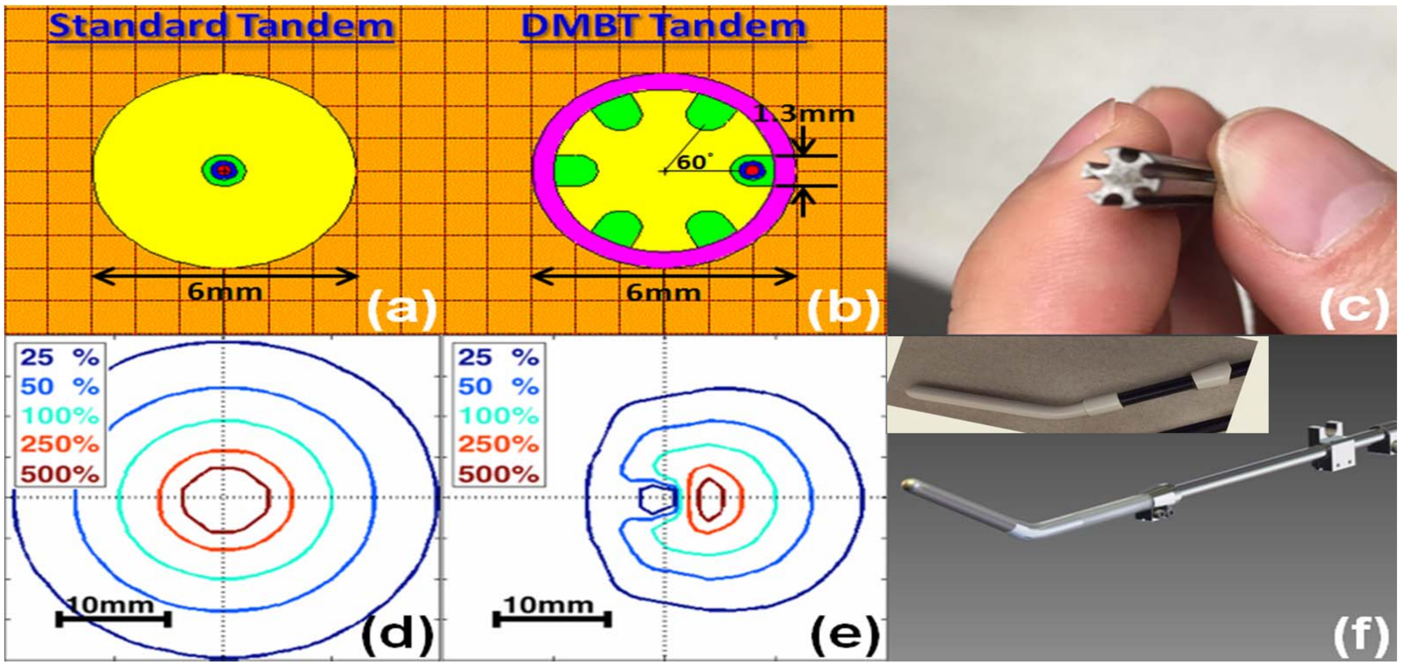




What is DMBT?

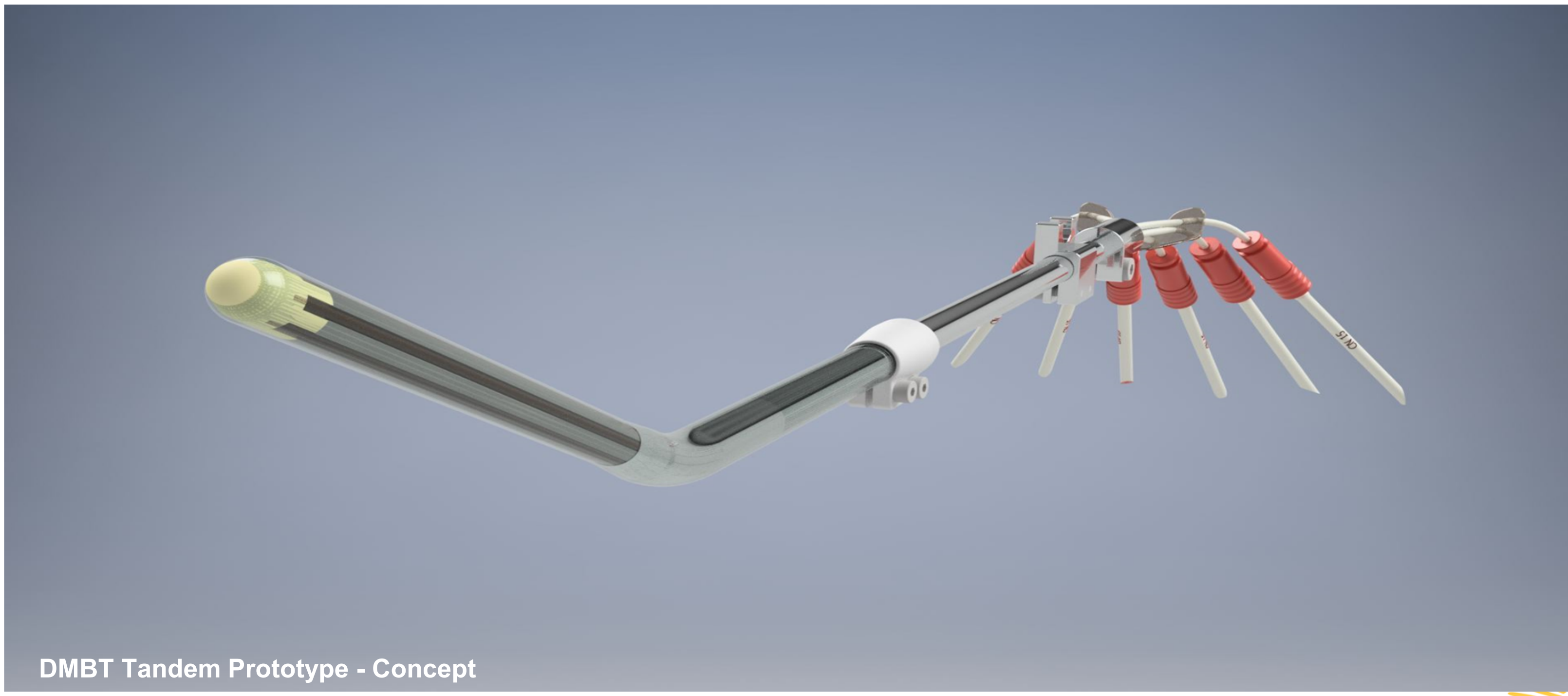
- ***D**irection **M**odulated **B**rachy**T**herapy*
- ***DMBT**?*
  - Intensity modulation through inverse planning of ***directional*** ^{192}Ir source dose profile achieved via intelligently-designed collimated shielding (*possibly* with ***beam direction*** & ***energy dynamically controlled*** by robotics) – Sound familiar?
  - Benefits in ***cervical and rectal cancers*** are demonstrated – *today*

DMBT Design



Han *et al*., Int J Radiat Oncol Biol Phys 2016;96(2):440-448.

DMBT Design



DMBT Tandem Prototype - Concept

Shield Selection

Table 1. Susceptibilities of water, tissue, and selected materials [25,44,49,68]

Material	Density (g/cm³)	Susceptibility (ppm)
Gold	19.3	–34
PEEK	1.3	–9.33
Water (37°)	0.933	–9.05
Human tissues	~0.92-1.05	~(–11.0 to –7.0)
Air (NTP)	1.29×10^{-3}	0.36
Aluminum	2.7	20.7-20.9
Tungsten	19.3	77.2-80
Titanium	4.54	182
Stainless steel (nonmagnetic, austenitic)	8.0	3520-6700

PEEK – polyether ether ketone, NTP – normal temperature [20°C] and pressure [101.325 kPa]

Soliman *et al.*, J Contemp Brachy 2016;8(4):363-369.

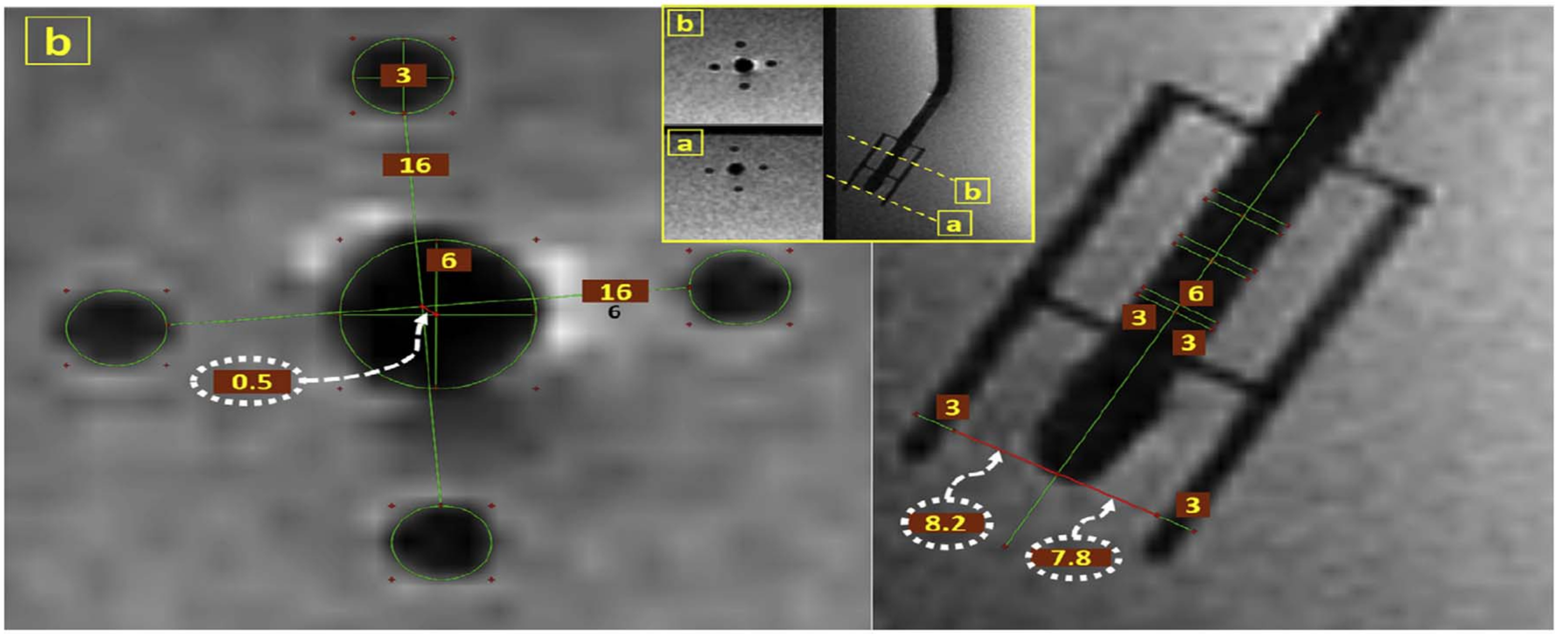
List of sintered heavy tungsten alloy samples in the market:

	Elemental composition (wt.%)				
Sample	W	Fe	Ni	Cu	Grade
F_xN_x	...	...	...	...	MLC
$F_{3.0}N_{7.0}$	90.0	3.0	7.0	0.0	MT17F[a]
$F_{1.5}N_{3.5}$	95.0	1.5	3.5	0.0	MT18F[a]
$F_{1.5}N'_{3.5}$	95.0	1.5	3.5	0.0	HE395[b]
$F_{0.9}N_{2.1}$	97.0	0.9	2.1	0.0	MT185[a]
$F_{0.0}N_{6.0}$	90.0	0.0	6.0	4.0	MT17C[a]
$F_{0.0}N_{4.0}$	95.0	0.0	4.0	1.0	HA195[b]
$F_{0.0}N_{3.5}$	95.0	0.0	3.5	1.5	MT18C[a]

Kolling *et al.*, Med Phys 2014;41(6):061707.

