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Use of MR for Brachytherapy Target Definition and Planning--Cervix Cancer

AAPM Spring Clinical Meeting 2015

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- No disclosures

ABS Consensus Guidelines

"Where do we go for guidance?"

- 2012 Viswanathan et al:
- Locally advanced cervix cancer
- Advances in 3D imaging
  - 3D tissue contouring guidelines
  - New dosimetry nomenclature
  - Improved outcomes (initial reports)
- For implementation
  - 3D contouring
  - image-based treatment planning
  - dose reporting
- ABS Consensus Guidelines recommend adoption of the GEC-ESTRO recommendations

Viswanathan and Thomadsen, *Brachytherapy.* 2012;11:33-46.
Viswanathan et al, *Brachytherapy.* 2012;11:47-52.

GEC-ESTRO Recommendations

- 2005 Haie-Meder et al
  - 3D-image-based approach and terminology for GTVs and CTVs
  - Based on the clinical experience of 3 different institutions
- 2006 Potter et al
  - 3D dose-volume parameters (D0.1cc, D2cc, EQD2 sums)
- 2010 Hellebust et al
  - Applicator reconstruction in 3D images (CT vs MR)
- 2012 Dimopoulos et al
  - MR imaging principles & technique

Haie-Meder et al, *Radiotherapy & Oncology.* 2005;74:235-245.
Potter et al, *Radiotherapy & Oncology.* 2006;78:67-77.
Hellebust et al, *Radiotherapy & Oncology.* 2010;96:153-160.
Dimopoulos et al, *Radiotherapy & Oncology.* 2012;103:113-122.

Clinical Implementation ca 2007

- First assessment of use of 3D-image based brachy (in mostly the U.S.) in 2007
- 133 ABS physician members surveyed
- 119 members were from U.S.
- Distribution of **imaging modalities** used specifically for dose specification

	All members (n =133)	U.S. members only (n=119)
Imaging modality used for target dose specification		
Plain film	43% (57)	43% (51)
CT	55% (73)	56% (67)
MRI	2% (3)	<1% (1)

Viswanathan and Erickson, *IJROBP.* 2010;76:104-109.

Clinical Implementation ca 2007

- How were they **specifying** dose on these images?

	All members (n =133)	U.S. members only (n=119)
Prescription, target		
Point A	76% (101)	77% (92)
mg/h/Point A	3% (4)	3% (3)
Volumetric	14% (19)	13% (15)
Point A and volumetric	7% (9)	8% (9)
Prescription, OAR		
ICRU	52% (69)	54% (64)
DVH	19% (25)	16% (19)
Both	29% (39)	30% (36)

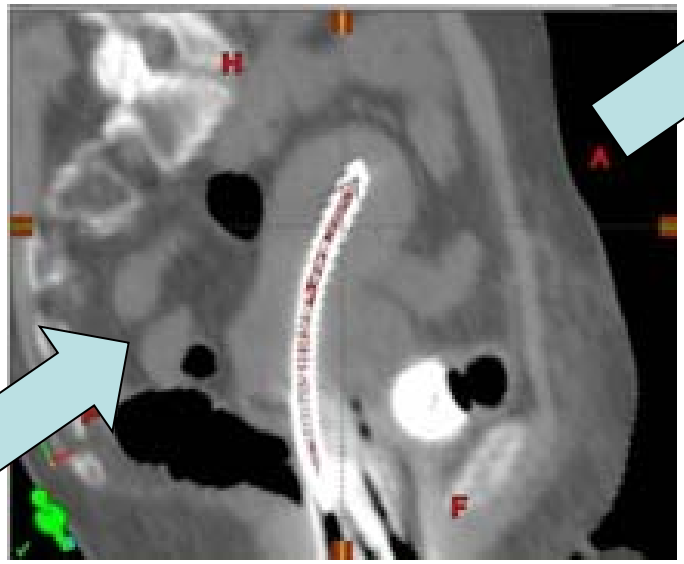
- How were they **modifying** dose?
  - More common to modify based on OARs: ICRU points vs DVHs
  - "Very disparate" criteria for target dosing: Point A vs CTV or GTV and what dose?

Viswanathan and Erickson, *IJROBP.* 2010;76:104-109.

