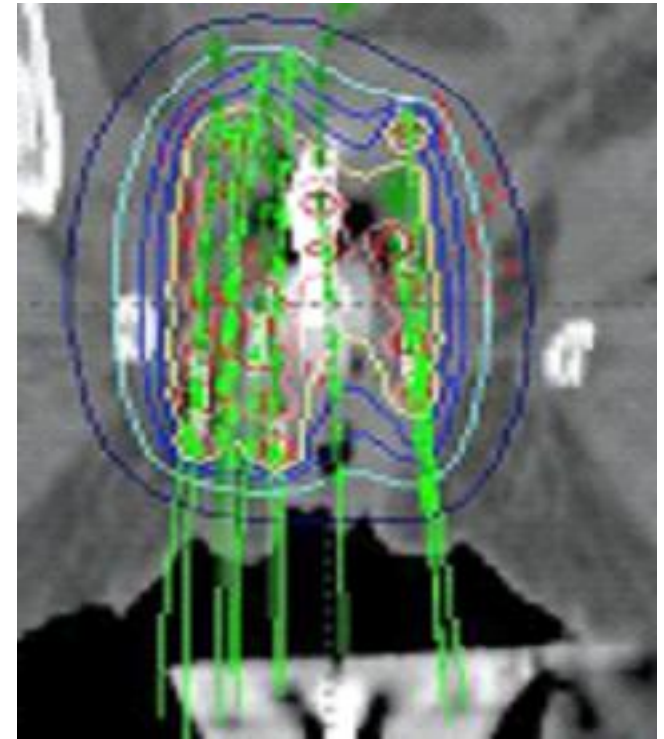


Interstitial Brachytherapy



Akila Viswanathan, MD MPH

BWH/Dana-Farber Cancer Institute

Harvard Medical School

January 30, 2016

Challenges to 3D interstitial ACCESS

1. Expertise
2. Applicators (precision, expense)
3. Imaging (CT, MRI, PET...)

TREATMENT PLANNING

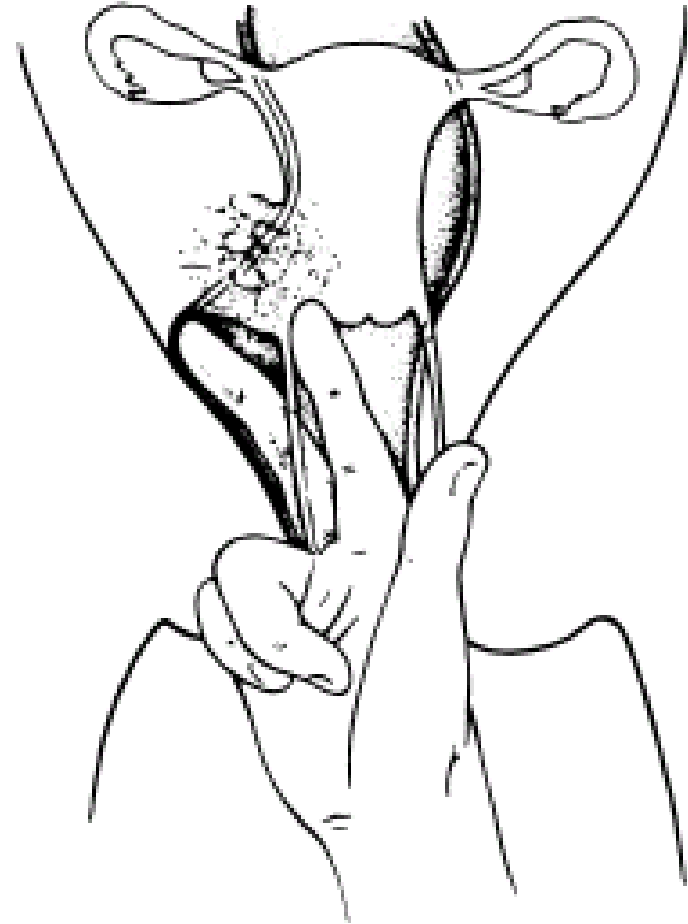
3. Utilization of images or contouring (relevant information)
4. Treatment planning systems (variability)
5. Treatment planning parameters (standardization)

OUTCOMES

6. Outcome measures (#s, local control, toxicity)
7. Patient quality of life (inpatient, bedrest)
8. Time (physician and physicist)

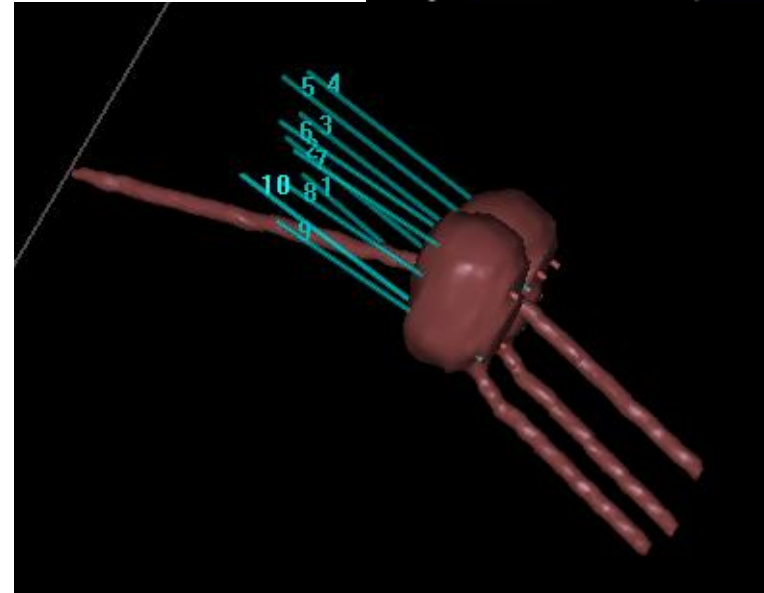
Patient Assessment

- **Speculum**
 - Assess vaginal disease
 - Place gold seed at inferior extent
- **Manual**
 - Assess vaginal width
 - Tumor size
 - Fixation to one side
 - Fistula



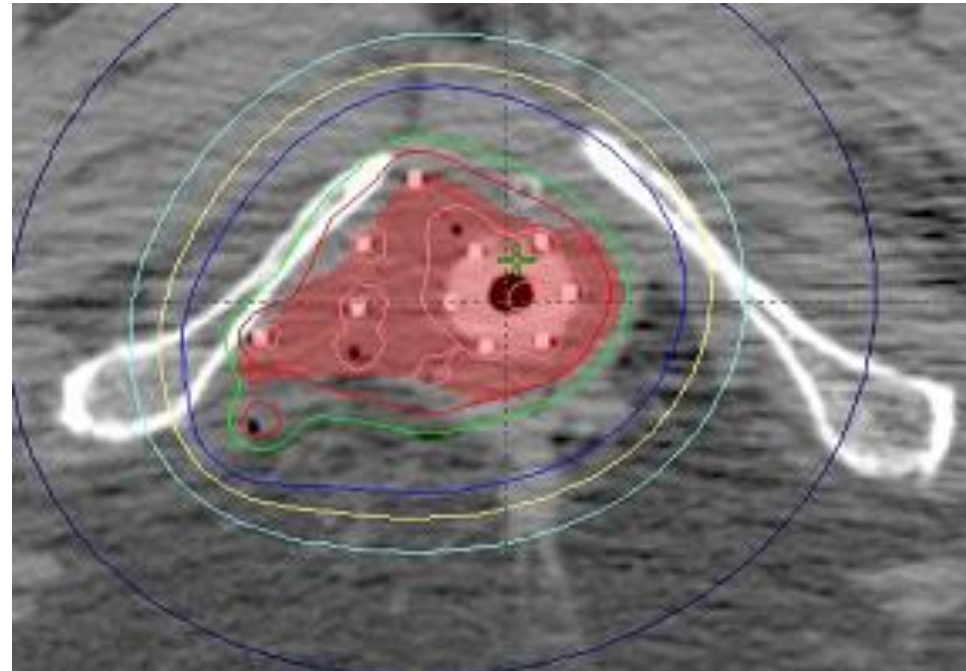
Indications for Interstitial

- **Large Cervical Ca**
 - Vaginal involvement
 - Sidewall involvement
 - Bladder involvement
- **Vaginal Cancer**
(**>5mm thickness**)
- **Vulvar Cancer with**
vaginal extension
- **Urethral Cancer,**
Bladder Cancer



Indications

- Postop recurrence
- Recurrent endometrial cancer in vagina
- Ovarian recurrence in vagina
- Extensive distal vaginal involvement from any ca
- Large pelvic mass
- Fistula

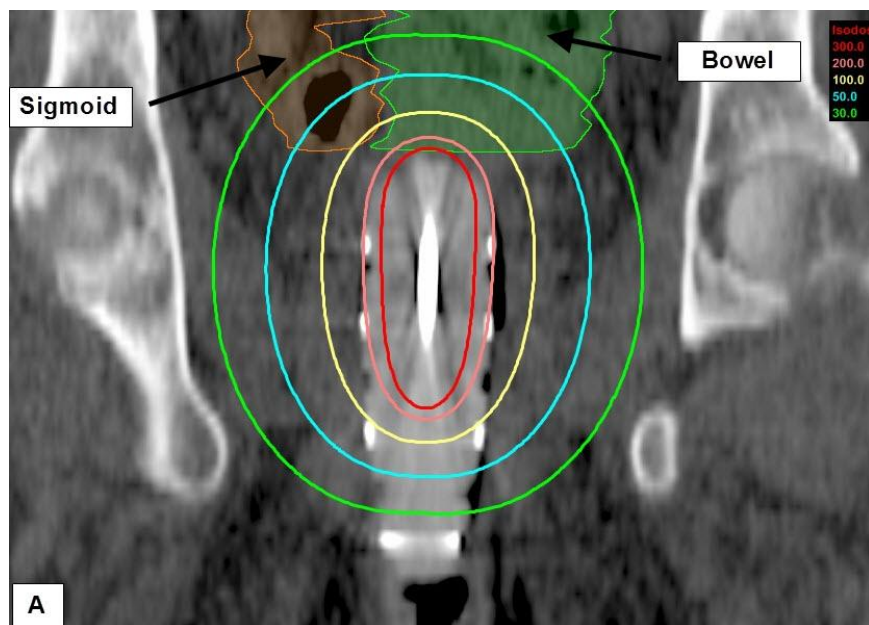


- **Historically, either laparoscopic, laparotomy or no guidance**
- **10% toxicity rate** (Syed IJROBP 2002; 54:67-78)
- **11% rate bowel insertion** (Eisbruch 1998)
- **Long-term fistula formation ~4-10%**
- **Imaging: US, MR or CT improves outcomes**