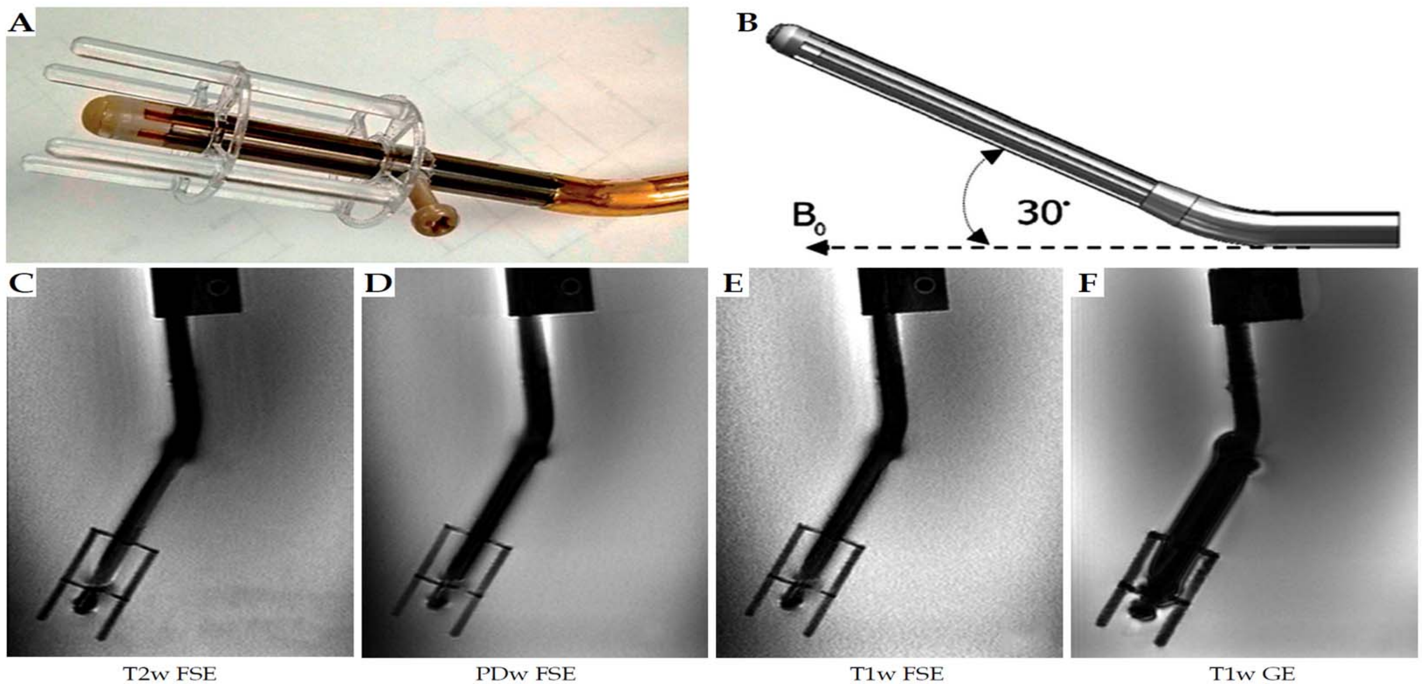
- Density = 18.0 g/cm³ (high)
- W is (weakly) paramagnetic
- Ni is (weakly) ferromagnetic
- Fe is (strongly) ferromagnetic

1.5T MRI



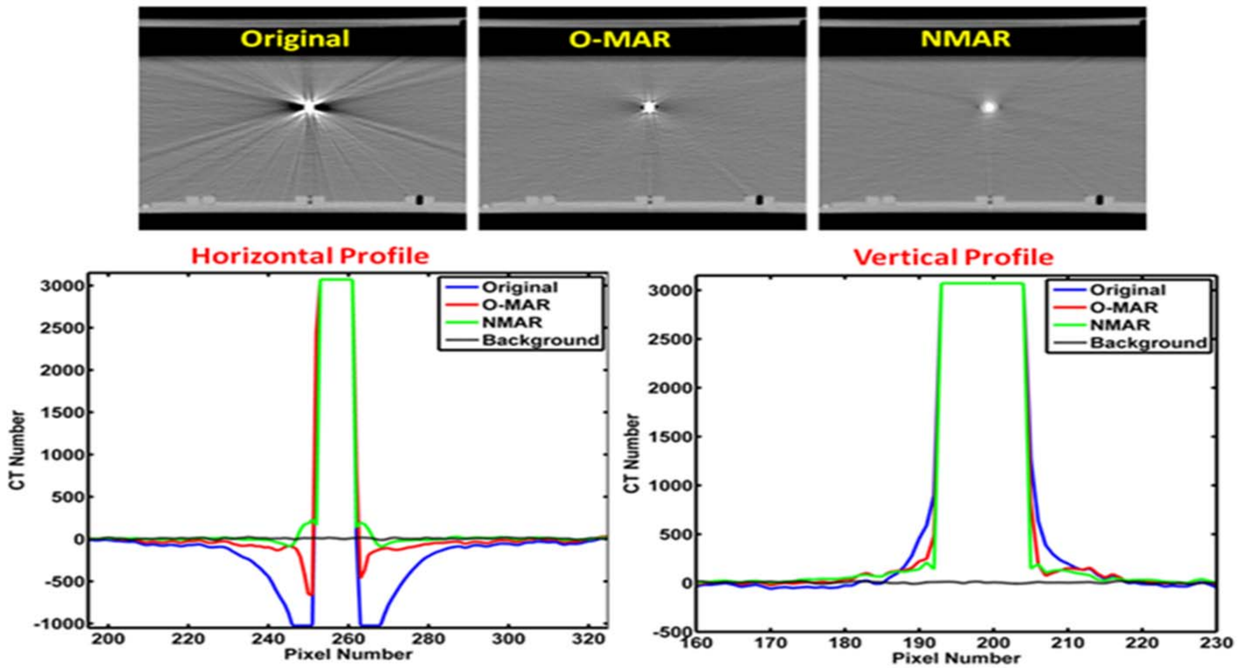
Soliman *et al.*, Radiother Oncol 2016;120(3):500-506.

3T MRI



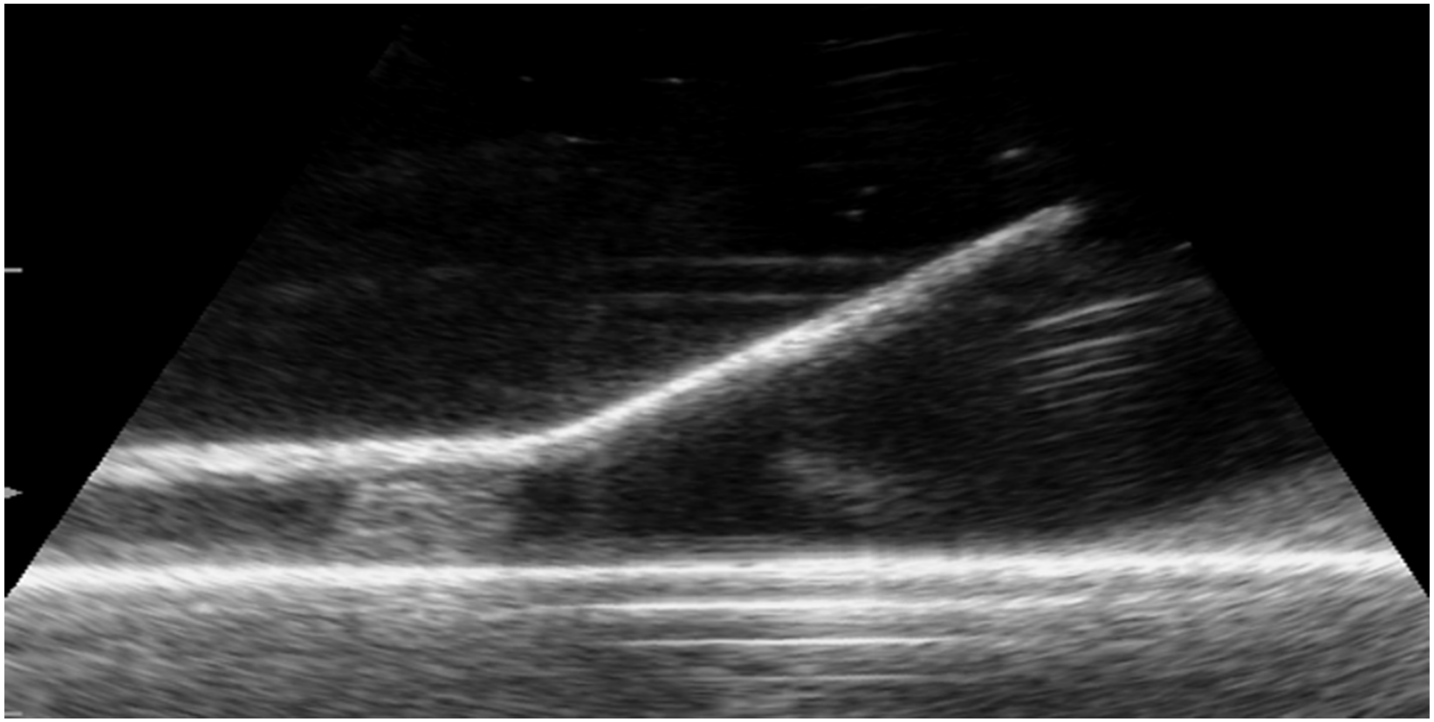
Soliman *et al*., J Contemp Brachy 2016;8(4):363-369.