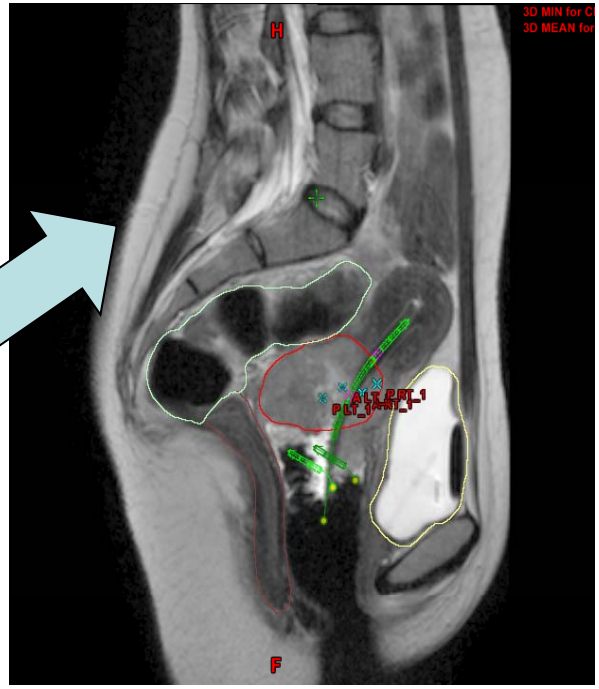
HDR Cervix Cancer Brachy at WUSM

1997

2007



2009

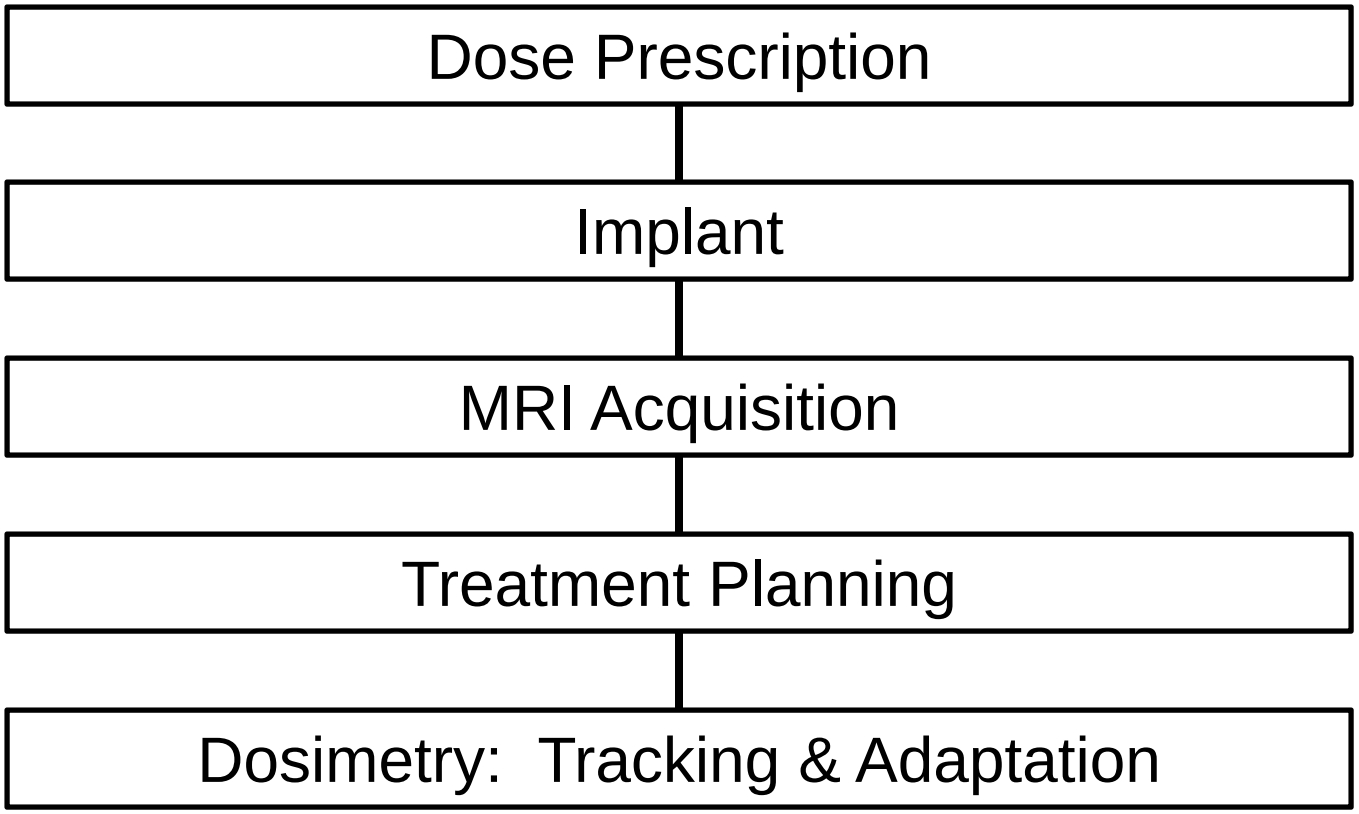


How to image with MRI?
How to plan with MRI?
GEC-ESTRO/clinical experience

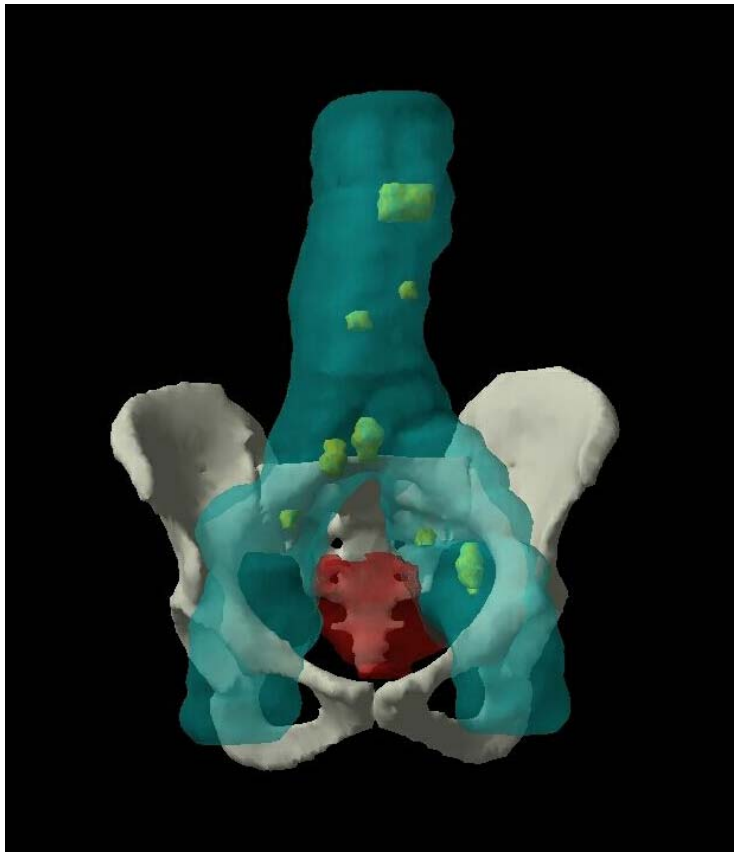
Learning Objectives

- To learn about one example of an implementation of an MRI-based technique for cervix cancer brachytherapy (at WUSM)
- To learn about aspects of this technique in the context of published recommendations and literature
- → To gain an understanding of how MRI can be used for target definition and adaptive treatment planning

Overview of Technique at WUSM



Dose Prescription



J. Esthappan et al., IJROBP 2008; 72,1134-1139.
Kidd et al., IJROBP 2010;77(4):1085-1091.

- Tumor stage & size
- IMRT
  - PTV (pelvic and para-aortic lymph node bed) 50.40 Gy at 1.8 Gy fraction, 28 fx
  - MTV Cervix (FDG-PET) 20.0 Gy concurrent
- HDR Brachy in 6 fx
- Timing (Concurrent):
  - IMRT 4 fx per week
  - Brachy 1 fx per week
  - 53 days (Fyles et al.) or else tumor control dropped by 1% per day