Cylinder vs Interstitial

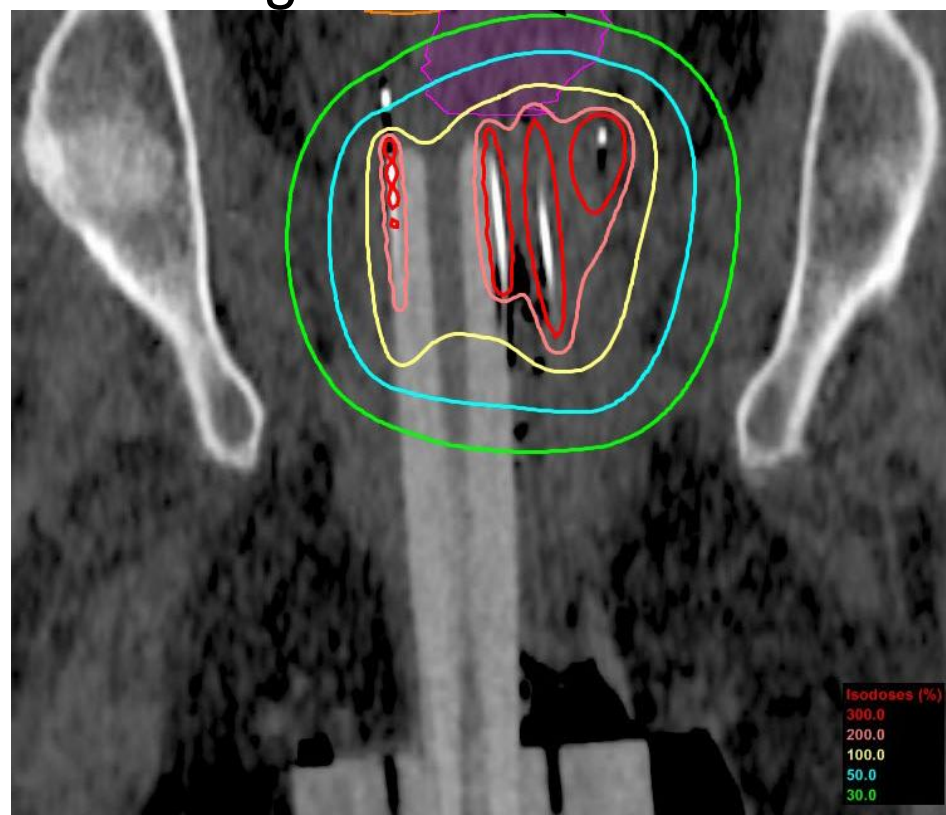
Cylinder

- For postop endo ca



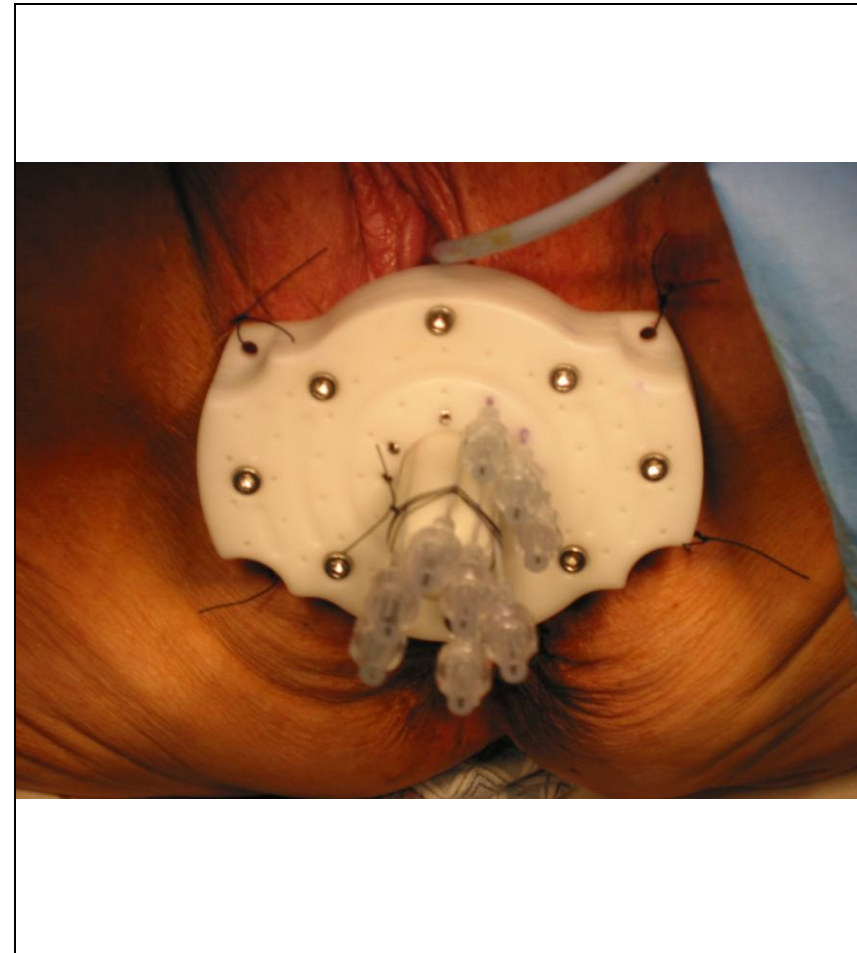
Interstitial

- For gross disease



Clinical preparation

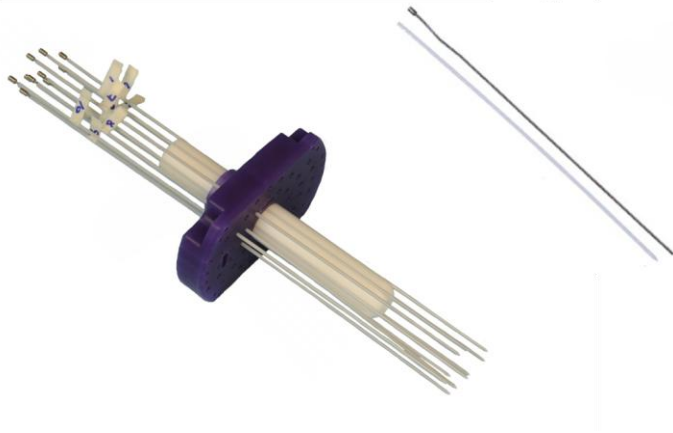
- Post EB exam, H/P
- Seed placement
- Pre-op anesthesia check
- Bowel prep
- NPO
- Baseline toxicity assessment
- DVT prophylaxis



Applicators: Individualize Selection

- **Syed**
 - Circular formation
- **Martinez**
 - Angled insertion to cover parametria
 - No obturator/not for vaginal ca
- **Ring or ovoids with needles**
 - Short needles to cover
 - Not for extensive vaginal ca
- **Cylinder with catheters (multichannel)**
- **Free hand**
 - Customized design

Applicators



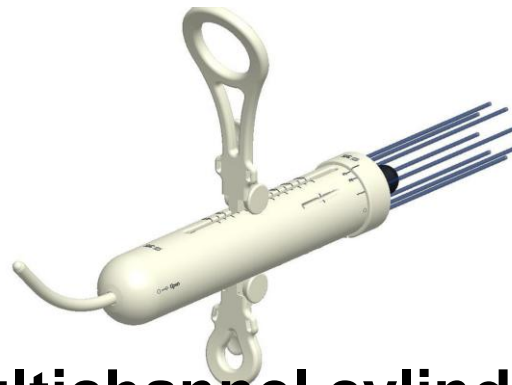
Tempalte Interstitial



Tandem and Ring



Tandem and Ovoids



Multichannel cylinder

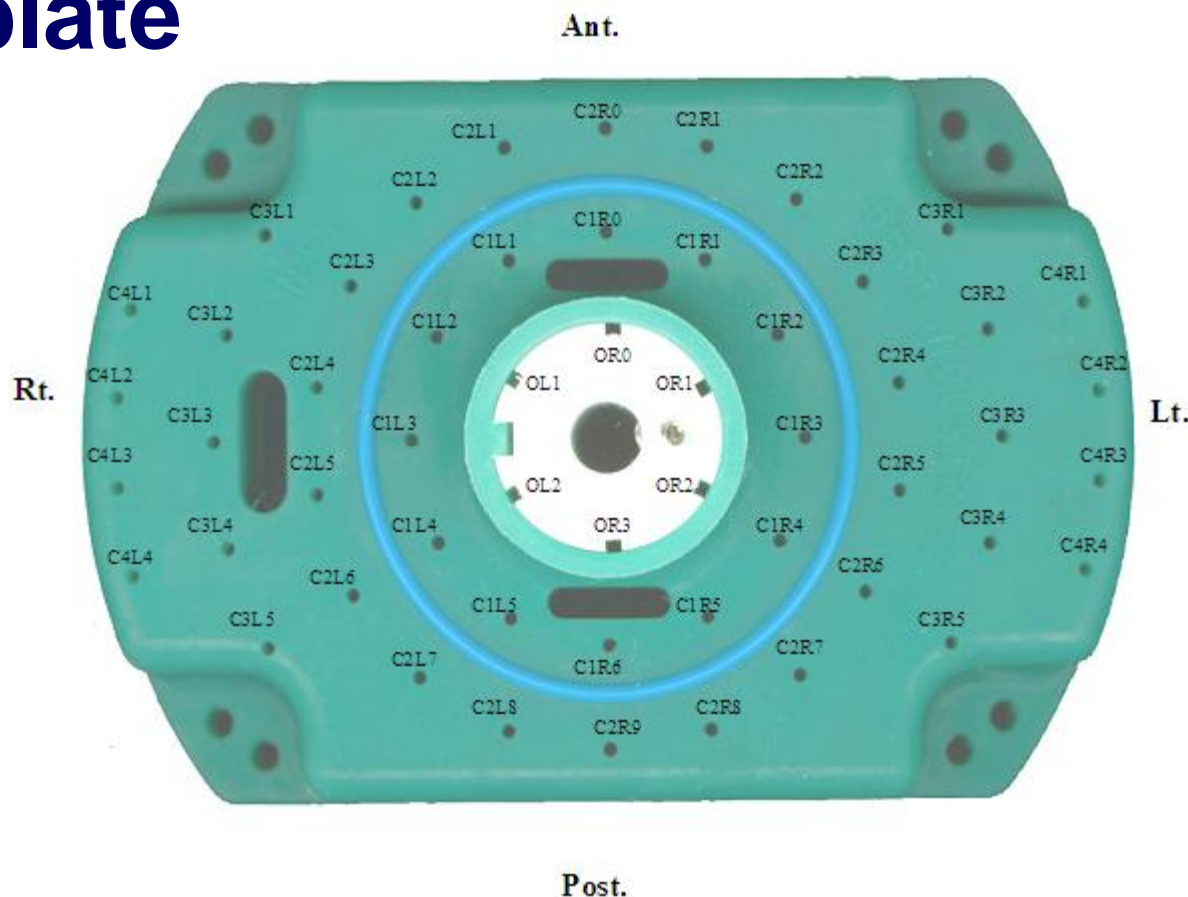
Need for central tandem

- **70 pts cervical cancer pts**
 - **All IIIB**
- **EBRT+LDR**
- **Tandem used in 73%**
- **Only sig predictor of OS on MVA was use of a tandem (HR 0.46)**

ABS guidelines recommend use of central tandem

Int J Gynecol Cancer. 2009.

Applicators: Syed Template



Fleming et al. Obst Gyn 55(4):525-530, 1980

Anesthesia



- **Bowel Prep, NPO**
- **Informed Consent**
- **Spinal**
 - Patient mobility
 - High-risk if anti-coagulated
- **General**
 - Quick to start
 - No patient motion
- **Epidural – hold anticoagulation**
 - Inpatient
 - DVT prophylaxis SQ Heparin, TEDs, pneumoboots OK