CT



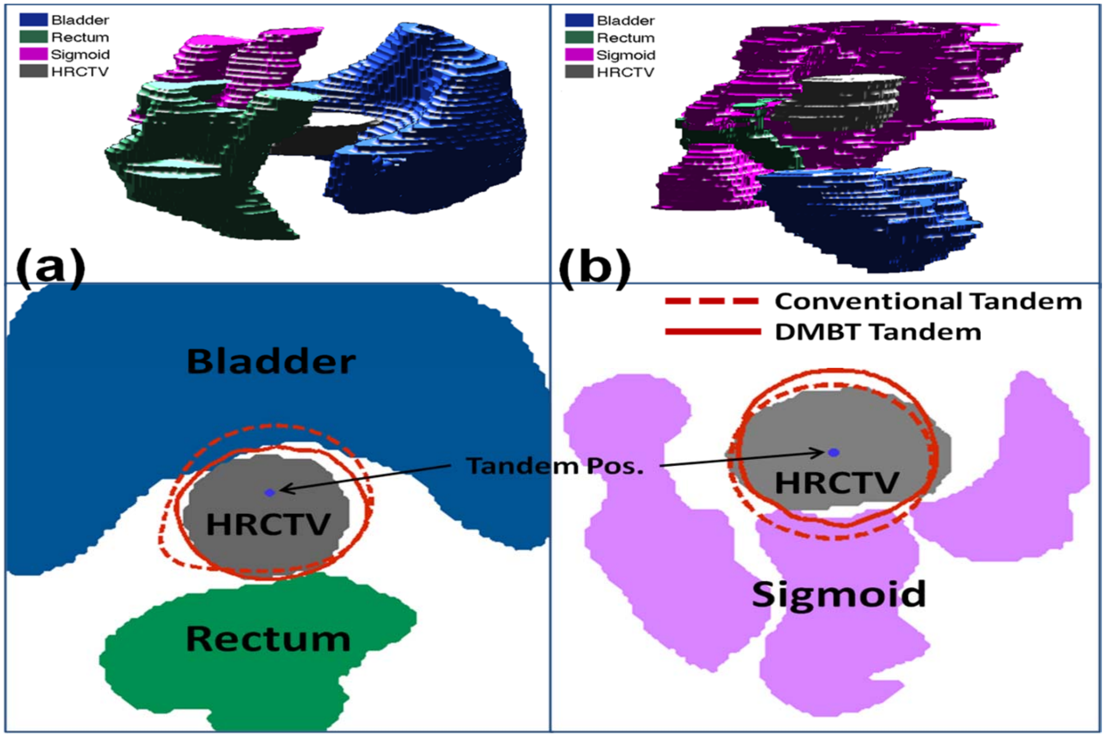
Elzibak *et al*., 2017 (*in preparation*).

Ultrasound-Guided Insertion



Elzibak *et al.*, 2017 (*in preparation*).

T&O vs DMBT



Han *et al.*, Int J Radiat Oncol Biol Phys 2014;89:666-673.

On average, D_{2cm3} reductions for 75 plans from UCSD:
Bladder 8.5% $\pm$ 28.7%
Rectum 21.1% $\pm$ 27.2%

Best single-plan reductions:
Bladder 40.8%
Rectum 40.1%

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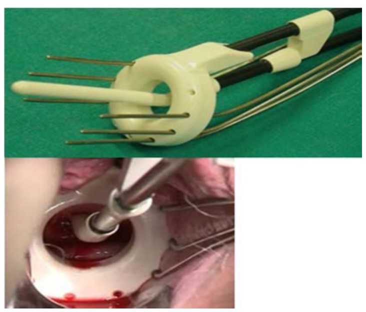
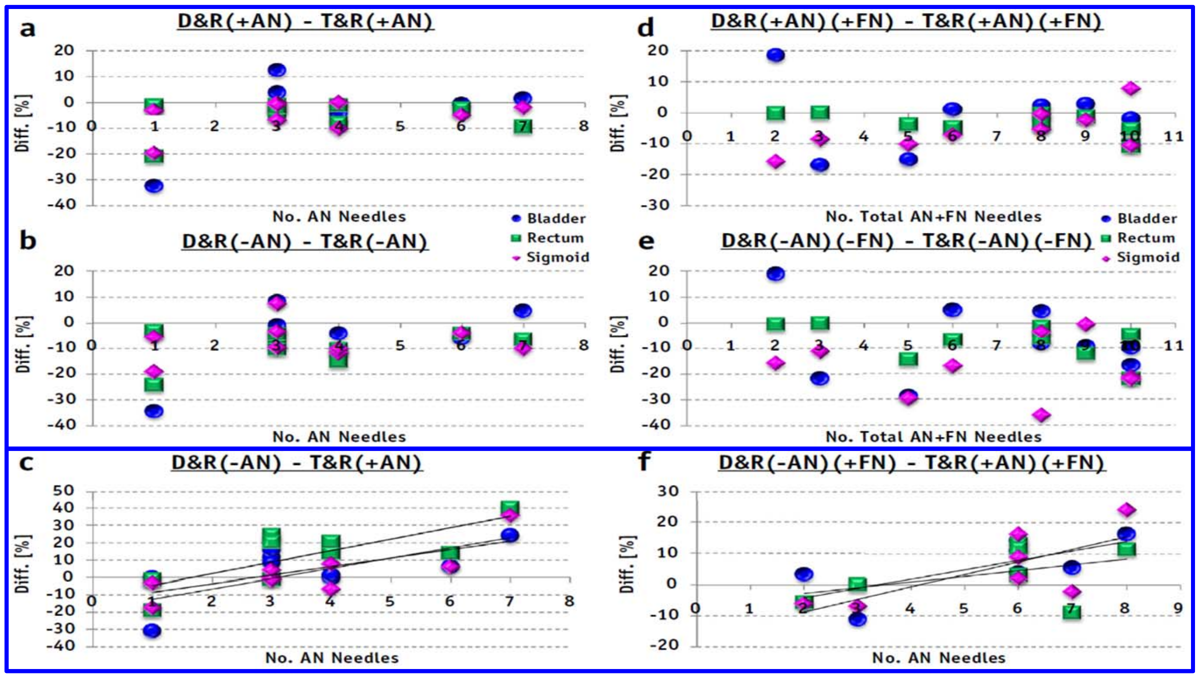
T&R+Needles vs DMBT



Vienna Applicator



Han *et al*., Int J Radiat Oncol Biol Phys 2016;96(2):440-448.

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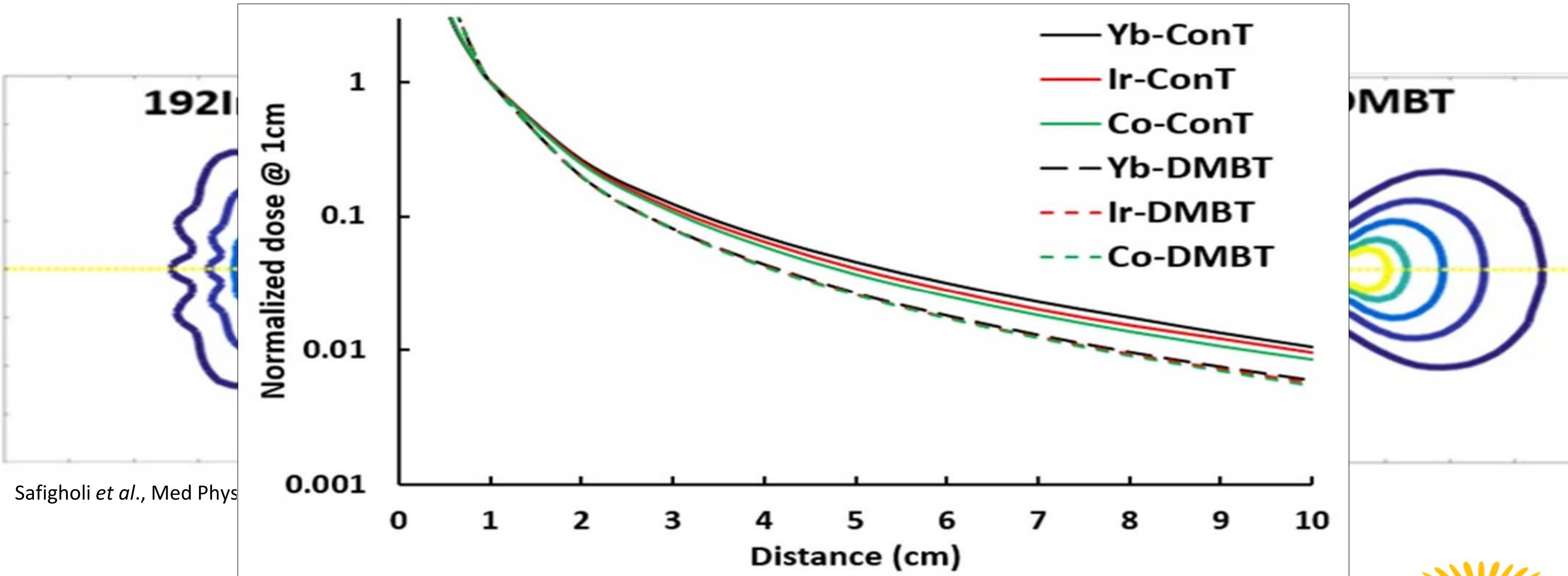
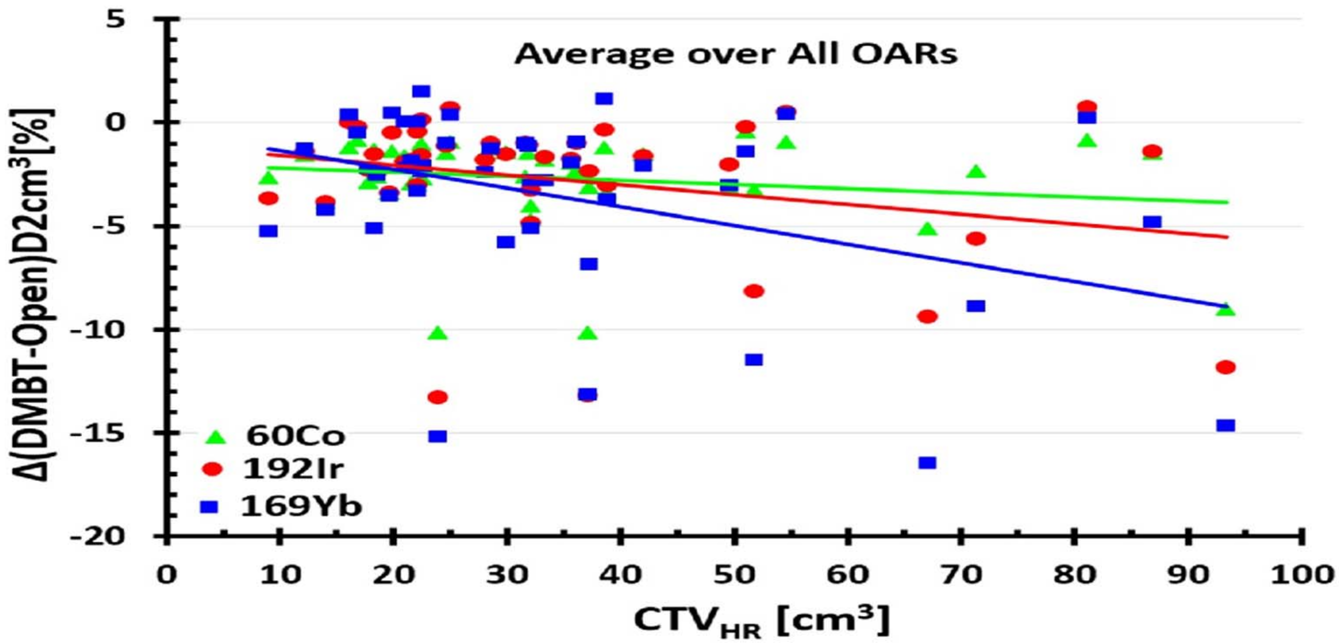
Multi-Source Afterloader?