Implant

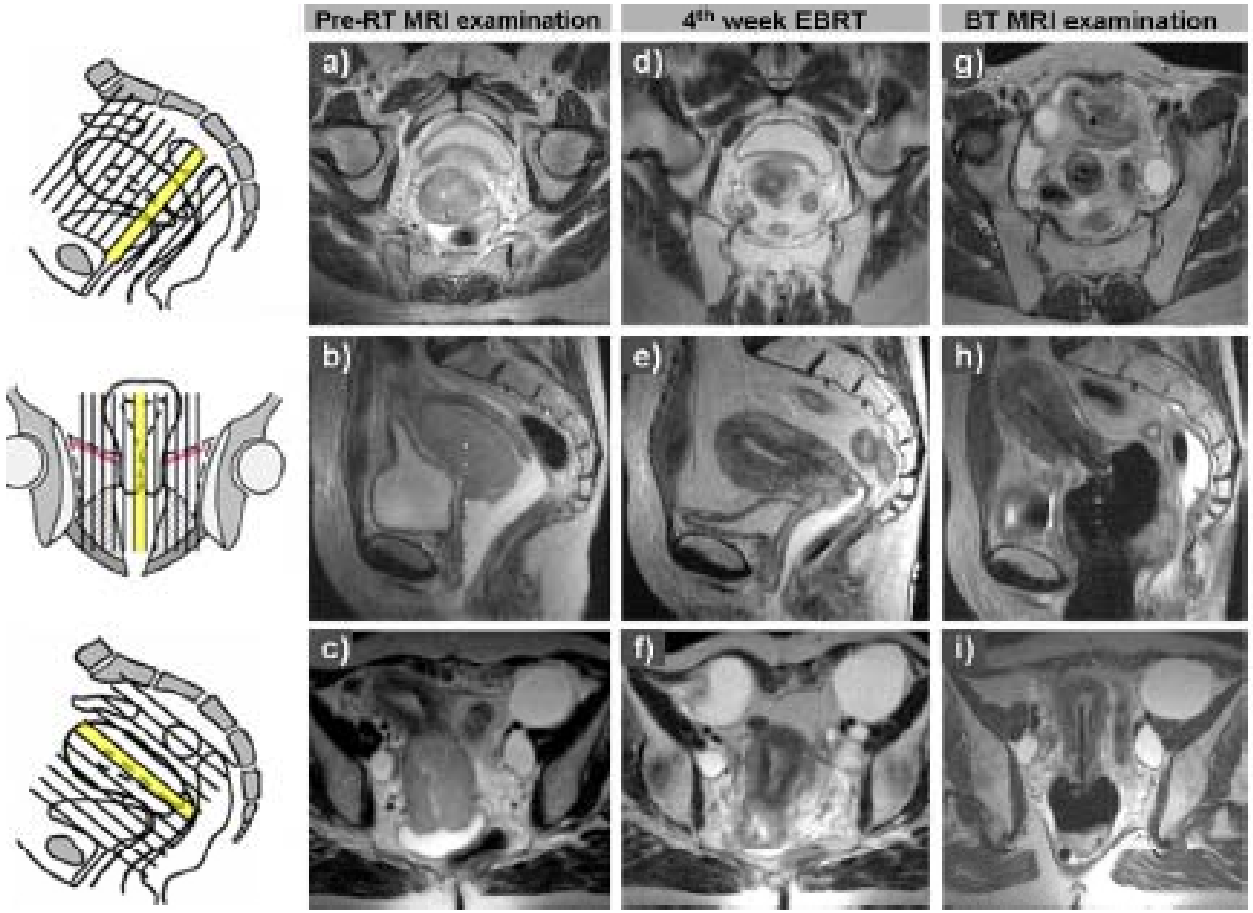
- Semi-sterile
- In HDR suite

- Titanium tandem and ovoids

Vendor Applicator Catalog

- Packing
  - Dry gauze, saline-soaked gauze, commercially available balloons

GEC ESTRO: T2W-MRI



- T2W – "**golden standard**" for visualization of tumor and OARs
- Complementary MRI sequences – **optional**

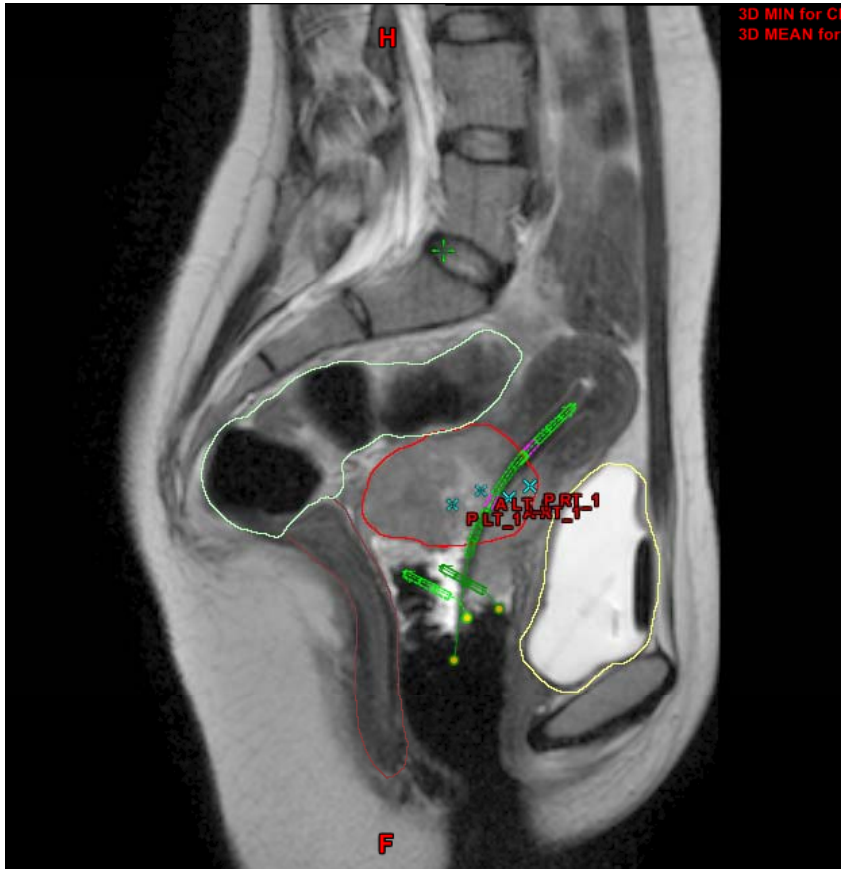
Dimopoulos et al, *Radiotherapy & Oncology.* 2012;103:113-122.

WUSM: Multi-sequence MRI

- 1.5-T MRI, 4-channel pelvic coil, respiratory triggering
  - T2-weighted (T2W) turbo spin-echo (TSE) imaging
  - Single-shot diffusion-weighted (DW) echo-planar imaging
  - Proton-density weighted (PDW) TSE imaging
- Para-sagittal acquisitions
- 3-6 minutes per sequence
- Image datasets exported to TPS
- Images registered based on DICOM coordinates (checked to see if patient moved between scans)

T2W: Primary Dataset for Planning

- WUSM & GEC-ESTRO
  - T2W-MRI is the primary dataset for planning
  - Points (e.g., point A)
  - OARs (bladder, rectum, and sigmoid)
- Target volume
  - GEC-ESTRO: GTV as well as HR-CTV defined on T2W-MRI (JKS's talk)
  - WUSM: GTV defined using T2W and **Diffusion-weighted MRI** sequences



Diffusion-weighted MRI

- DW-MRI
  - Add diffusion-weighted gradients to T2W → DWI → sensitive to the motion of water molecules
  - Water diffusion properties of different tissues can be quantified on the DWI as an Apparent Diffusion Coefficient (ADC) value

$$S_{DW} = S_o e^{-b*ADC}$$

  - $\boldsymbol{S_{DW}}$ and $\boldsymbol{S_o}$ are signal intensities measured with and without diffusion-weighted gradients, respectively
  - *b*-value is the diffusion factor (sec/mm^2) -- characterizes strength of the diffusion gradients