Template and Catheter Placement

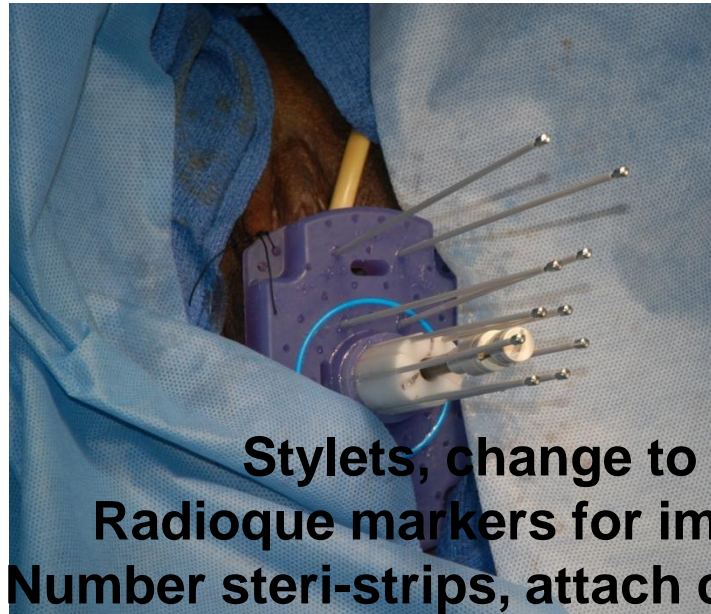
Ultrasound



**Stitch at vaginal apex
for countertraction**

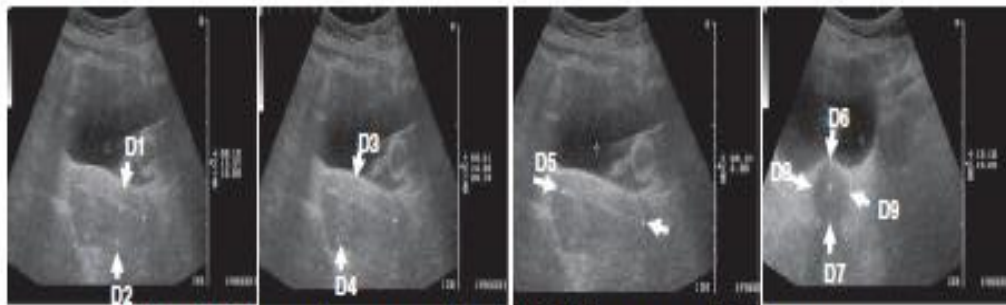


Stitch template

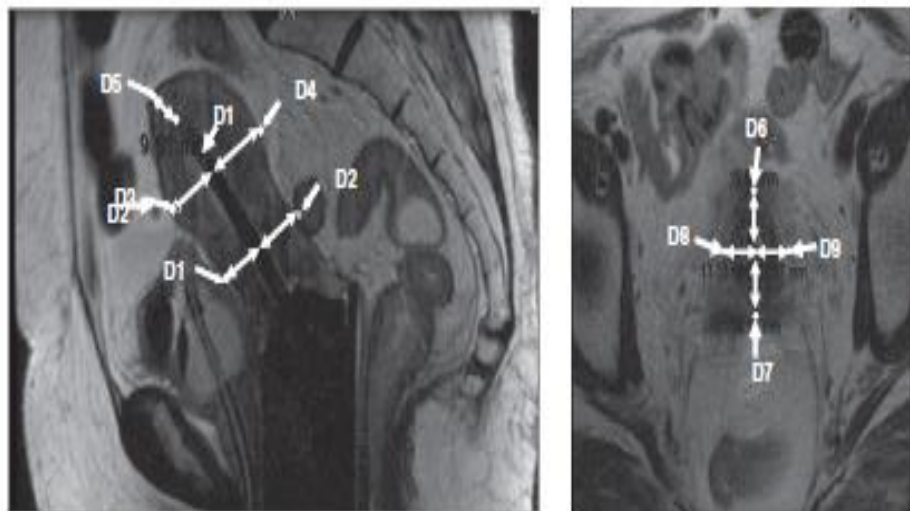


**Stylets, change to
Radioque markers for imaging
Number steri-strips, attach clockwise**

U/S and MRI lesion correlation

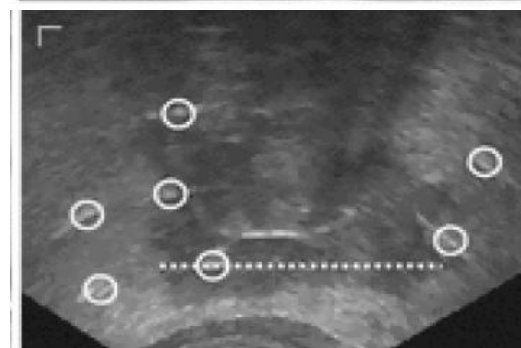


(a) : Various reference points and distances on US Images



(b) : Various reference points and distances on MR Images

Fig. 2. Shows various reference points and distances on: (a) US Images and (b) MR Images.



Mahantshetty U et al. Radiotherapy and Oncology. 2012. Schmid MP et al. Strahlenther Onkol. 2013.

Cervix Cancer Education Symposium, January 2016, Bangkok, Thailand

Iterative Insertion: US, CT or MR

MR Workflow:
Diagnostic series:

T2 a/s/c
T1 contrast
DWI

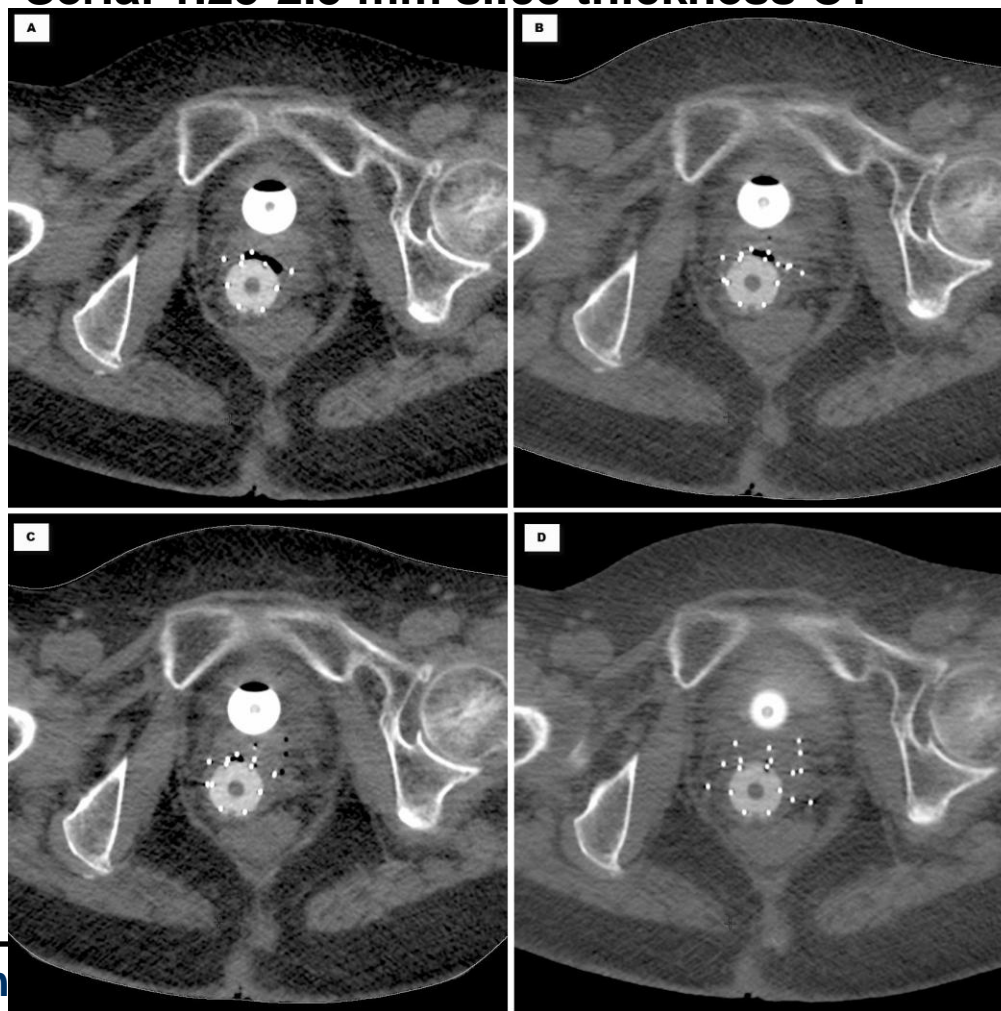
Intra-procedure:

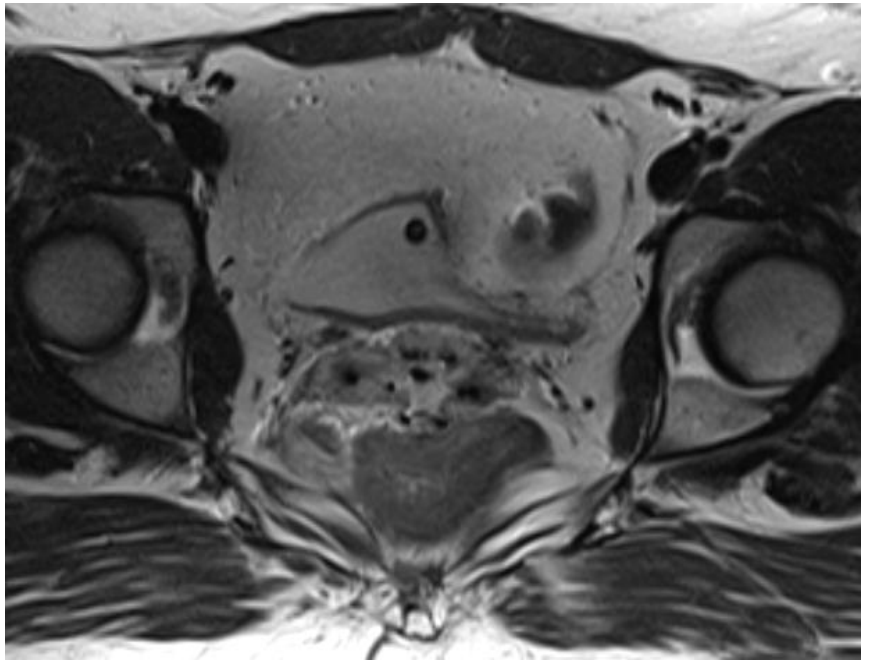
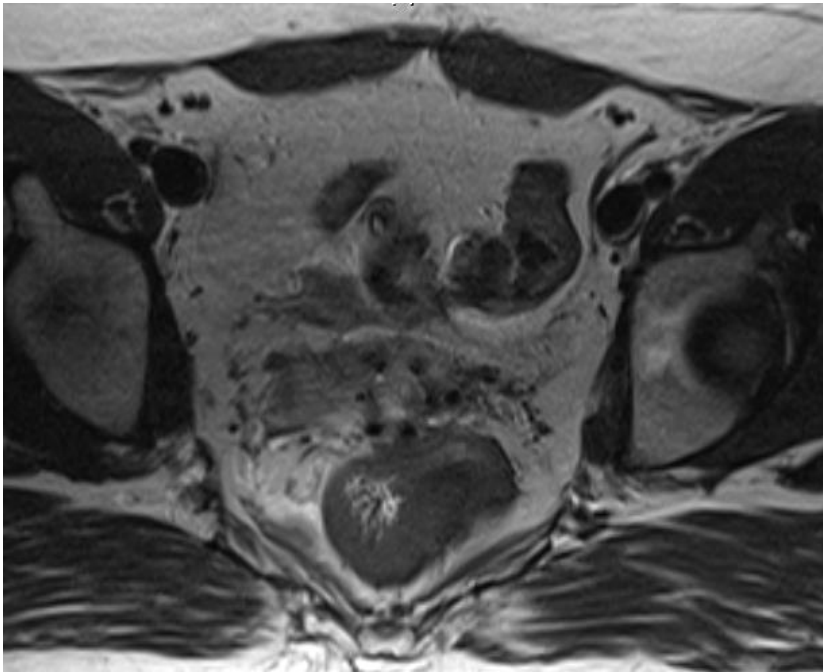
bSSFP Sagittal
bSSFP Axial
T2 axial

Final series:

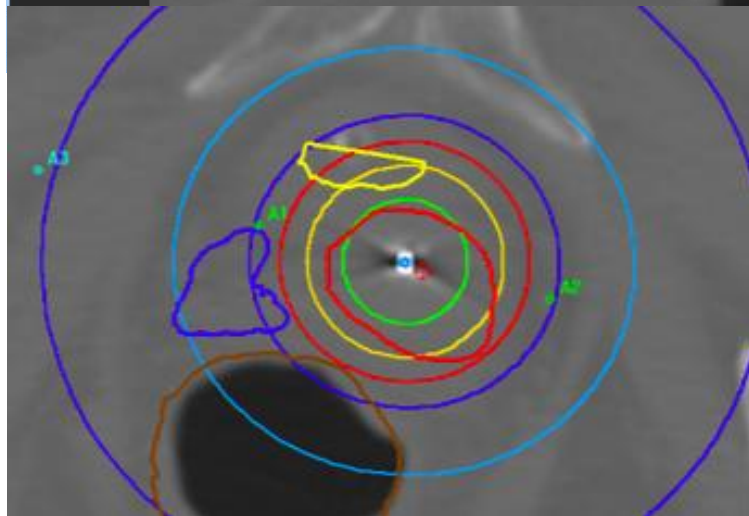
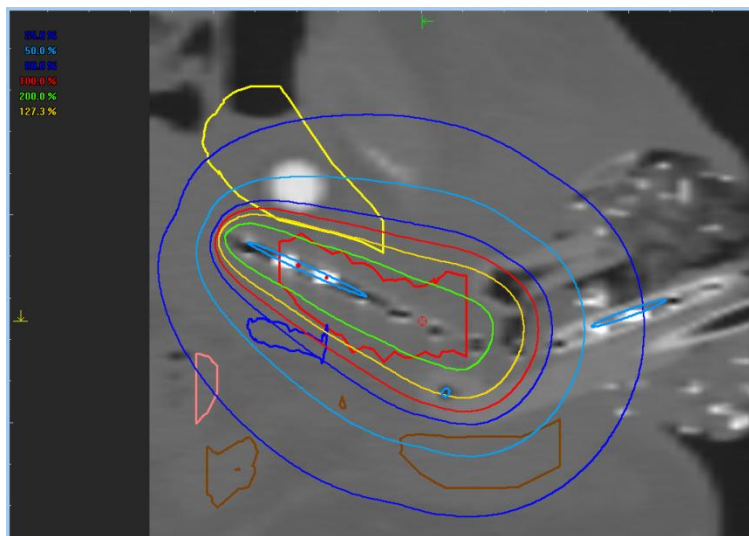
T2 axial/sag/cor
for planning
1.6mm thick
cover template