Safigholi *et al.*, Med Phys

Multi-Source Afterloader?



Safigholi *et al.*, Med Phys 2016 (AAPM Abstract).

TG43 → TG186 (MBDCA)

- TG43 – *Homogeneous water medium*
- TG 186 – *Came out in 2012*

Report of the Task Group 186 on model-based dose calculation methods in brachytherapy beyond the TG-43 formalism: Current status and recommendations for clinical implementation

Luc Beaulieu[a)]
Département de Radio-Oncologie et Centre de Recherche en Cancérologie de l'Université Laval, Centre hospitalier universitaire de Québec, Québec, Québec G1R 2J6, Canada and Département de Physique, de Génie Physique et d'Optique, Université Laval, Québec, Québec G1R 2J6, Canada

Beaulieu *et al*., Med Phys 2012;39(10):6208-6236.

- <u>M</u>odel <u>B</u>ased <u>D</u>ose <u>C</u>alculation <u>A</u>lgorithms
    1. Monte Carlo
    2. Collapsed Cone Convolution (ACE®)
    3. Grid Based Boltzmann Solver (Acuros BV®)

4.2.4 Shielded applicators

While the above sections look at the differences due to tissue heterogeneities and lack of scatter medium, here we briefly discuss the effects due to shielding. Accounting for the effects of shielding on the dose distribution can be done by using the Applicator Library for Oncentra Brachy. By placing an ACE supported applicator into the treatment plan, the geometry and location of the applicator and all applicator materials are automatically taken into account by the dose calculations. Figure 12 shows a comparison between the dose distributions calculated with TG-43 and ACE for the Fletcher CT/MR Shielded applicator. The figure shows both dose distributions and the corresponding DVH curves. Further information regarding this applicator and its use in combination with ACE can be found in White paper "Fletcher CT/MR Shielded applicator with ACE" (document number 888.00627 MKT).

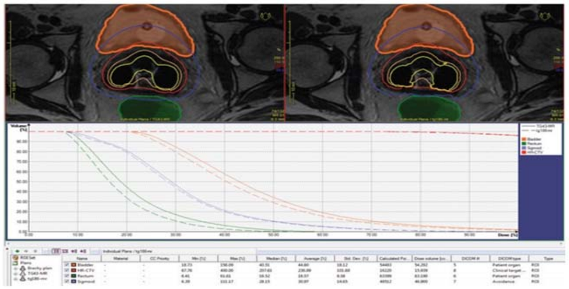


Figure 12: Comparison of dose distributions calculated with TG-43 and ACE. Top left: TG-43 dose distribution. Top right: ACE dose distribution. Bottom: Comparison of DVH curves for the two dose distributions.

van Veeleen *et al*., "ACE" – White paper by Elekta

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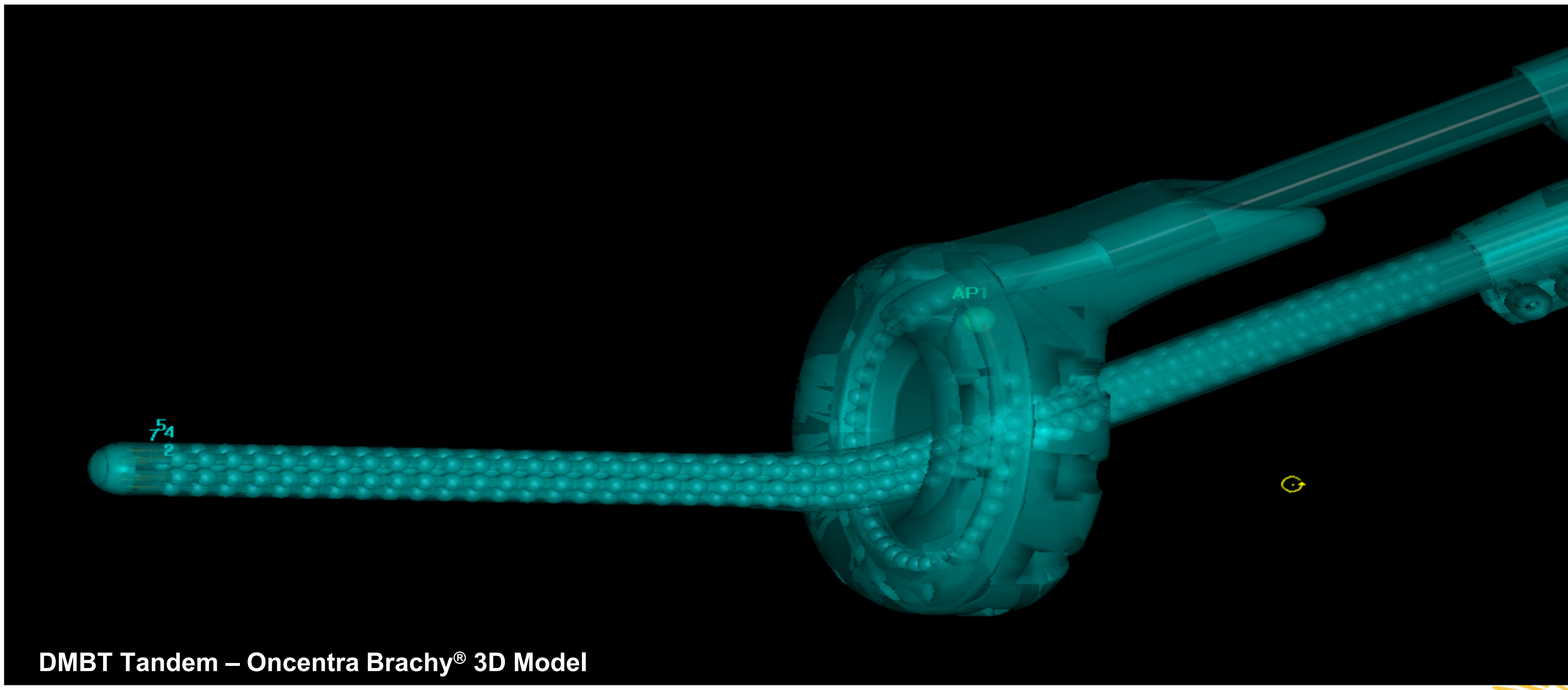
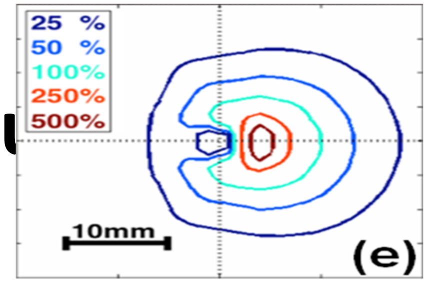
3D Virtual Model