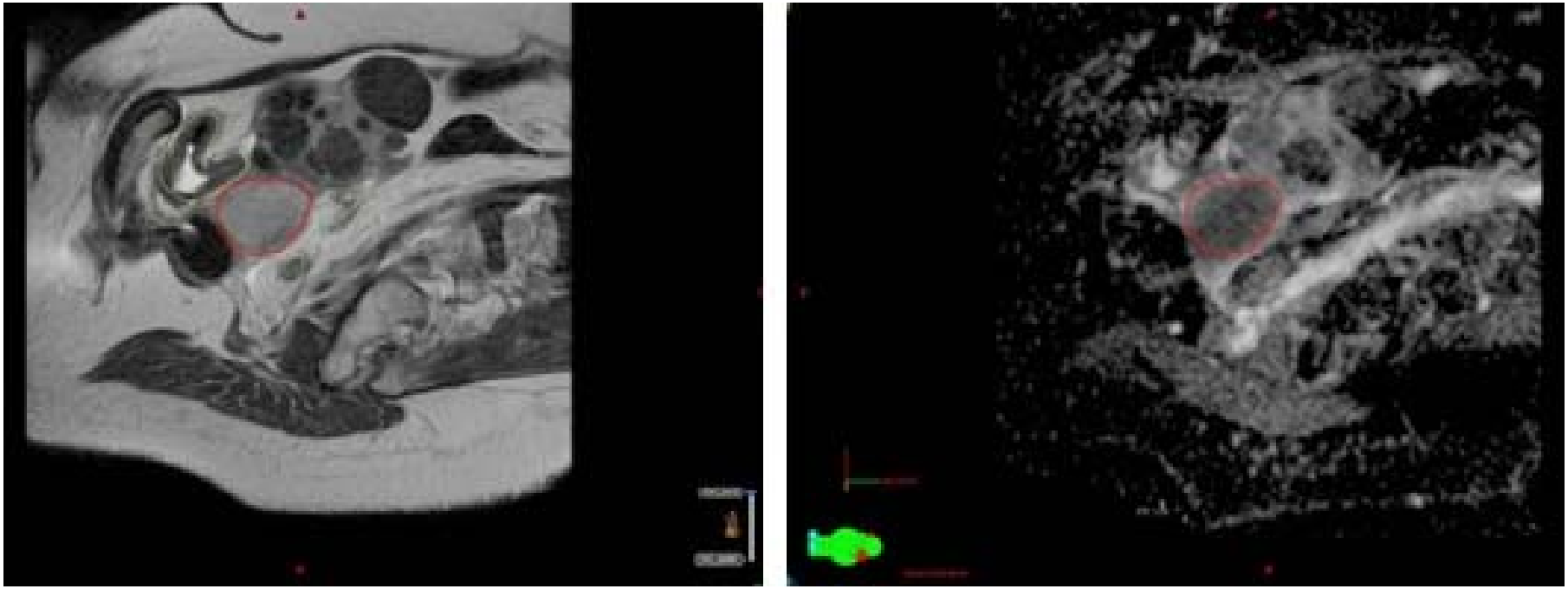
→DW-ADC maps

Diffusion-weighted ADC Maps

- DW-ADC maps
  - Cervix tumors have been shown to have significantly **lower ADC** values than normal cervix
  - More cellularly dense→restricts diffusion→ lower ADC value **→appears darker**
  - WUSM: DW-ADC maps fused with T2W images for the delineation of GTV
  - → Examples

Naganawa et al., Eur Radiol (2005)15:71-78.
Payne et al., Gyn Onc (2010)116:246-252.
McVeigh et al., Eur Radiol (2008)18:1058-1064.
Harry et al., Gynecol Oncol;116:253-261