Serial 1.25-2.5 mm slice thickness CT

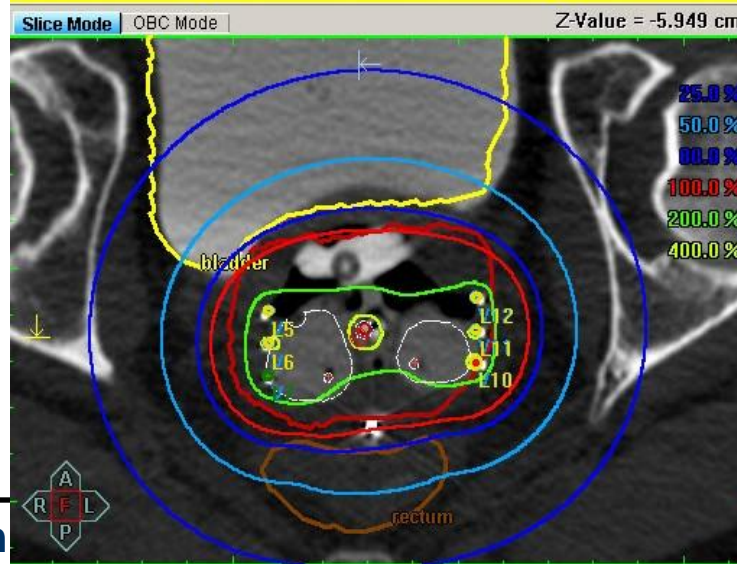
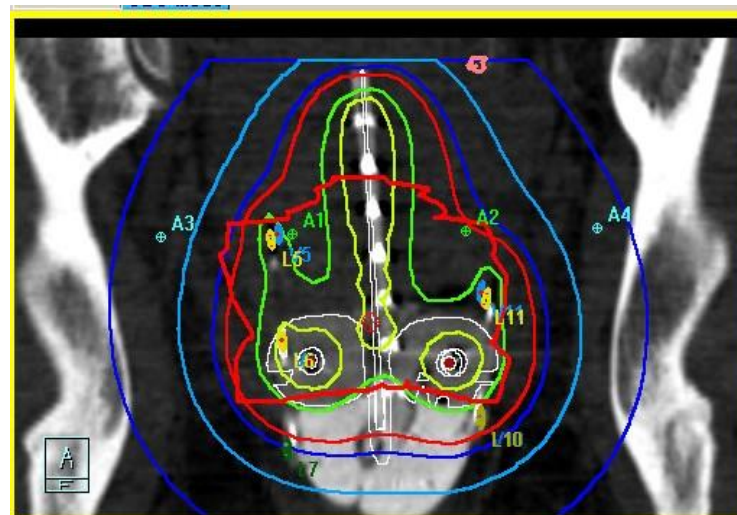




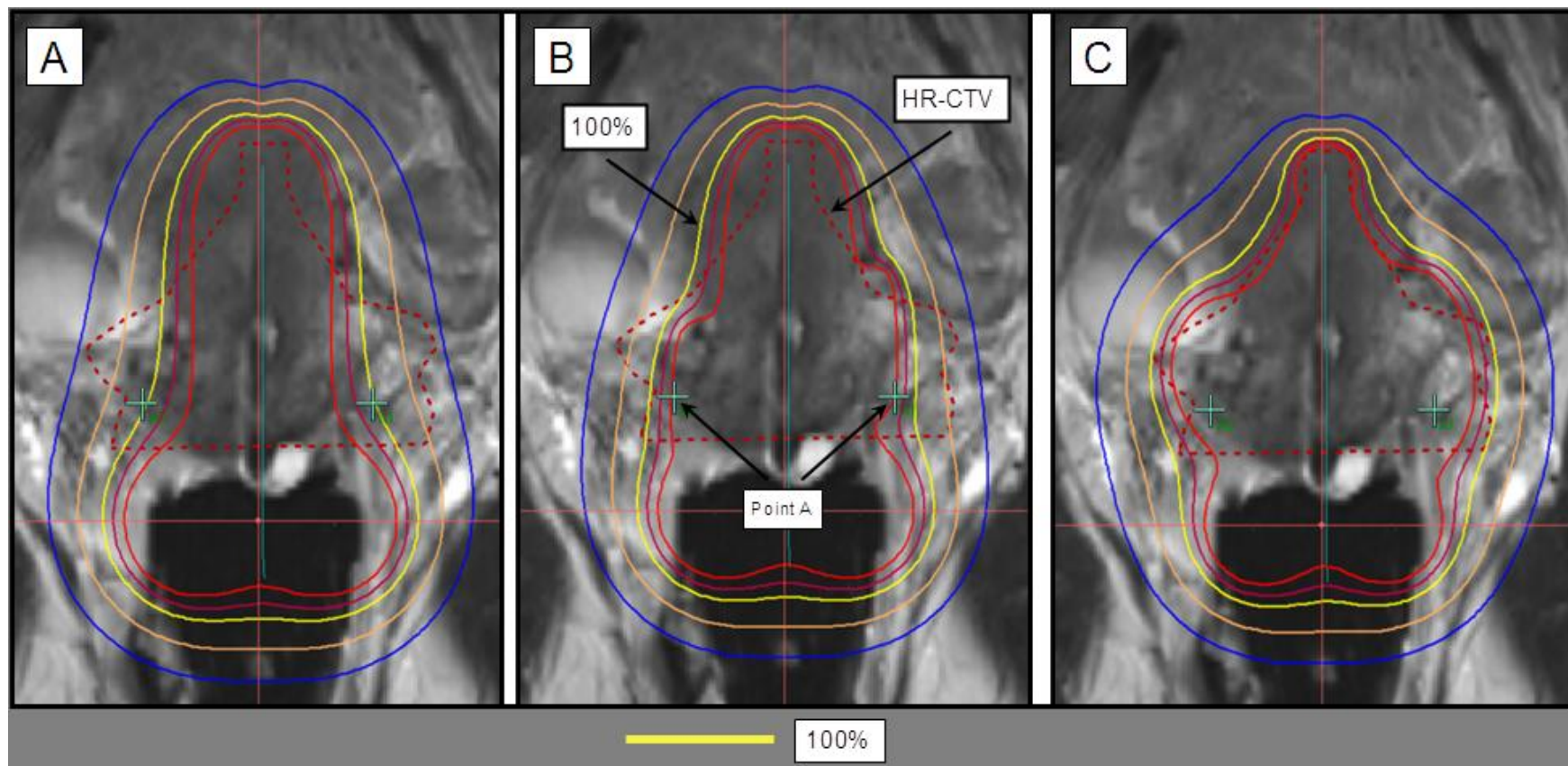
Point A vs. 3D Narrow cvx



Wide cvx

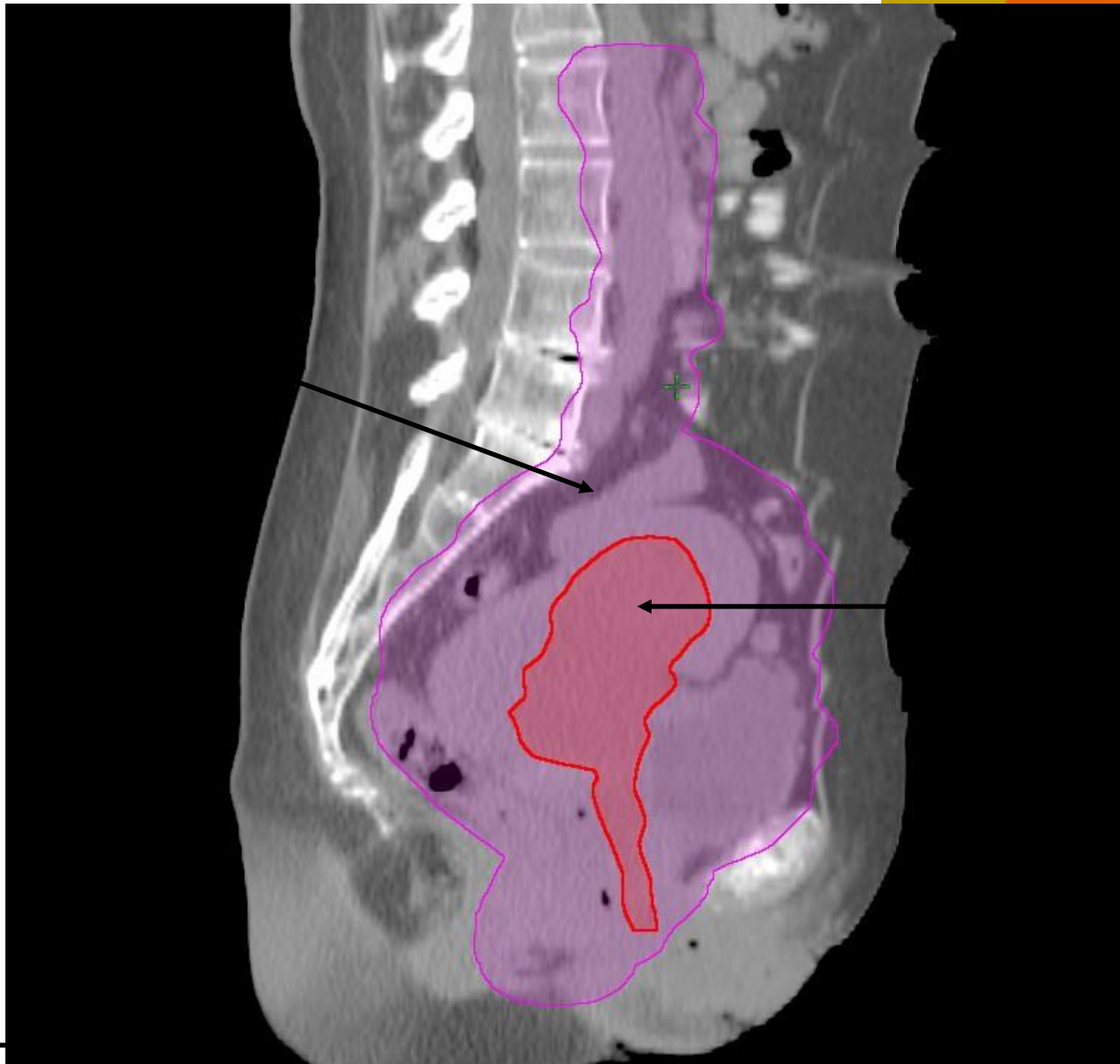


3T MR Treatment Planning

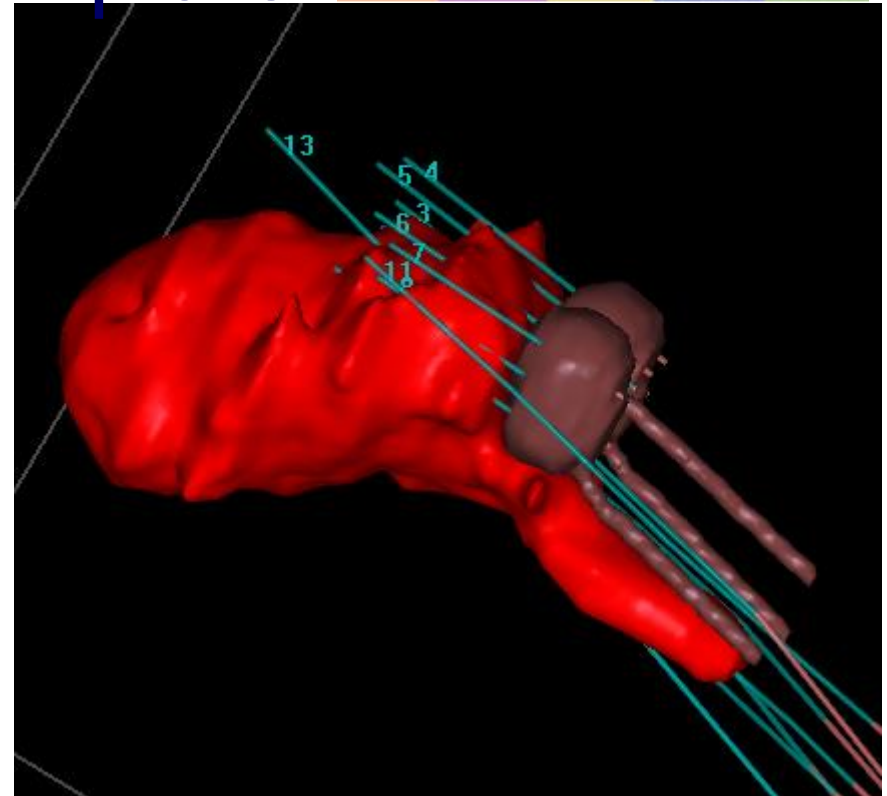
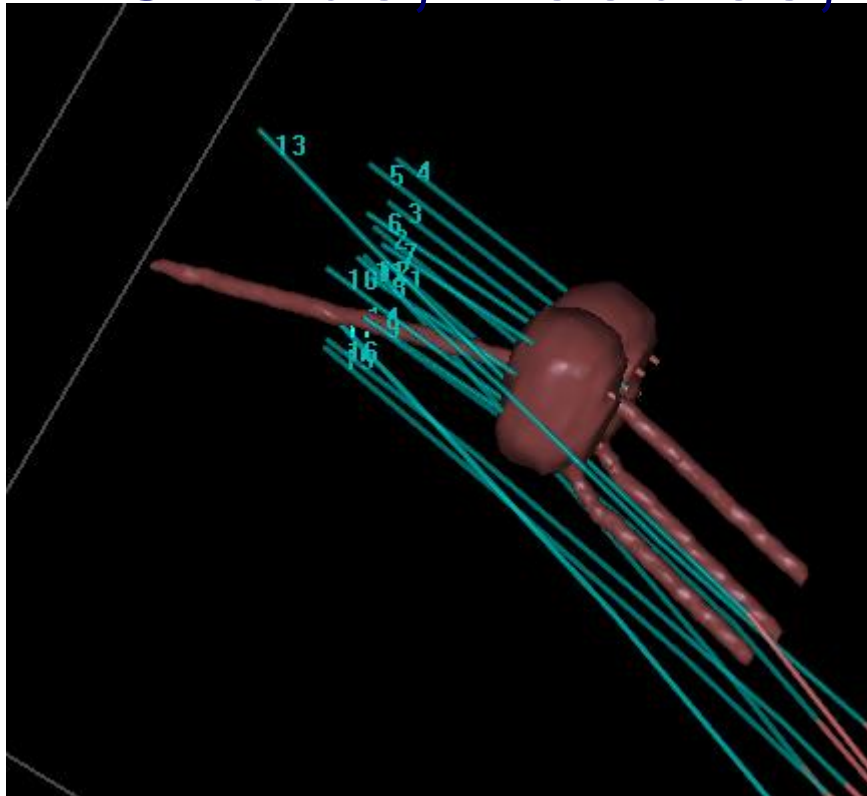