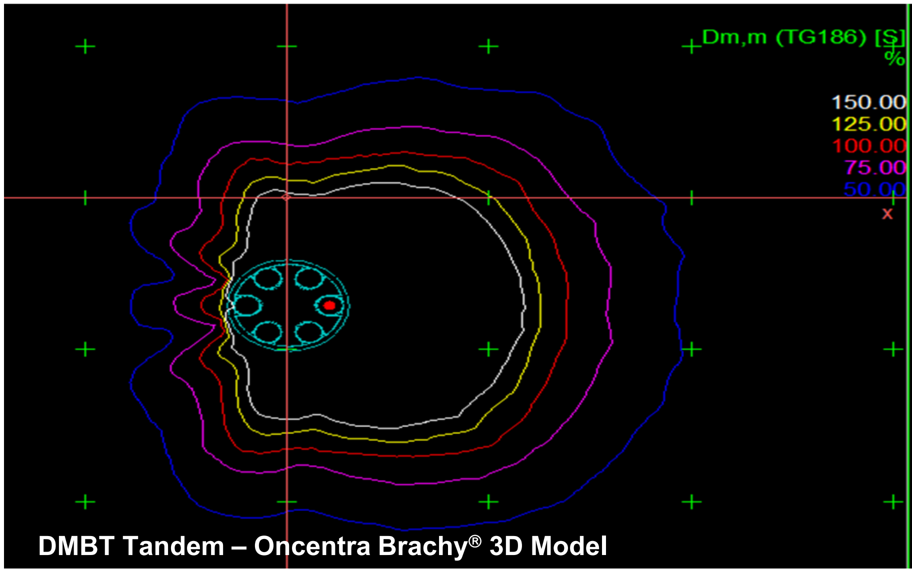


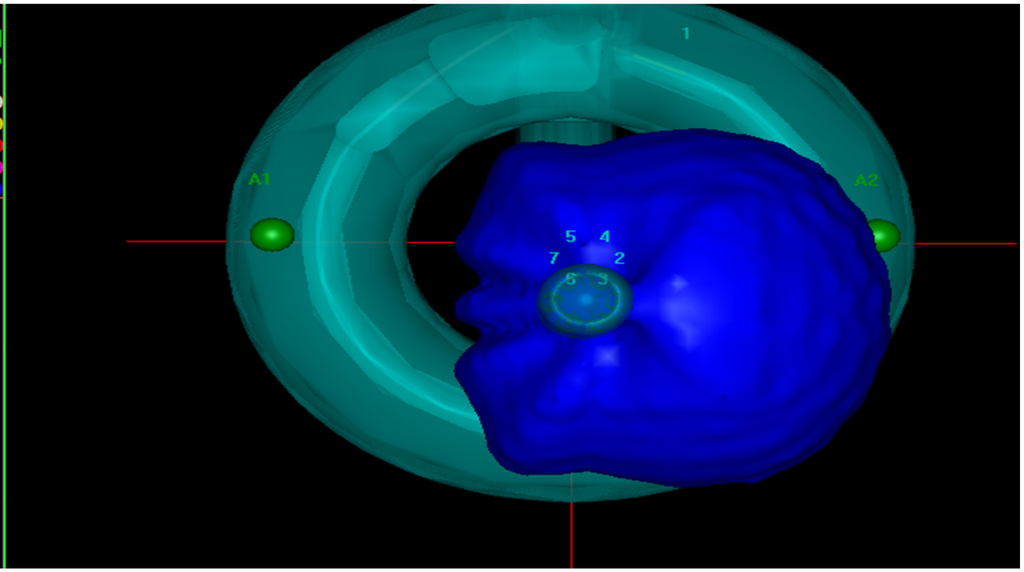
DMBT Tandem – Oncentra Brachy® 3D Model

3D Virtu

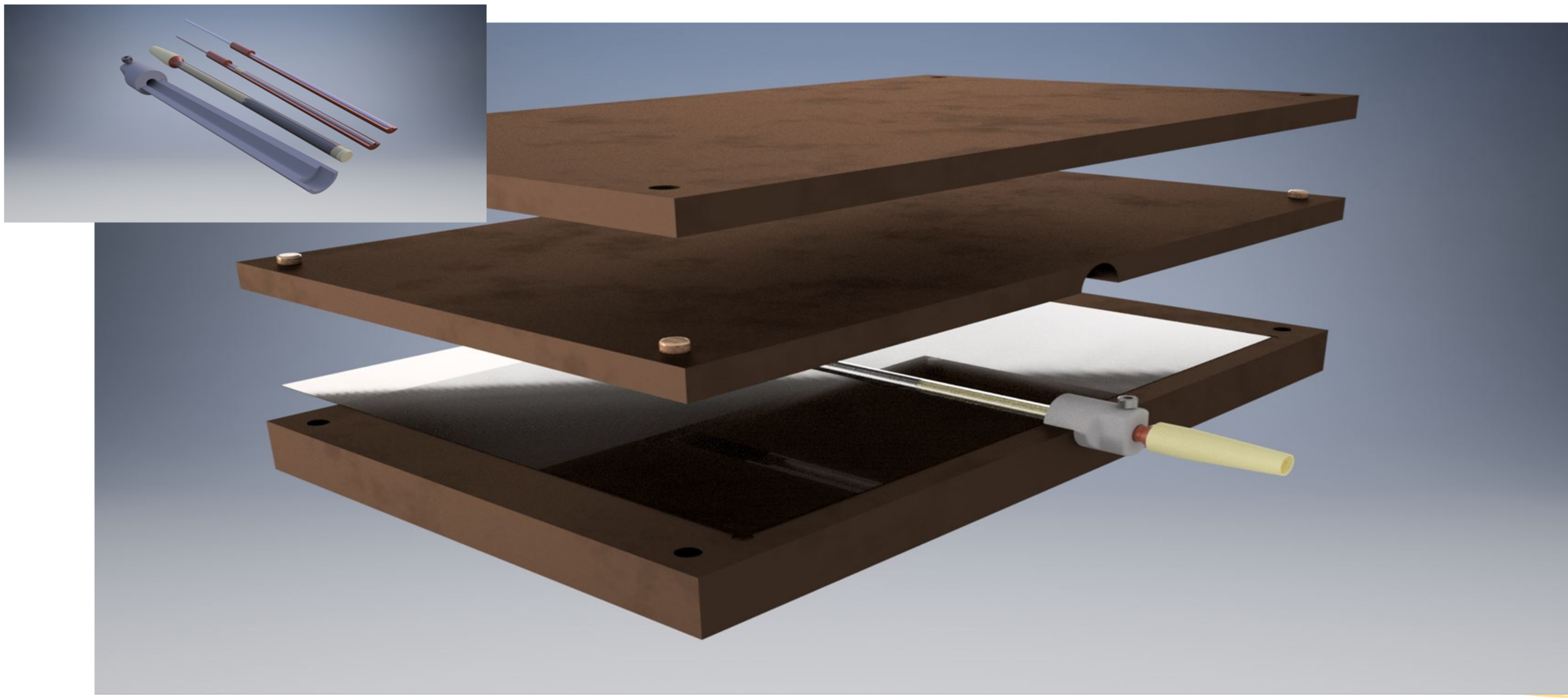


Han *et al.*, Int J Radiat Oncol Biol Phys 2016;96(2):440-448.