Exp: ADC Maps + T2W MRI → GTV_B

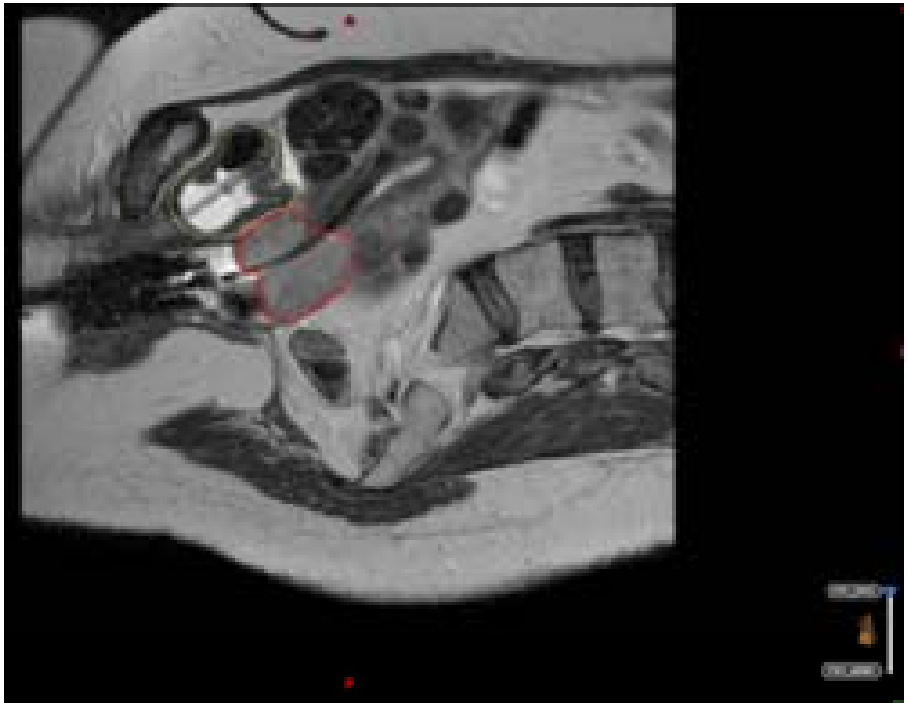


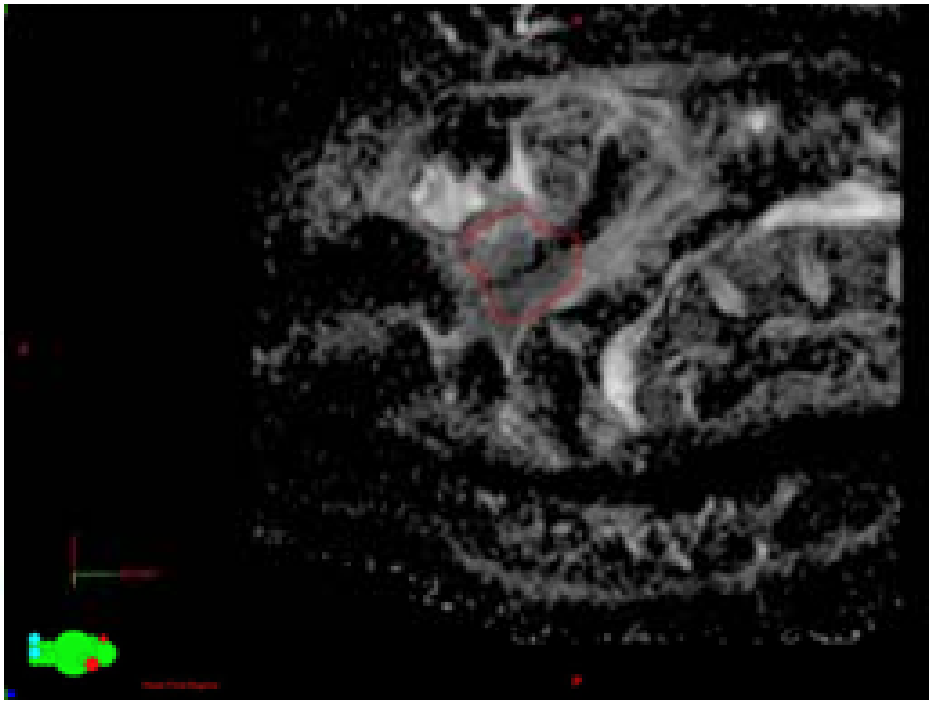
Good agreement

A para-sagittal slice in the T2W-MRI (a) and corresponding ADC map (b) about 1.5 cm lateral to the tandem for Patient 1. GTV_B defined using both datasets – good agreement between the contour and the image.

*Esthappan et al, Journal of Contemporary Brachytherapy, **3**, 193-198, 2011.*
*Olsen et al, Journal of Magnetic Resonance Imaging, **37**, 431-4, 2013.*

Exp: ADC Maps + T2W MRI → GTV_B



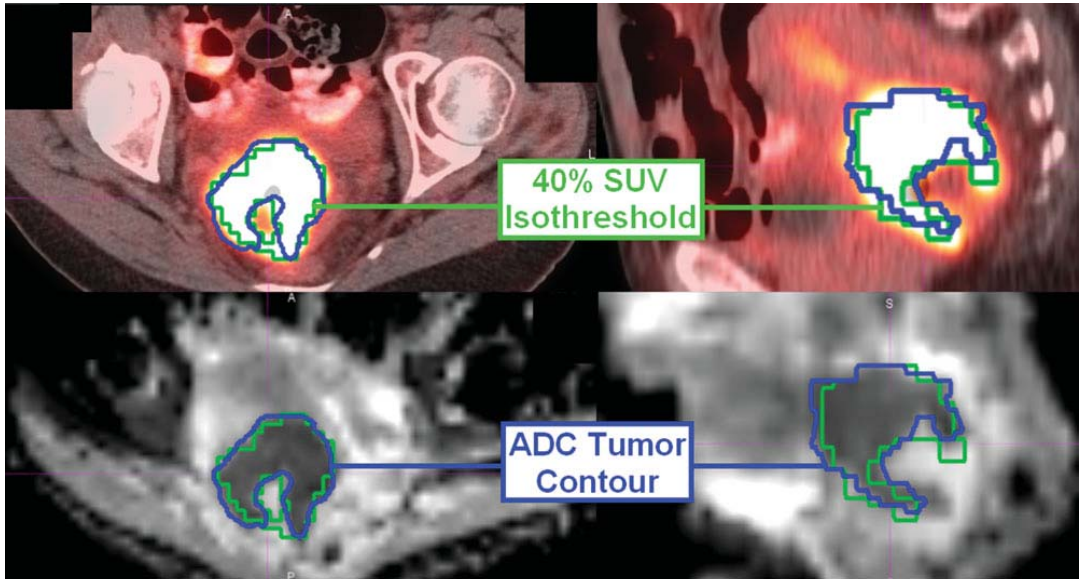


Fair agreement—but use with caution!!!

Same patient, same scan, different slice, which contains the tandem. **Pitfall:** ***DWI highly sensitive to metal susceptibility artifacts. ADC map and T2W should be used together for GTV_B definition, but the ADC used with caution when near metal.***

WUSM: Target Volume Definition

- 2013 Olsen et al: Pretty good agreement between FDG-PET (bright) and DW-ADC maps (dark)



- 2014 Dyk et al: GTV only-- dose to GTV from our treatment approach is highly correlated with local control

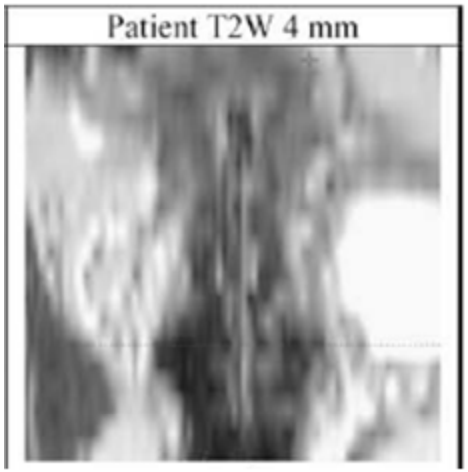
Olsen et al *J MRI*, 2013;37(2):431-434.
Dyk et al, *IJROBP* 2014;90(4):794-801.

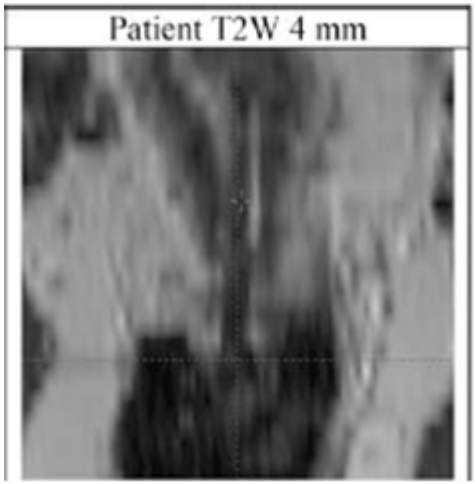
Esthappan et al, *JCB 2*011;3(4):193-198.