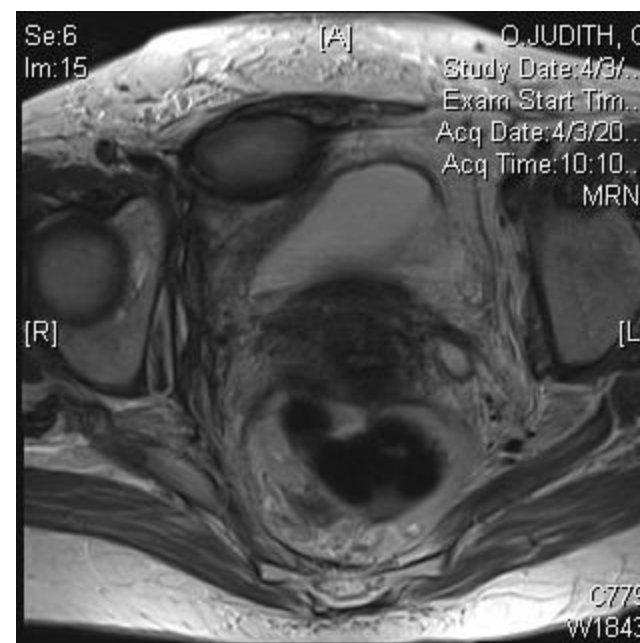
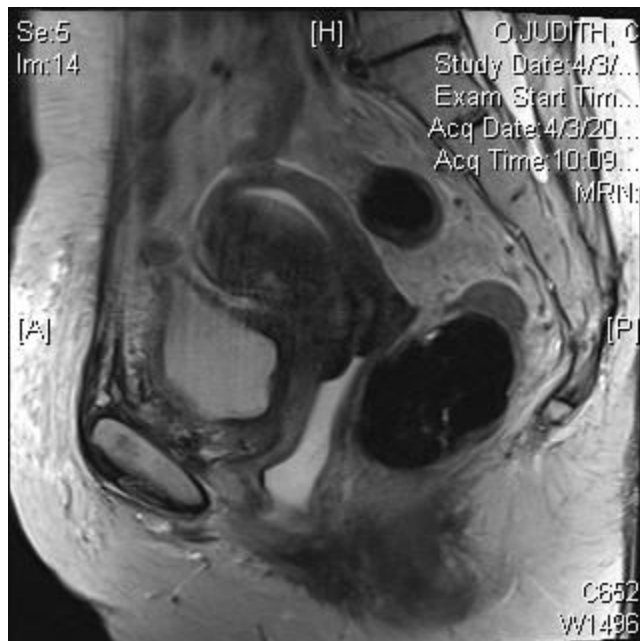
Case: Pre and post EB Sag MR



Ovoids, Needles, Template

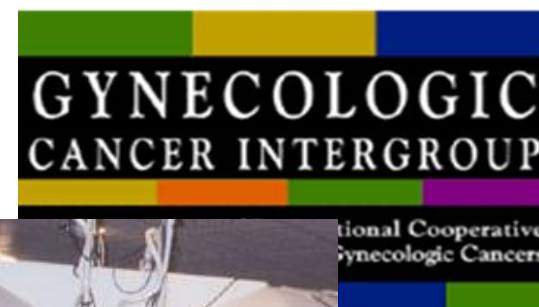


Follow-up 5 months later



Biopsies Gyn Onc and Urology (EUA and Cysto): all negative

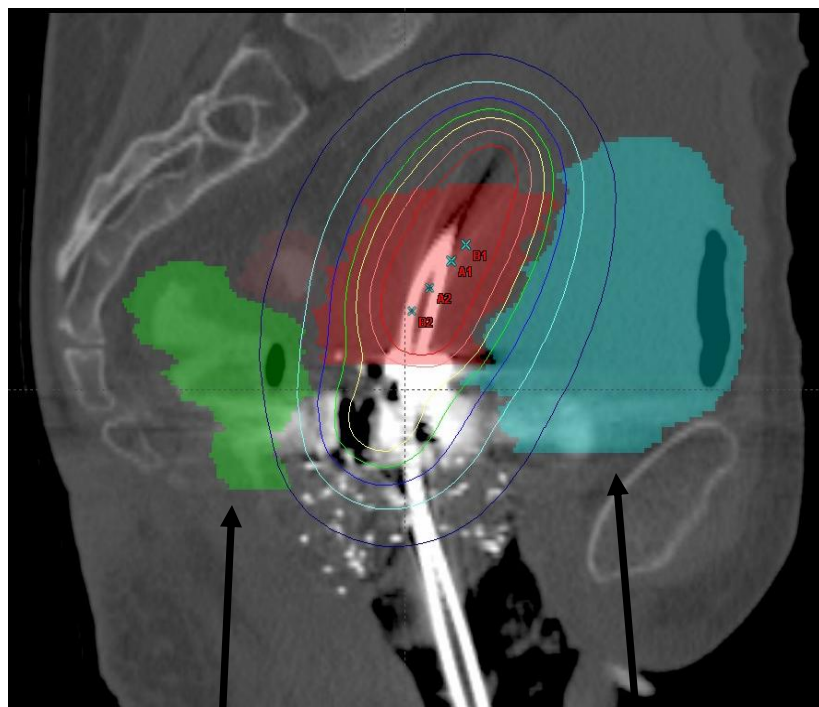
MR-Interstitial Outcomes



- First prospective trial in IGBT
- Real-time guidance
- 2004-2006
- 25 patients
- 15 recurrent ca
- All Interstitial
- 0.5 T MR
- 2 yr PFS 65%
- 2 yr OS 60%
- 2 persistent disease
- [No Local Recurrence](#)

Brachytherapy 2013 May-Jun;12(3):240-7

Contouring

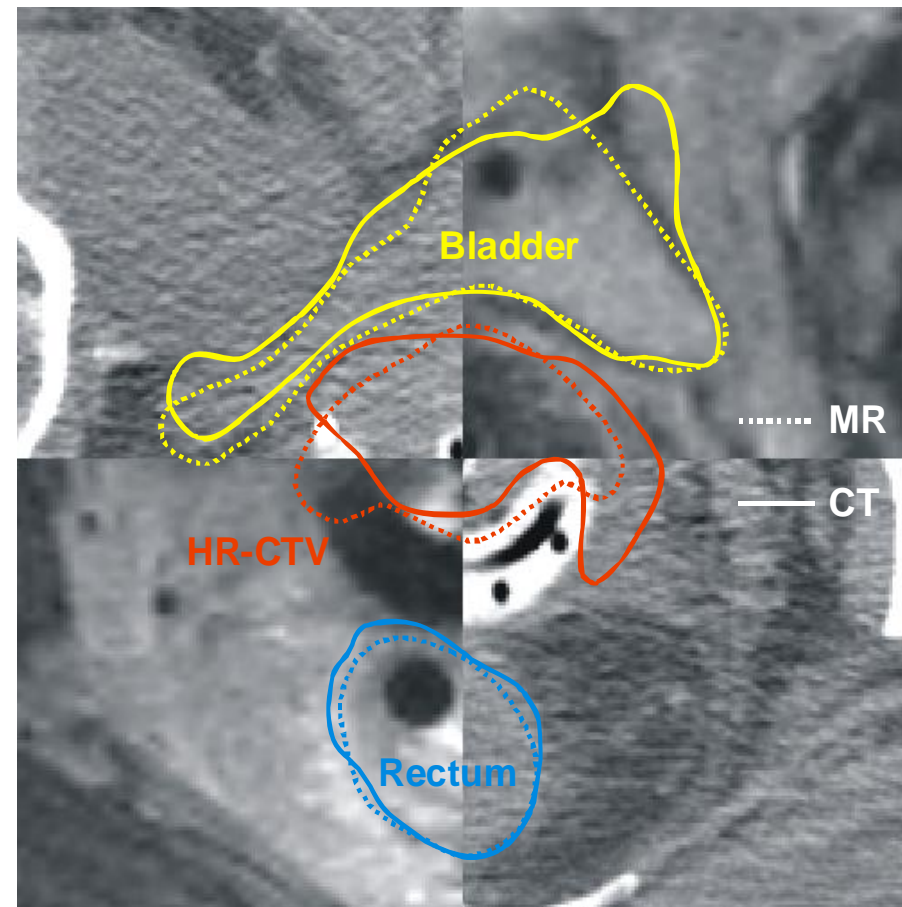


- OAR contrast for CT: rectum, sigmoid, bladder
- Primary
 - Tumor mass (HR-CTV):
 - Pre-implant imaging
 - Caution: applicator distortion
 - Exam, fiducials
 - Entire cervix
 - Secondary:
 - Vagina or uterus

Rectum Bladder

CT versus MR contouring

- CT larger than MR
- CT with contrast clear OAR delineation
- CT interface bowel/cervix difficult
- MR visualize GTV
 - Still treat entire uterus

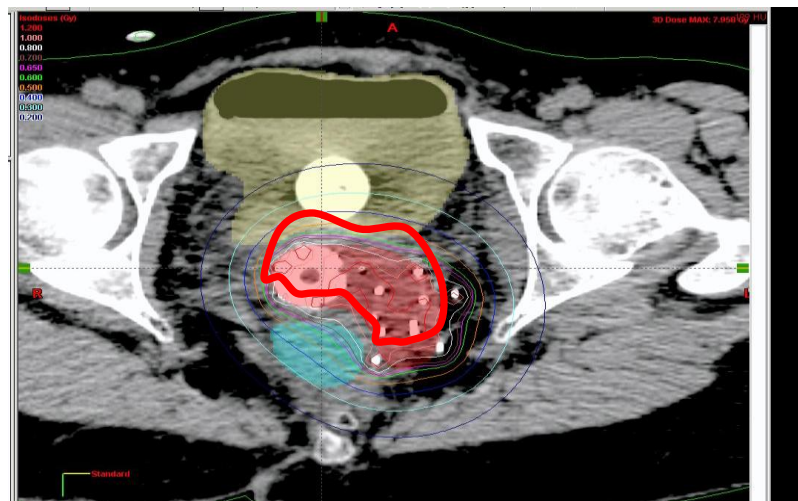


Int J Radiat Oncol Biol Phys 2007 Jun 1;68(2):491-8

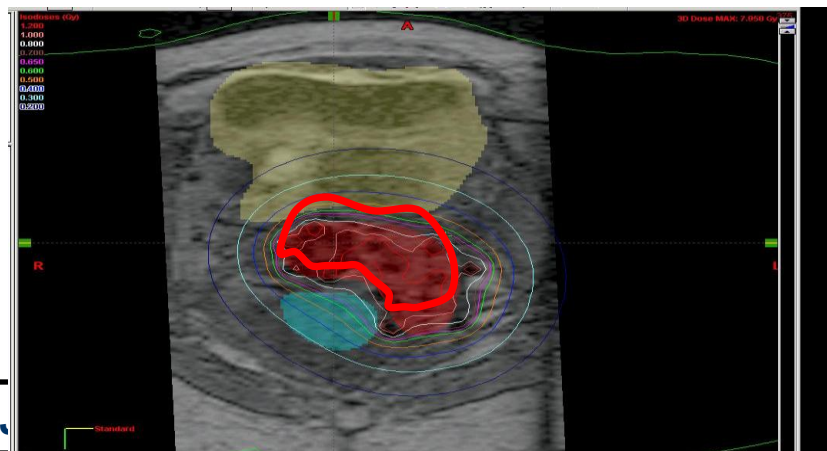
Treatment planning parameters

- CTV - Contour entire visible mass (70-80Gy)
- IR-CTV: entire vagina (60Gy)
- D90
- V100, V150, V200
- OAR: D0.1cc, D2cc
 - Rectum, Sigmoid <70Gy;
 - Bladder < 90 Gy