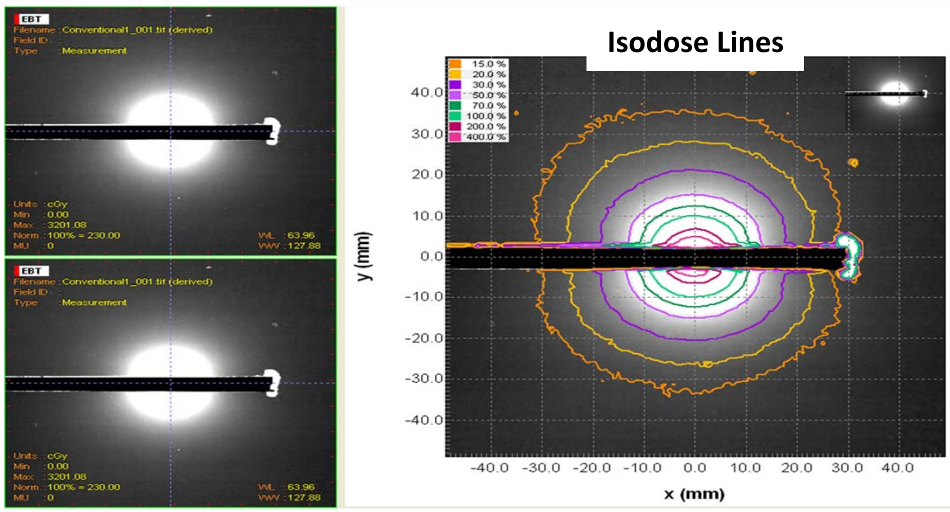




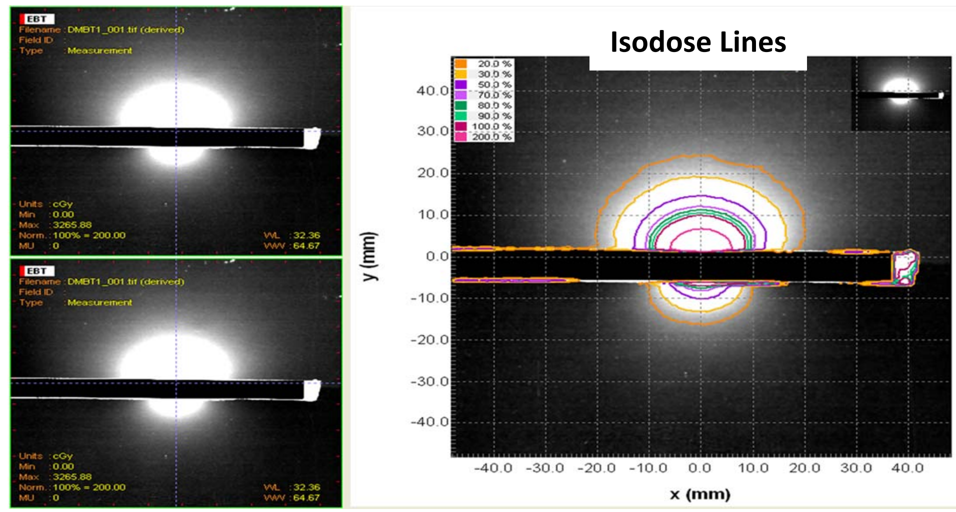
Dosimetric Verification w/ Film



Dosimetric Verification w/ Film



Open Conventional Tandem – Single Dwell



DMBT Tandem – Single Dwell

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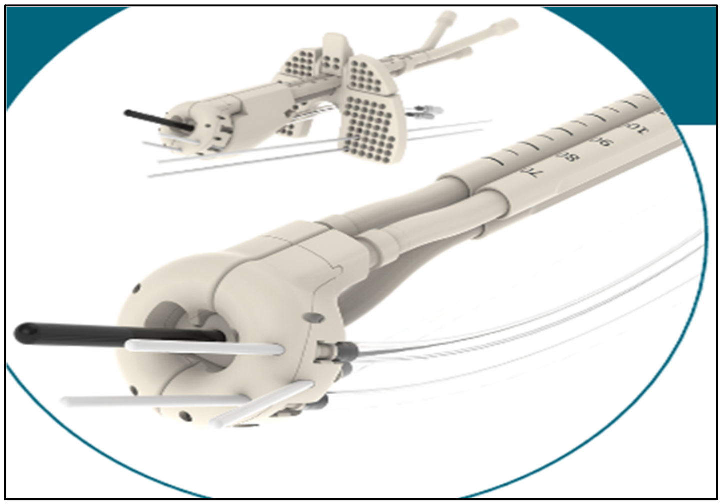
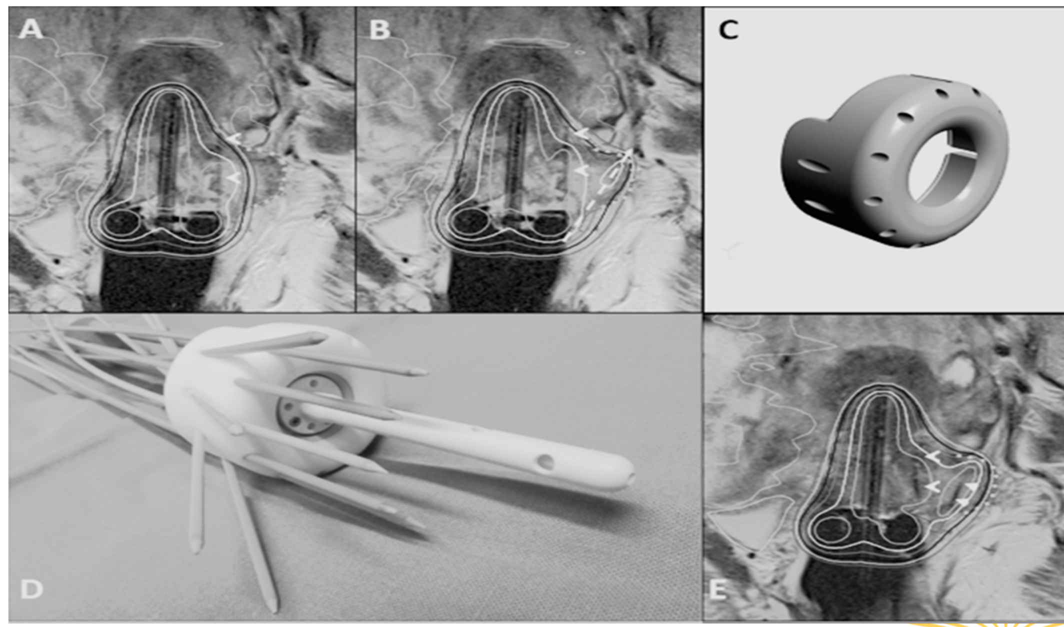
State-of-the-Art Applicators

What is consistently **not** changing?



Venezia™ (Elekta Brachytherapy)



Lindegaard *et al.*, Radiother Oncol 2016;118(1):173-5.

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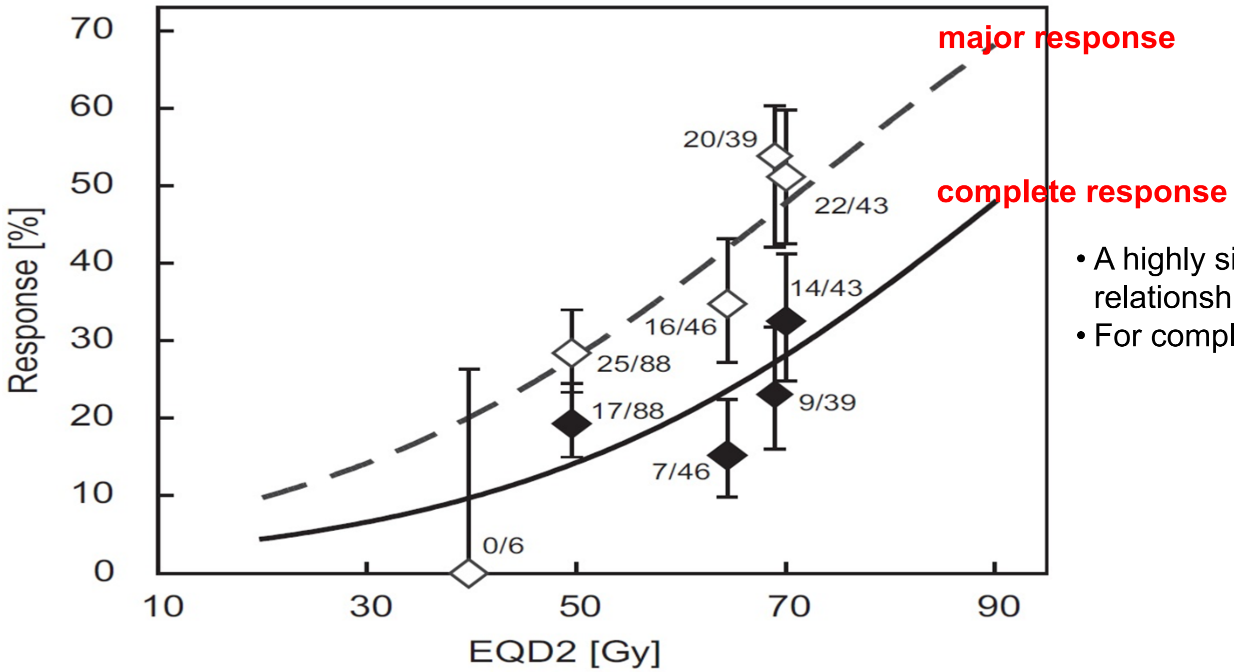
Rectal Cancer

- Recurrences after surgery occurs mostly **within the tumor bed**; therefore, eradicating local disease is critical [Mendenhall et al., IJROBP 1983;9:97-]
  - HDR can be given as an **additional boost** to standard CRT for subpopulation of resistant tumors
- McGill phase II trial [Vuong et al., *Semin Colon Rectal Surg* 2010;21:115-119]
  - Neoadjuvant HDR **only** (no CRT); 650x4, 285 patients treated (mostly T3, Nx)
  - 27% pCR compared with RT/CT regimens…
  - Grade 3 acute proctitis occurred in only 1% vs 25-30% in CRT

Rectal Cancer



Appelt *et al.*, Int J Radiat Oncol Biol Phys 2013;85:74-80.

- A highly significant **dose-response** relationship is found ($p<0.002$)
- For complete response, ***D_{50}=92Gy EQD2***

Treatment Options

Treatment Techniques	Dose Conformality?	Non-Invasive?
External Beam Radiation Therapy (EBRT)	✓	✓✓✓✓✓
Single-Channel Intracavitary HDR	✓✓	✓✓✓✓
Interstitial LDR/HDR	✓✓✓	✓
Segmented Shielding HDR	✓✓✓	✓✓✓
Intra-Operative Brachytherapy	✓✓✓✓	✓
Superficial X-ray (Papillon Technique)	✓✓✓✓	✓✓✓
CAPRI Applicator (13 Channels) HDR	✓✓✓✓	✓✓✓
Intracavitary Mold Applicator (8 Channels) HDR	✓✓✓✓	✓✓✓
Direction Modulated Brachytherapy (DMBT) HDR	✓✓✓✓✓	✓✓✓

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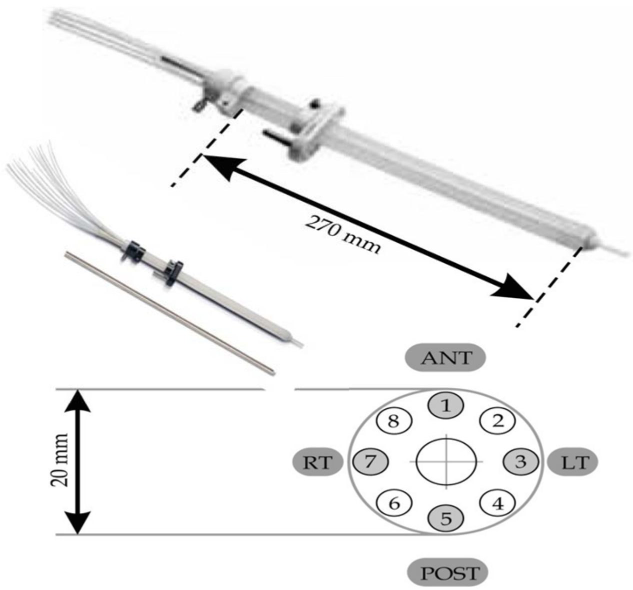
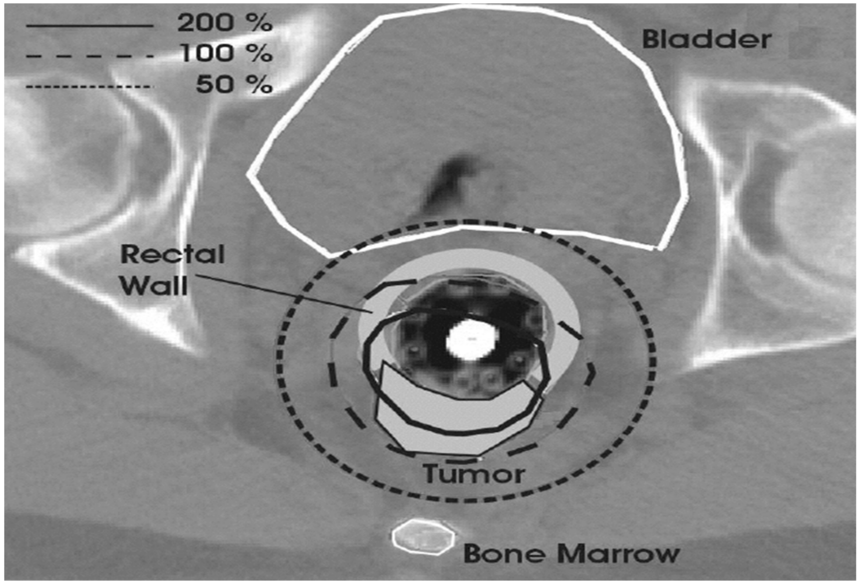
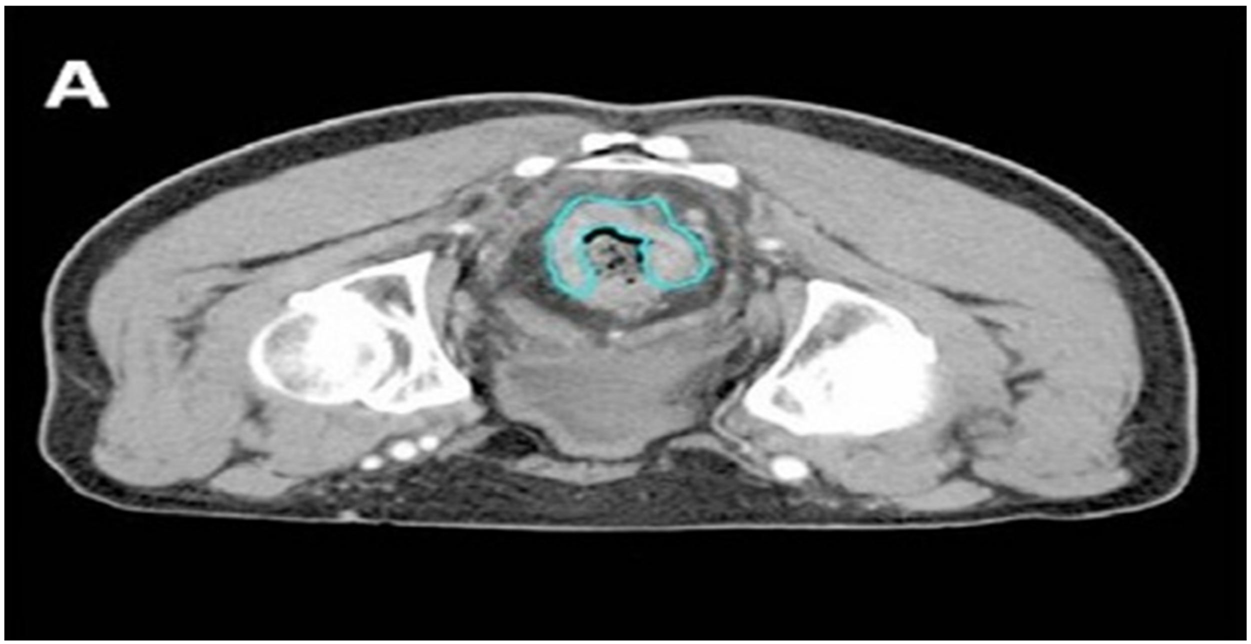
Intracavitary Mold Applicator (ICMA)