Applicator Reconstruction

GEC-ESTRO and published literature…

- GE: Centers used T2W-MRI and plastic applicators
- GE: Mentions differences between Plastic vs Titanium applicators:
  - More info: 2009 Haack et al
    - Plastic: weak signal on T2W, use of markers
    - Titanium: susceptibility artifact, can introduce more distortions

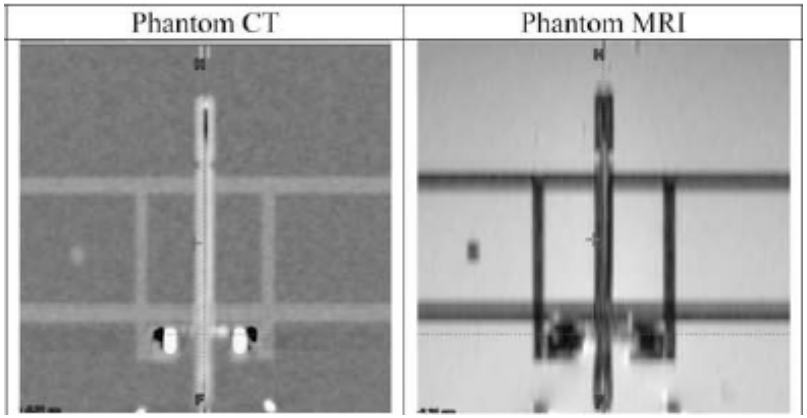




Haack et al, *Radiotherapy and Oncology* 2009;91:187-193.

Applicator Reconstruction

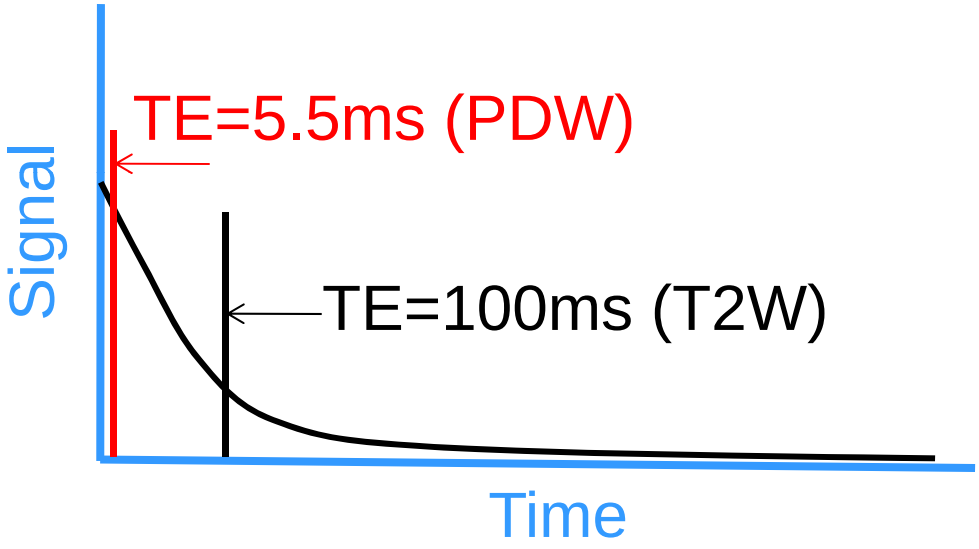
- GE: Centers used “low” (0.1-0.5 T) and “high” (1.0-1.5-T)
- GE: Mention Ti artifacts and increase at higher Tesla
  - More info: 2011 Kim et al
    - 3-T MRI units offers higher SNR
    - Artifacts increase with higher magnetic strength
    - Worse on T2W (6.9 ± 3.4 mm) vs. T1W (2.6 ± 1.3 mm)
- GE: Phantom MRI scans of Ti using clinical sequences fused against CT



- GE: Alternative planning strategy for Ti: CT or additional MRI sequences fused to the T2W-MRI

Haack et al, *Radiotherapy and Oncology* 2009;91:187-193. Kim et al, *IJROBP* 2011;80(3):947-955.

Proton Density-Weighted MRI



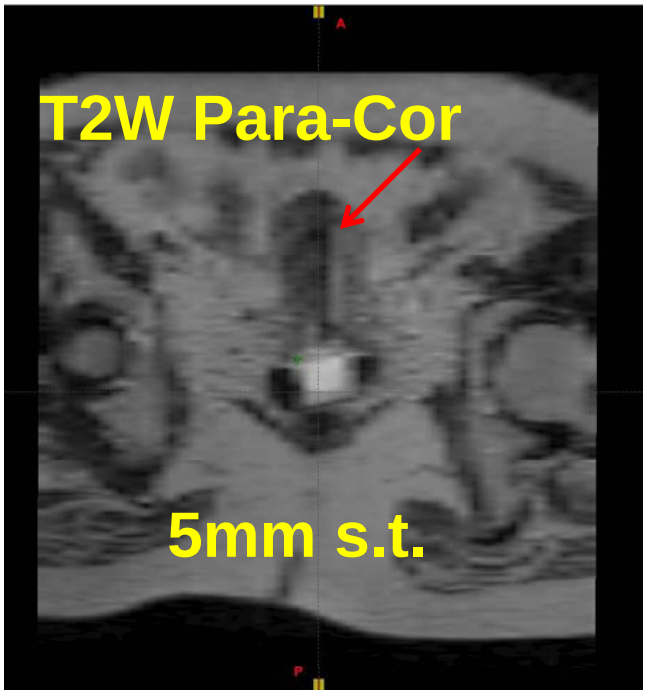
- WUSM: PDW sequence fused to the T2W-MRI for applicator reconstruction
- TE for PDW << TE for T2W sequence
- Data is acquired at this very short time point
- Signal from tissues in PDW sequence is higher than T2W sequence

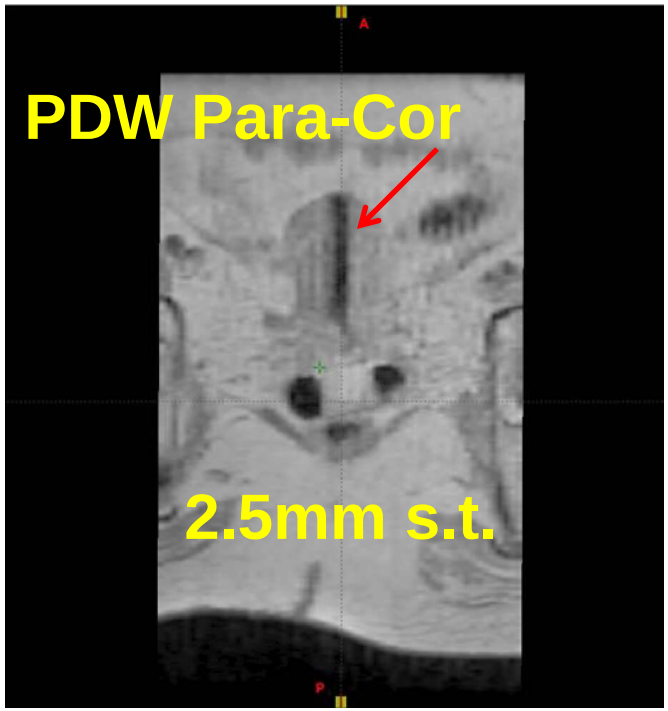
Courtesy of Y. Hu

WUSM: Applicator Reconstruction

- Tissues brighter in PDW
- Applicator appears dark in both sequences
- → Higher contrast between applicator and tissues in PDW images
- Better visualization of applicator in the PDW images
- Less distorted in PDW images