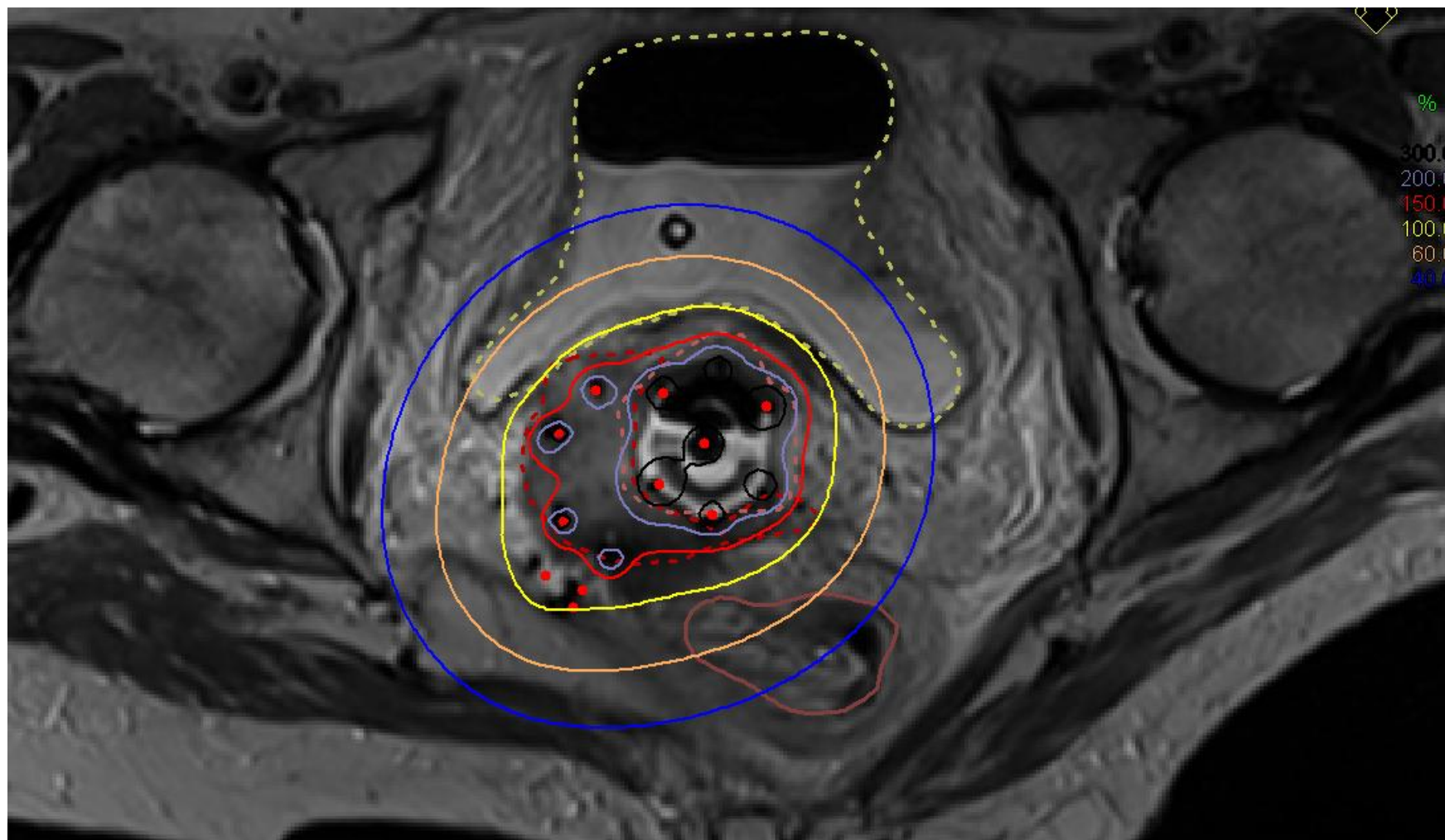
CT



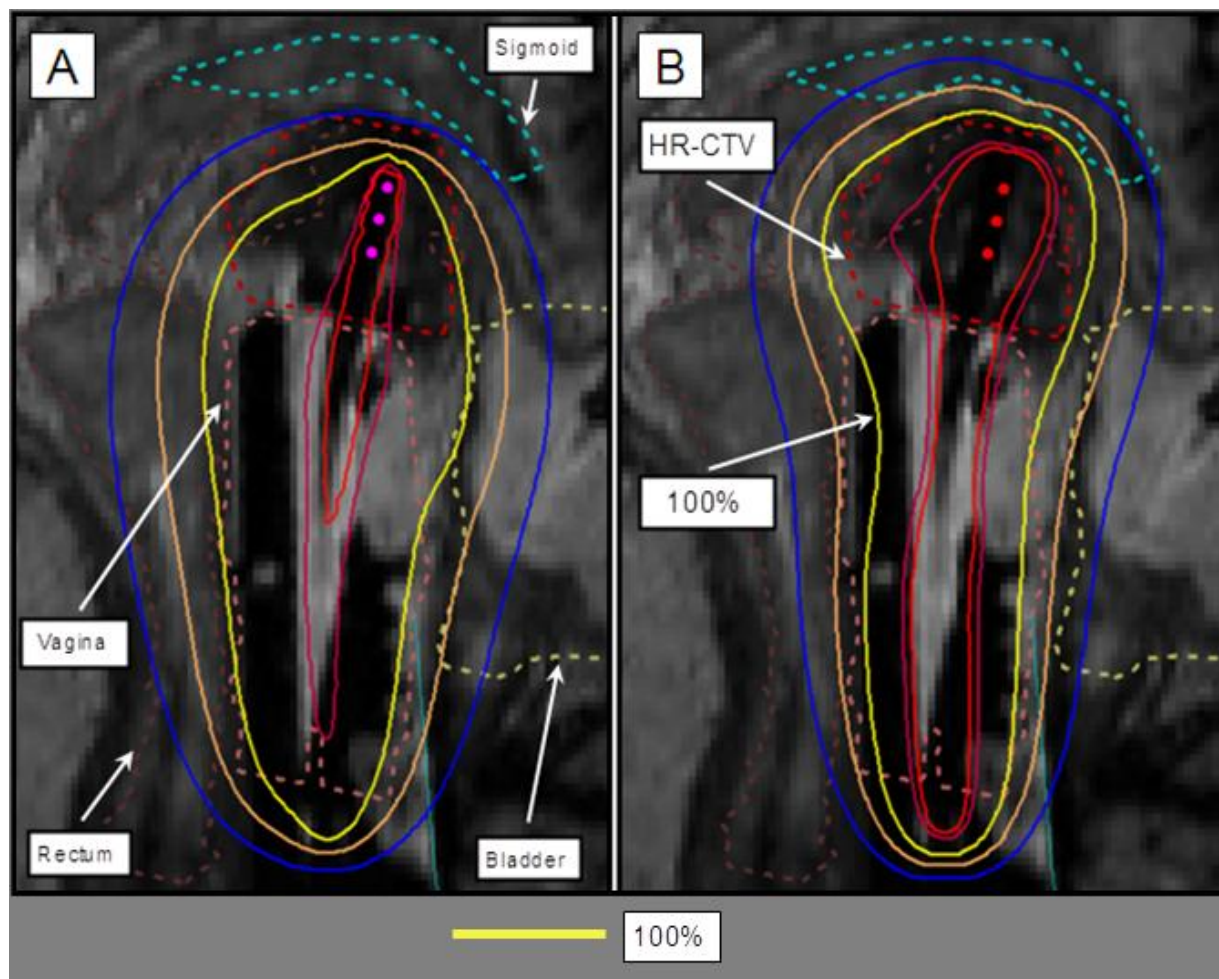
MRI



Evaluate isodose distributions

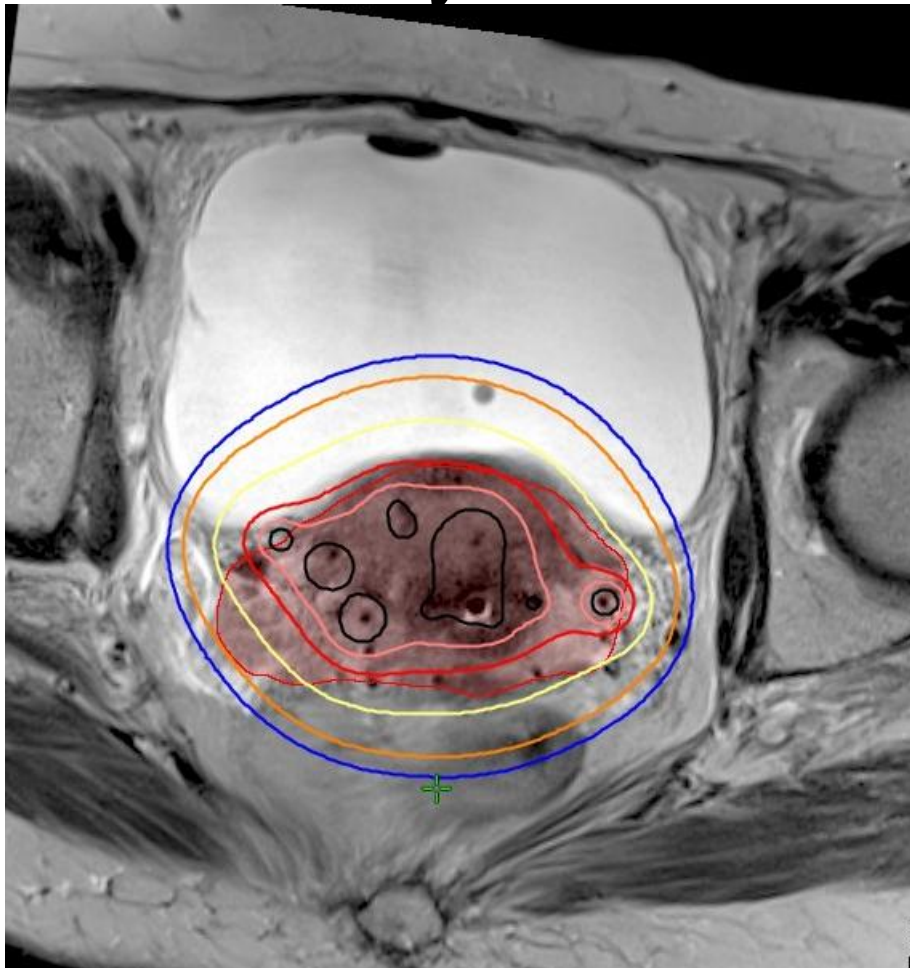


Optimization

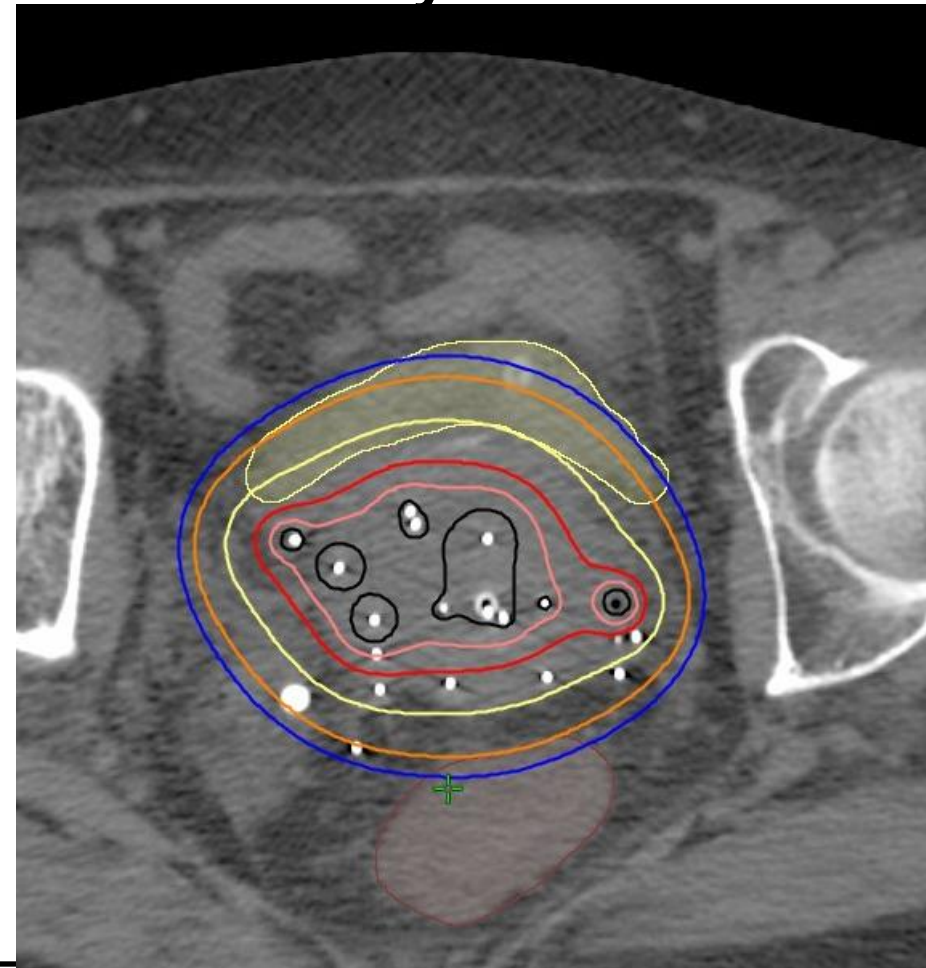


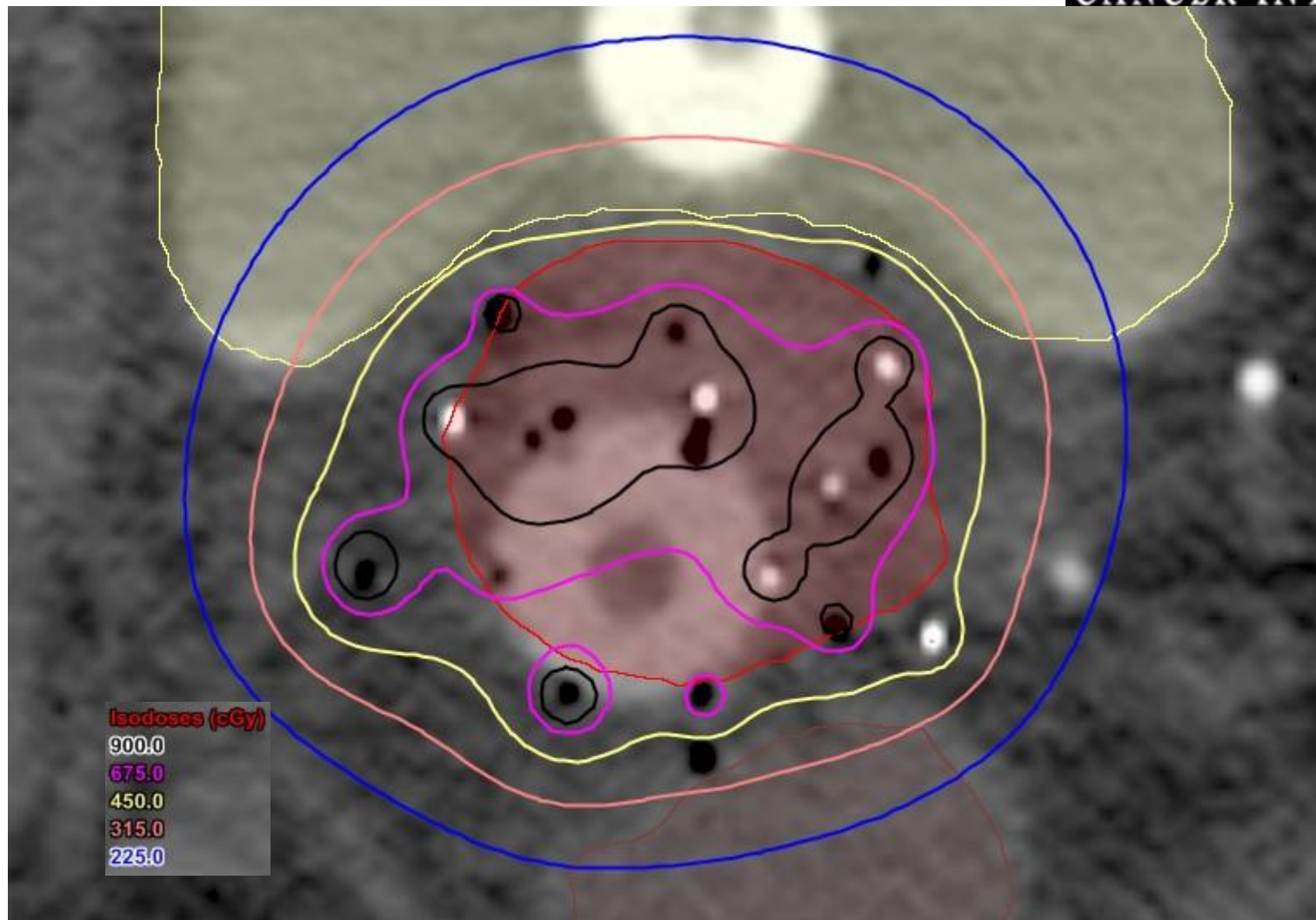
MR versus CT

MR: Identify tumor



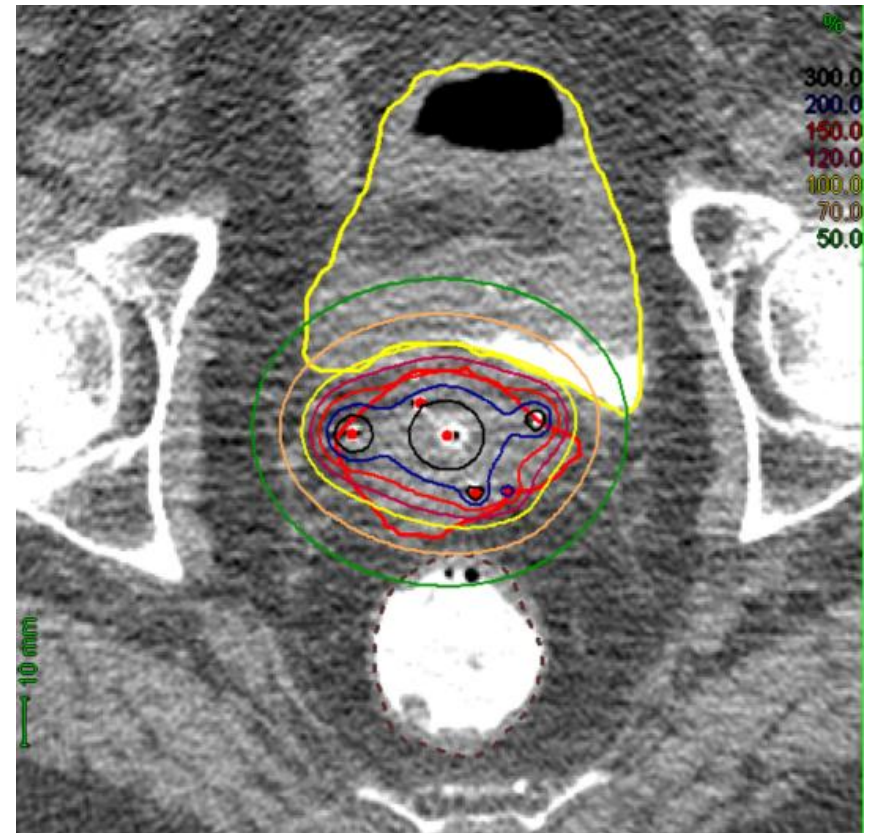
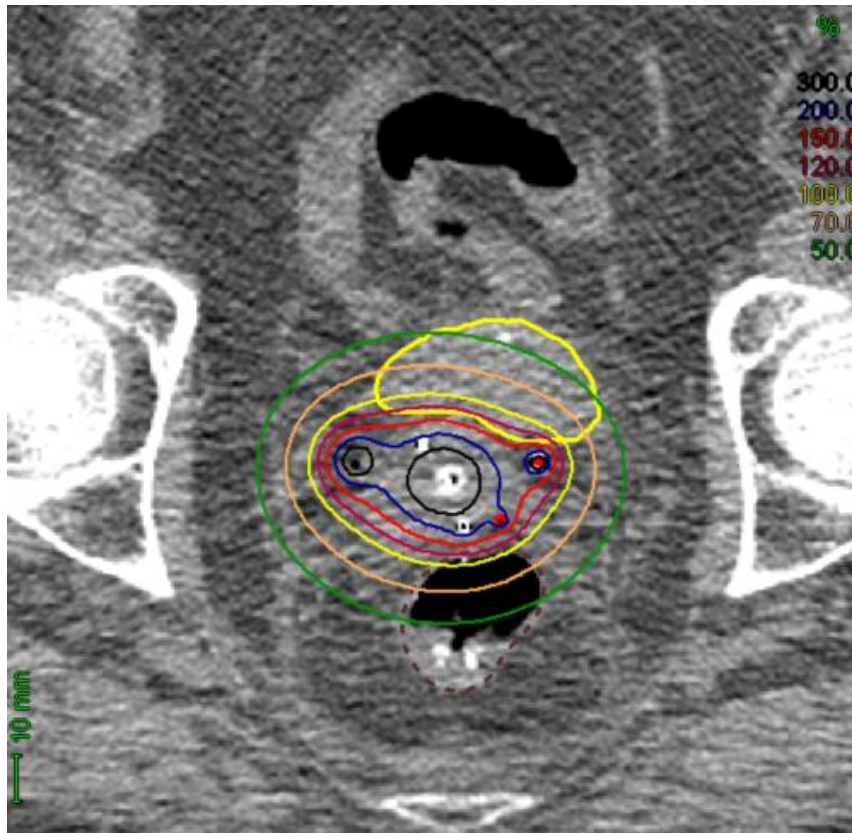
CT: identify catheters



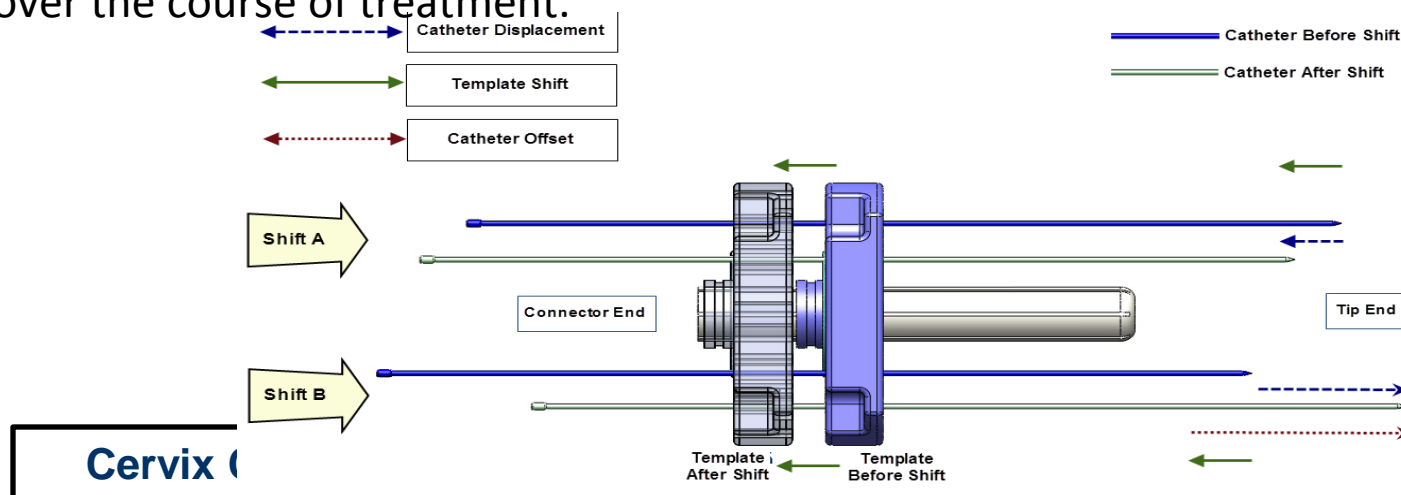


Central hot spots may be a desired feature

Normal Tissue Variation



- 198 catheters analyzed
 - 43% caudal (5.0 ± 2.0 mm), 22% cranial (7.9 ± 4.0 mm), 14% anterior (6.3 ± 2.1 mm), 48% posterior (8.7 ± 3.1 mm), 7% left (4.8 ± 0.4 mm), 9% right (5.4 ± 0.9 mm).
 - Catheter offsets were: 3% caudal (7.2 ± 6.3 mm), and 11% cranial (6.1 ± 2.6 mm).
 - Template shifts were: 43% caudal (5.2 ± 1.6 mm) and 14% cranial (6.6 ± 4.0 mm).
 - Deformations were: 10 shrinkages (4.7 ± 0.9 mm), and 32 expansions (4.7 ± 0.5 mm).
 - Dosimetric changes were: $5.2 \pm 10.8\%$ for rectum D_{2cc} , $-1.1 \pm 18.5\%$ for bladder D_{2cc} , and $-5.1 \pm 6.7\%$ for tumor D_{90} .
- On average, less than 1 cm displacements and deformations of the implant occurred over the course of treatment.