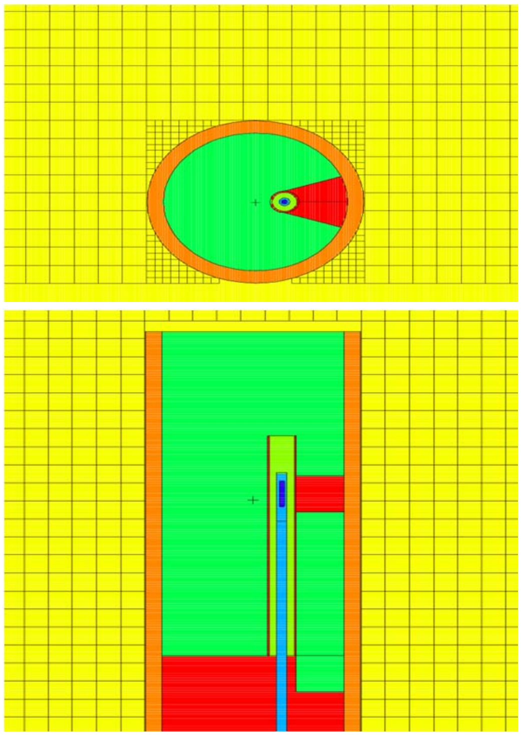
Devic *et al*., JACMP 2005;6(2):44-49.

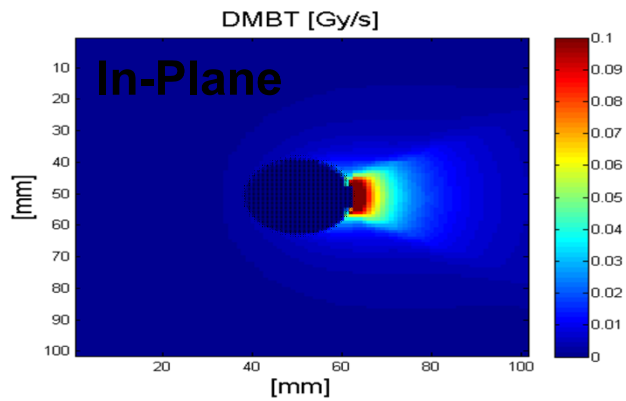
Why DMBT?

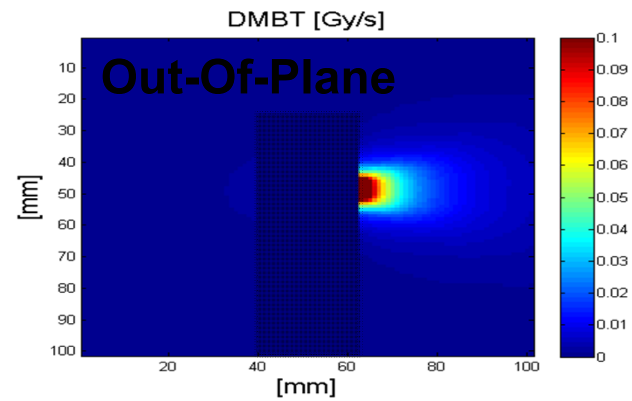


Lambrecht *et al*., Radiother Oncol 2010;96:339-346.

DMBT Design







- Tungsten=18.5g/cc; 1.9-cm diameter & 4.5-cm length
- This results in **~<u>2.5% transmission</u>** in the shielded-end

- Use voxel sizes of 2.5mm^2 within 5cm, and 5mm^2 outside
- 80 million particle histories are used to insure variance of ≤ 5% everywhere
    - This takes about, using 8 CPUs, ~2.5 days
- Geometric symmetry is exploited for speeding up calculations
- Measure [MeV/g], per voxel, per history

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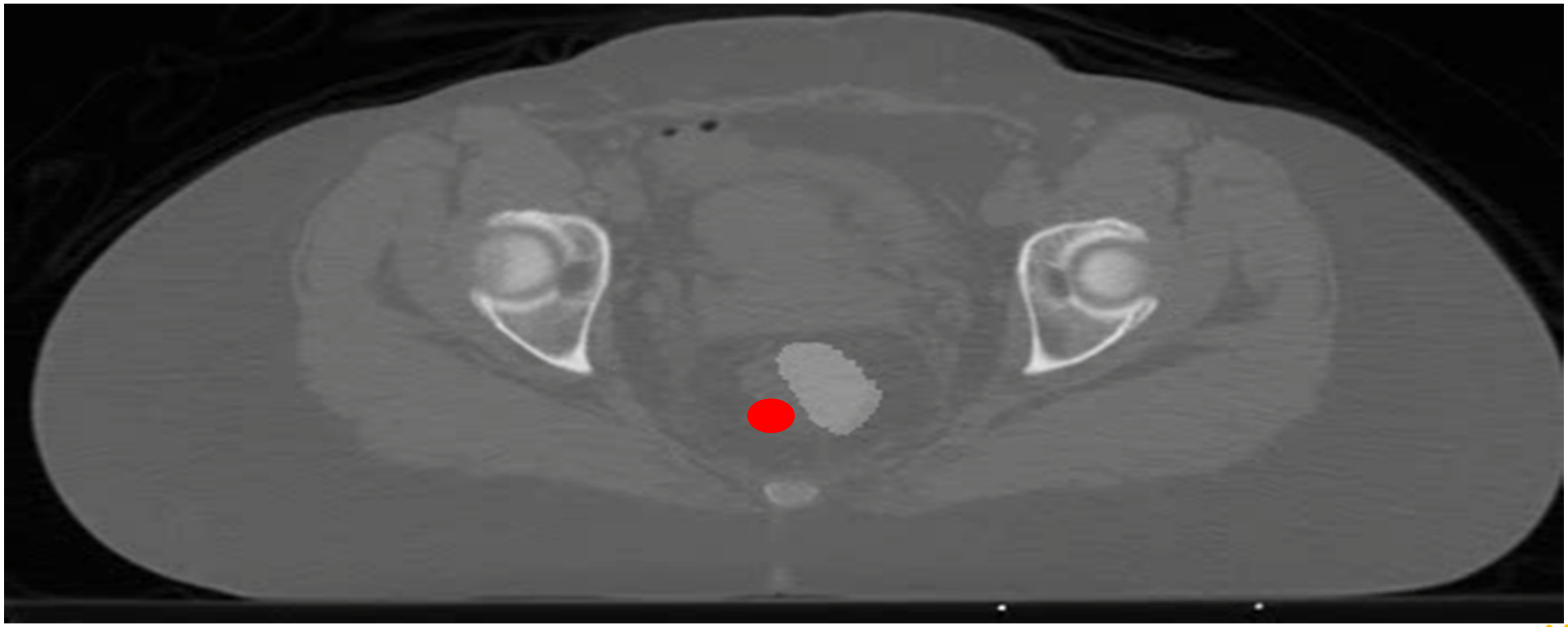
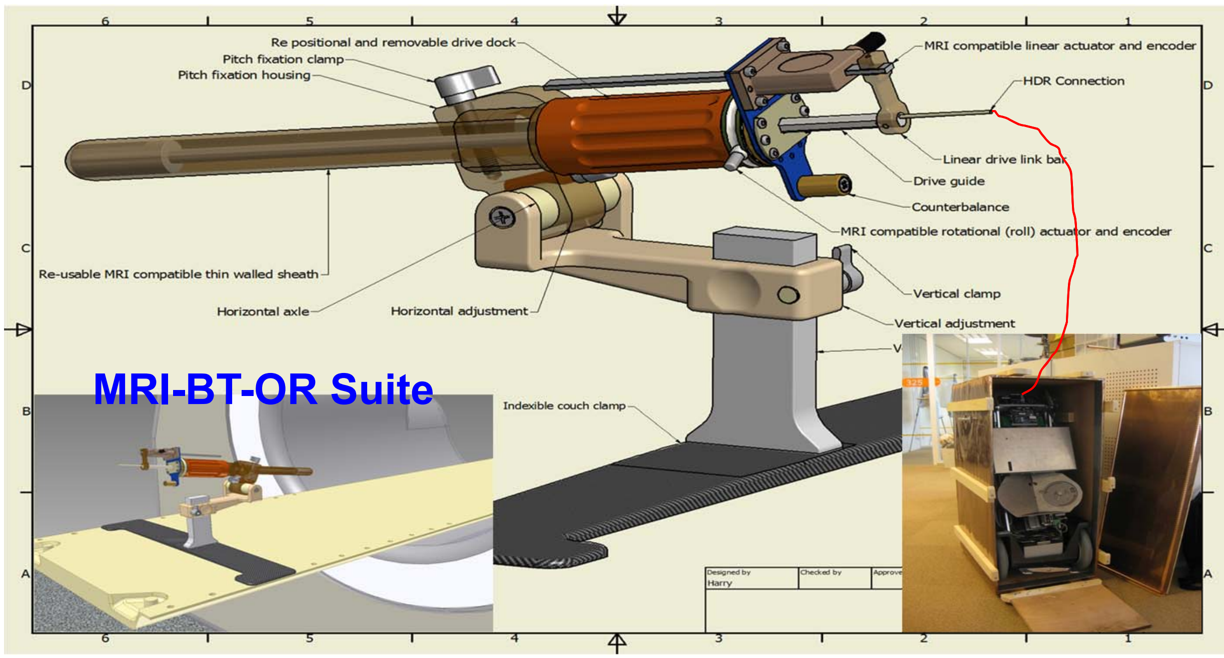
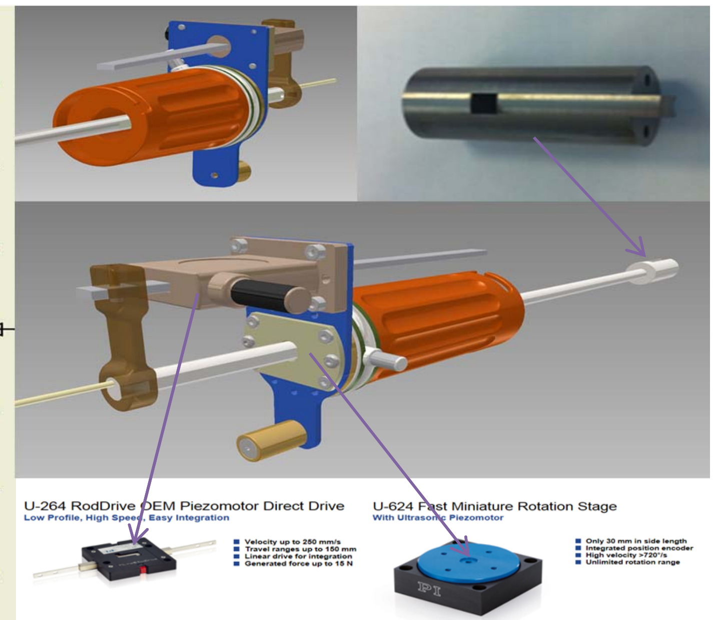
My Vision