WUSM: Applicator Reconstruction





- Higher signal in PDW → thinner slices
- 5 mm vs 2.5 mm
- Better visualization of applicator in reconstructed views in PDW
- "Lose" tandem in T2W

Hu and Esthappan et al, *Radiation Oncology* 2013: 8:16

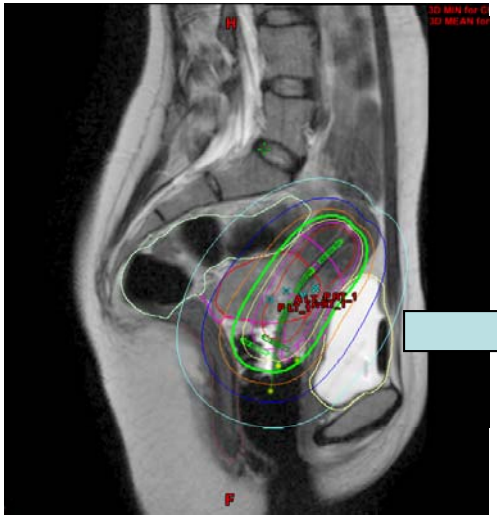
Dosimetry (GEC-ESTRO & Vienna Group)

- 2006 GEC-ESTRO
  - Dose-volume metrics: D2cc – dose to maximally exposed 2 cm^3 of the OARs, D90 GTV and HR-CTV
  - "Equivalent dose" and summation: EQD_2 : physical → BED → normalized to equivalent dose delivered in 2 Gy fractions of EB
  - Adapting dose to improve target coverage
- 2007 Lang et al
  - Summation spreadsheets with full EB dose, dose constraints
- 2005 Kirisits et al
  - Dose constraints & dose adaptation schemes
  - Start with standard loading, then 4 options:
    - » Symmetric scaling via point A
    - » asymmetric (A_L vs A_R)
    - » changing of dwell positions (ring)
    - » changing dwell weights individually

Lang et al, *IJROBP* 2007;69(2):619-627.

Kirisits et al, *IJROBP* 2005;62(3):901-911.

WUSM: Dose Tracking



OAR-Bladder

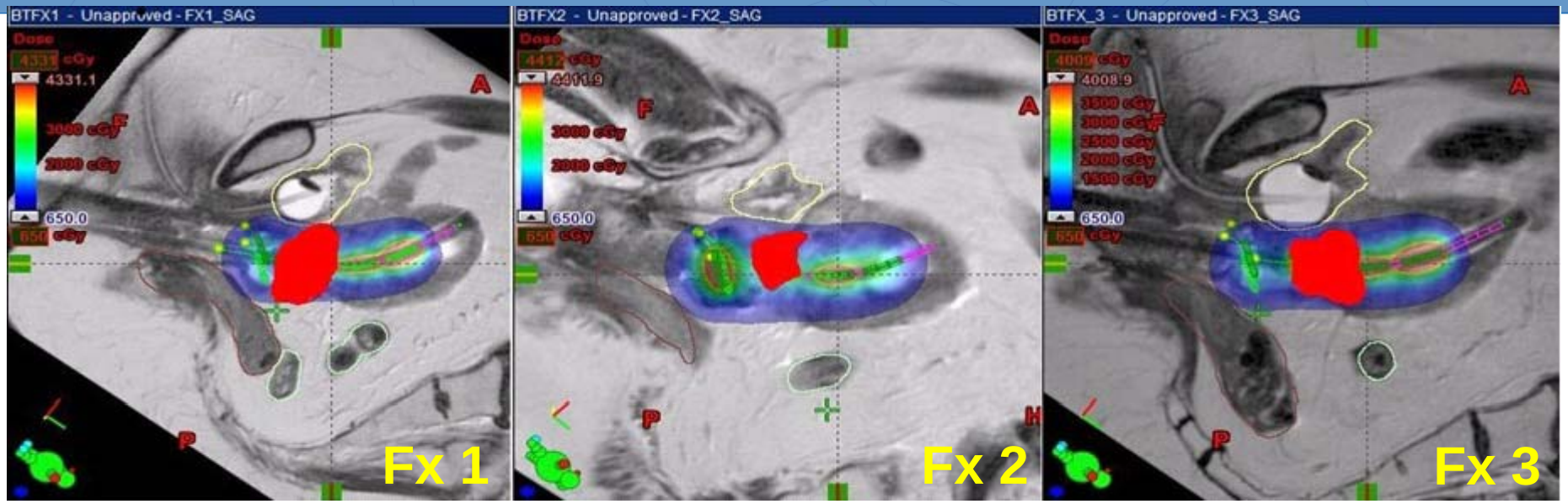
	BTFX1	BTFX2	BTFX3	BTFX4	BTFX5	BTFX6	BTX AVG	BTX+Mean EB (MTV CERVIX)
Vol (cc)	80.63	100.06					90.34	
D100(Gy)	0.56	0.49					0.53	27.47
D90(Gy)	0.96	0.96					0.96	30.08
D2cc (Gy)	4.14	4.17					4.15	49.25
EQD(Gy),D100	0.40	0.34					0.37	24.25
EQD (Gy),D90	0.76	0.76					0.76	26.58
EQD (Gy),D2cc	5.90	5.97					5.93	57.63
Ratio(D2cc/A_AVG Dose)	0.64	0.64					0.64	
Ratio:EQD(D2cc)/EQD(A_AVG)	0.66	0.66					0.66	

- Export of DICOM RT files to an in-house developed tool → a tracking spreadsheet (Baozhou et al IJROBP 2014;90(1):S490).
- BT dose tracked per fraction (D2cc bladder)
- Ratios to Point A (e.g., D2cc B < 80%)
- Mean brachy doses projected out to end of treatment and summed with mean IMRT dose
- Kirisits: D2cc B< 90 $Gy_{\alpha\beta3}$,D2cc R & S<75 $Gy_{\alpha\beta3}$, D90 GTV >=80-85 $Gy_{\alpha\beta10}$

WUSM: Dose Adaptation

- Start with standard loading schemes normalized to point A
- (1) Applicator Optimization:
  - Customize dose by modifying the applicator geometry based on tumor/anatomy
    - e.g., use of mini-ovoids or tandem alone for the latter fractions
  - Can also be used to decrease OAR dose predicted by Dose Tracker
- (2) Loading Optimization:
  - Another way to decrease OAR dose predicted by Dose Tracker
  - Tumor dosing takes priority, loading rules followed for the first 3 fx, **regardless of OAR dose**
  - **After fraction 3**, given adequate tumor volume shrinkage (50%), if D2cc out of tolerance…
  - Scale down loading uniformly by either 10% or 20%, while maintaining target coverage

Exp: Dose Tracking & *App Optimization*



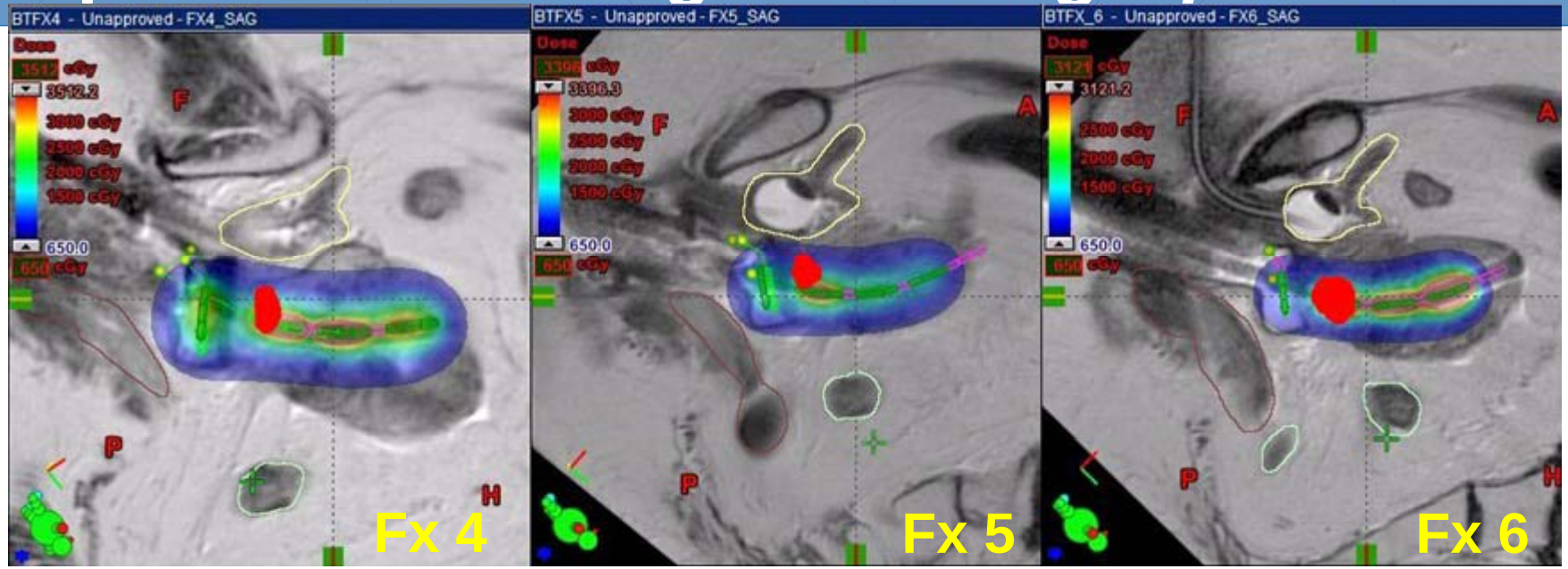
Fx 1 – 3:
Rx isodose colorwash
GTV in red
High bladder doses
Mini ovoids by Fx3

Courtesy of C. Bertelsman

OAR-Bladder

	BTFX1	BTFX2	BTFX3
Vol (cc)	51.21	41.86	44.34
D100(Gy)	1.29	1.30	1.18
D90(Gy)	1.88	1.91	1.73
D_Mean (Gy)	3.40	3.62	3.20
D_Max (Gy)	6.81	6.75	6.92
D2cc (Gy)	6.02	5.99	5.78
EQD_2(Gy),D100	1.10	1.12	0.98
EQD_2(Gy),D90	1.83	1.87	1.63
EQD_2(Gy),D_Mean	4.35	4.78	3.95
EQD_2(Gy),D_Max	13.33	13.14	13.70
EQD_2(Gy),D2cc	10.84	10.75	10.13
Ratio(D2cc/A_AVG Dose)	0.91	0.87	0.97
Ratio:EQD(D2cc)/EQD(A_AVG)	1.18	1.10	1.27

Exp: Dose Tracking & *Loading Optimization*



Fx 4-6:
Still high bladder dose
Sufficient target shrinkage

Fx 4-5: 10% reduction
Fx 6: 20% reduction
Reduce bladder dose
Maintain target coverage

OAR-Bladder

	BTFX1	BTFX2	BTFX3	BTFX4	BTFX5	BTFX6	BTX AVG	BTX+Mean EB (Bladder)
Vol (cc)	51.21	41.86	44.34	38.06	40.63	10.84	37.82	
D100(Gy)	1.29	1.30	1.18	0.96	1.13	0.99	1.14	46.31
D90(Gy)	1.88	1.91	1.73	1.54	1.52	1.20	1.63	49.24
D_Mean (Gy)	3.40	3.62	3.20	2.89	2.66	1.90	2.94	57.12
D_Max (Gy)	6.81	6.75	6.92	5.97	5.12	3.78	5.89	74.81
D2cc (Gy)	6.02	5.99	5.78	4.83	4.43	2.53	4.93	69.04
EQD_2(Gy),D100	1.10	1.12	0.98	0.76	0.93	0.79	0.95	40.48
EQD_2(Gy),D90	1.83	1.87	1.63	1.40	1.37	1.01	1.52	43.91
EQD_2(Gy),D_Mean	4.35	4.78	3.95	3.40	3.00	1.86	3.56	56.14
EQD_2(Gy),D_Max	13.33	13.14	13.70	10.69	8.30	5.12	10.71	99.07
EQD_2(Gy),D2cc	10.84	10.75	10.13	7.55	6.57	2.79	8.10	83.42
Ratio(D2cc/A_AVG Dose)	0.91	0.87	0.97	0.88	0.80	0.51	0.82	
Ratio:EQD(D2cc)/EQD(A_AVG)	1.18	1.10	1.27	1.07	0.92	0.46	1.00	

Courtesy of C. Bertelsman

Conclusions

- We have described a technique for MRI-based brachytherapy of cervix cancer patients:
  - Multi-sequence: T2W, DW-ADC, and PDW para-sagittal acquisitions
  - Improved visualization of OARs, GTV, and applicator
  - Dose adaptation
- We have described this technique in the context of GEC-ESTRO guidelines and published literature with key differences in:
  - MR image acquisition technique
    - Target definition
    - Applicator reconstruction
  - Dose adaptation