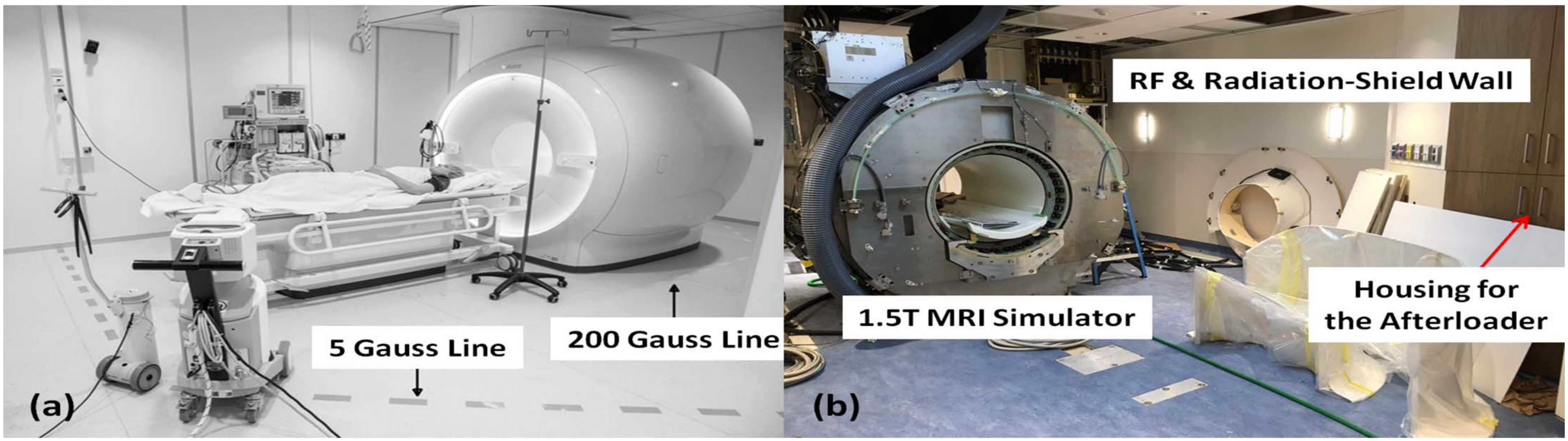
In-Room MR Compatible Design





MASSEY CANCER CENTER VCU

The Future of Brachytherapy Suites

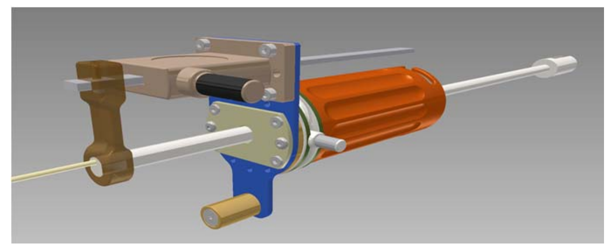


Utrecht Medical Centre, The Netherlands

Sunnybrook Hospital, Toronto, Canada (Sept 23, 2016)

36 Clinical Plans from JGH, Montreal

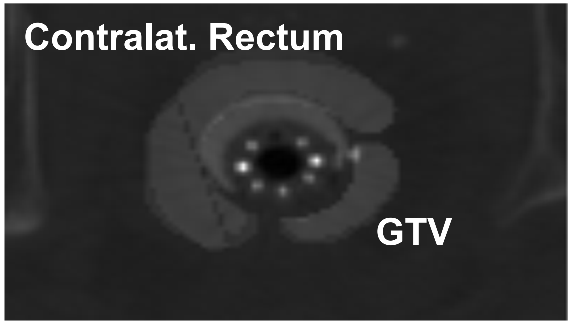
VS

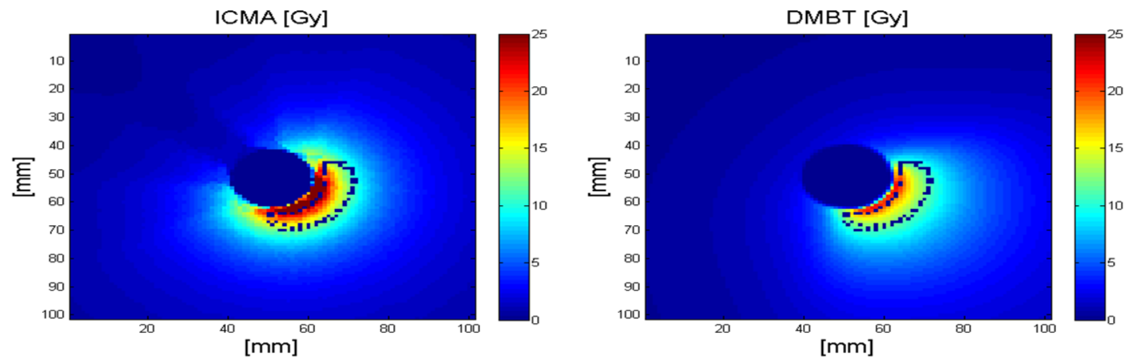


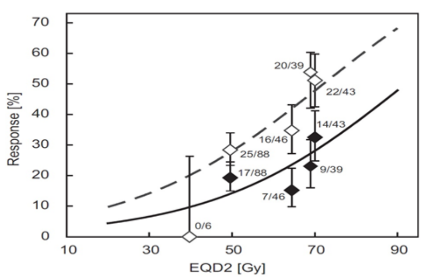
(ICMA)

(DMBT)

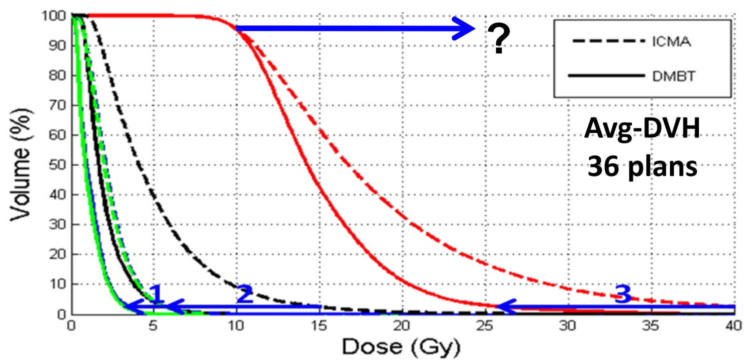
36 Clinical Plans from JGH, Montreal







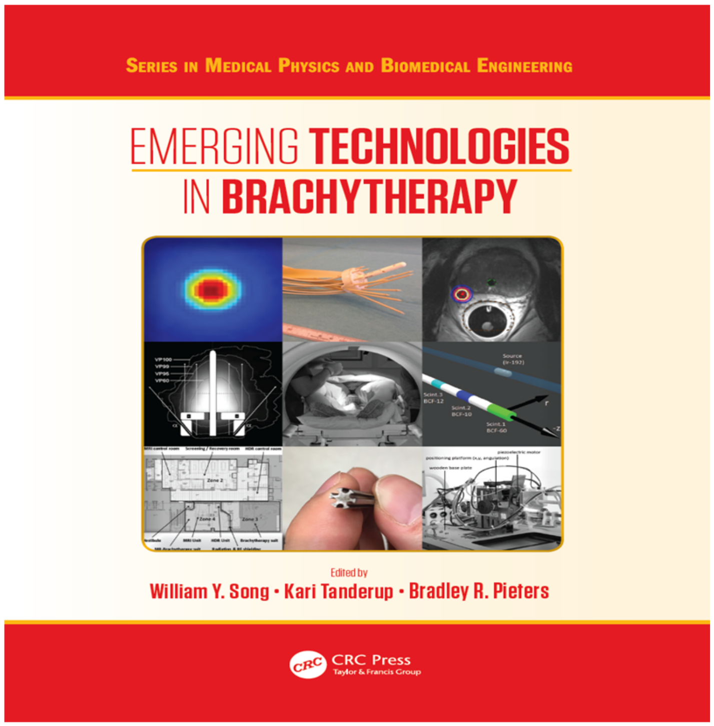
Appelt *et al.*, 2013



Webster *et al.*, Med Phys 2013;40:011718.

- Non-surgery cases
- Rx = 10Gy
- Total dwell times:
  - ICMA = 5.21±0.95 min.
  - DMBT = 15.94±3.97 min.

Emerging Technologies in Brachytherapy



- William Y Song, Kari Tanderup, Bradley Pieters - Editors
- 31 Chapters
- 100+ leading experts contributed from academia & industry
- Release Date: ***May 2017***

Questions?