HDR Fractionation

www.americanbrachytherapy.org/guidelines

| | | Dose of EBRT | HDR dose to CTV (Gy) | EQD2 to CTV | D2 cc per fx to rectum to limit EQD2 to ≤ 70 Gy |
|-------------------------|------------------|----------------------------|-------------------------|----------------|---|
| D90 | >90% | 36 Gy/18 fx ^a | 5 × 6 | 72.9 | ≤ 4.1 |
| | | | 5.5 × 6 | 78.0 | ≤ 4.1 |
| V100 | >90% | 39.6 Gy/22 fx ^a | 5 × 6 | 76.4 | ≤ 3.8 |
| | | | 5.5 × 6 | 81.5 | ≤ 3.8 |
| D2cc bladder | <90 Gy | 45 Gy/25 fx | 3 × 9 | 73.6 | ≤ 2.55 |
| | | | 3 × 10 | 76.8 | ≤ 2.38 |
| | | | 4.5 × 5 | 71.5 | ≤ 3.75 |
| | | | 5 × 5 | 75.5 | ≤ 3.75 |
| D2cc rectum | 70-75 Gy | | 5.5 × 5 | 79.8 | ≤ 3.75 |
| | | | 7 × 3 | 74.1 | ≤ 5.2 |
| | | | | | |
| D2cc sigmoid | 70-75 Gy | 50.4 Gy/28 fx | 4.0 × 5 | 72.9 | ≤ 3.25 |
| | | | 4.5 × 5 | 76.8 | ≤ 3.25 |
| | | | 5 × 5 | 80.9 | ≤ 3.25 |
| | | | 7 × 3 | 79.4 | ≤ 4.55 |

Brachytherapy, Jan 2012

http://www.americanbrachytherapy.org/guidelines/gyn_HDR_BT_docu_sheets.xls

| | Fx 1 | Fx 2 | Fx 3 | Fx 4 | Fx 5 |
|--|--------------|--------------|--------------|--------------|--------------|
| Date | 7/18/2012 | 7/19/2012 | 7/19/2012 | 7/20/2012 | 7/20/2012 |
| type of procedure | interstitial | interstitial | interstitial | interstitial | interstitial |
| Insertion Number | 1 | 2 | 3 | 4 | 5 |
| Dose Rate | HDR | HDR | HDR | HDR | HDR |
| Prescribed this fraction (Gy) | 5.5 | 5.5 | 5.5 | 5.5 | 5.5 |
| Prescribed BED ₁₀ [$\alpha/\beta=10$ Gy] | 0.0 | 0.0 | 0.0 | 0.0 | 0.0 |
| Interstitial? | yes | yes | yes | yes | yes |
| # needles inserted | 13 | 13 | 13 | 13 | 13 |
| #needles loaded | 10 | 10 | 10 | 10 | 10 |
| Prescription isodose line (Gy) | 5.5 | 5.5 | 5.5 | 5.5 | 5.5 |
| Total time this fraction (min) | 5.72 | 5.74 | 5.75 | 5.81 | 5.85 |
| total interstitial dose this fraction (Gy) | 5.5 | 11 | 16.5 | 22 | 27.5 |
| BLADDER | | | | | |
| D0.1cc | 5.2637 | 5.2637 | 5.2637 | 5.2637 | 5.2637 |
| D0.1cc BED ₃ [$\alpha/\beta=3$ Gy] | 14.5 | 14.5 | 14.5 | 14.5 | 14.5 |
| D2cc | 4.0849 | 4.0849 | 4.0849 | 4.0849 | 4.0849 |
| D2cc BED ₃ [$\alpha/\beta=3$ Gy] | 9.6 | 9.6 | 9.6 | 9.6 | 9.6 |
| D5cc | 3.4513 | 3.4513 | 3.4513 | 3.4513 | 3.4513 |
| RECTUM | | | | | |
| D0.1cc | 7.6716 | 7.6716 | 7.6716 | 7.6716 | 7.6716 |
| D0.1cc BED ₃ [$\alpha/\beta=3$ Gy] | 27.3 | 27.3 | 27.3 | 27.3 | 27.3 |
| D2cc | 4.2267 | 4.2267 | 4.2267 | 4.2267 | 4.2267 |
| D2cc BED ₃ [$\alpha/\beta=3$ Gy] | 10.2 | 10.2 | 10.2 | 10.2 | 10.2 |
| D5cc | 3.4879 | 3.4879 | 3.4879 | 3.4879 | 3.4879 |
| SIGMOID | | | | | |
| D0.1cc | 2.7803 | 2.7803 | 2.7803 | 2.7803 | 2.7803 |
| D0.1cc BED ₃ [$\alpha/\beta=3$ Gy] | 5.4 | 5.4 | 5.4 | 5.4 | 5.4 |
| D2cc | 1.7611 | 1.7611 | 1.7611 | 1.7611 | 1.7611 |
| D2cc BED ₃ [$\alpha/\beta=3$ Gy] | 2.8 | 2.8 | 2.8 | 2.8 | 2.8 |
| D5cc | 1.3919 | 1.3919 | 1.3919 | 1.3919 | 1.3919 |
| CTV | | | | | |
| V100 (cm ³) | 19.12 | 19.12 | 19.12 | 19.12 | 19.12 |
| D100 (Gy) | 1.8663 | 1.8663 | 1.8663 | 1.8663 | 1.8663 |
| V150 | 12 | 12 | 12 | 12 | 12 |
| V200 | 6.23 | 6.23 | 6.23 | 6.23 | 6.23 |
| D90 (Gy) | 3.2252 | 3.2252 | 3.2252 | 3.2252 | 3.2252 |
| D 90 BED ₁₀ [$\alpha/\beta=10$ Gy] | 4.3 | 4.3 | 4.3 | 4.3 | 4.3 |
| OTHER BOWEL | | | | | |

ABS IC vs IS Cervix Recommendations

Intracavitary vs Interstitial

Table 1

Examples of regimens frequently used in the United States for tandem and ovoid or t

| EBRT, dose to ICRU 52 point or median dose in case of IMRT | Fractionation to point A (Gy) | EQD2 (Gy) to the tumor (point A dose with $\alpha/\beta = 10 \text{ Gy}$) ^a |
|--|----------------------------------|---|
| 25 × 1.8 Gy | 4 × 7 Gy | 83.9 |
| 25 × 1.8 Gy | 5 × 6 Gy | 84.3 |
| 25 × 1.8 Gy | 6 × 5 Gy | 81.8 |
| 25 × 1.8 Gy | 5 × 5.5 Gy | 79.8 |

Table 3

Examples of potential dose fractionation regimens to consider for
template-based HDR interstitial brachytherapy after 45–50.4 Gy of
external beam

| Dose of EBRT | Brachytherapy dose ^a | EQD2 (Gy) to CTV |
|----------------------|---------------------------------|------------------|
| 45 Gy/25 fractions | 3.5 Gy × 9 | 79.7 |
| | 4.25 Gy × 7 | 79.6 |
| 50.4 Gy/28 fractions | 5 Gy × 5 | 75.5 |
| | 3 Gy × 9 | 78.8 |
| | 4.5 Gy × 5 | 76.7 |

Gynecologic Cancer InterGroup Cervix Cancer Research Network



| Publication | Total # of pts | Case Mix | Mean EQD2 Total Dose (EBRT+BT) | Median F/U (months) | Local Control |
|------------------------------------|----------------------|----------------------------------|------------------------------------|-------------------------------|--|
| Pinn-Bingham M <i>et al</i> , 2012 | 116 | Primary (100%) | 87 | 36 | 85% |
| Lee L <i>et al</i> , 2012 | 68 | Primary (50%) Recurrent (50%) | 75 | 17 | 2y - 86% |
| Kannan N <i>et al</i> , 2012 | 47 | Primary (100%) | 71 | 15 | 2y – 61% |
| Thibault I <i>et al</i> , 2012 | 43 | Primary (79%) Recurrent (21%) | 80 | 19 | 2y - 87% (primary) 2y – 45% (recurrent) |
| De Ieso P <i>et al</i> , 2012 | 37 | Primary (40%) Recurrent (60%) | 71 (definitive) 48 (palliative) | 27 (mean) | 2y – 74% 5y – 63% |
| Beriwal S <i>et al</i> , 2012 | 30 | Primary (57%) Recurrent (43%) | 74 | 17 | 2y – 79% |
| Fokdal L <i>et al</i> , 2011 | 28 | Recurrent (68%) Vaginal (32%) | 82 | 18 | 2 y - 92% |
| Yoshida K <i>et al</i> , 2010 | 18 | Primary (100%) | 70 | 18 | 83% |
| Diwanji A <i>et al</i> , 2010 | 18 | Primary (100%) | 70 | 18 | 83% |

Quality of Life

- Inpatient stay
- Bedrest
- Isolation for LDR
- After care
- Elderly

Collaboration with nursing



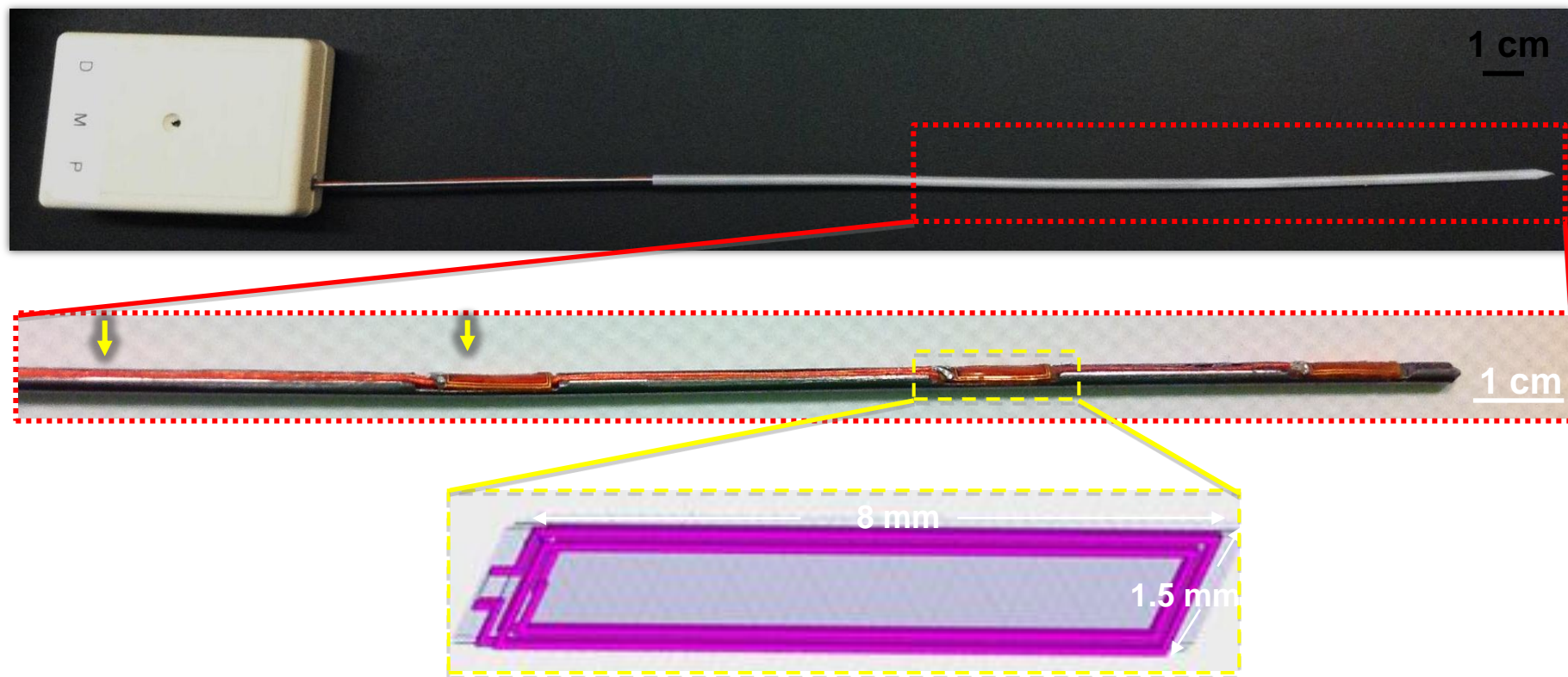
Follow-up

- On protocol, MRI at 3 and 6 months
- Off protocol, PET at 3 months
- Pap smear every 3 months for 2 years then 6 months for 3 years then every year



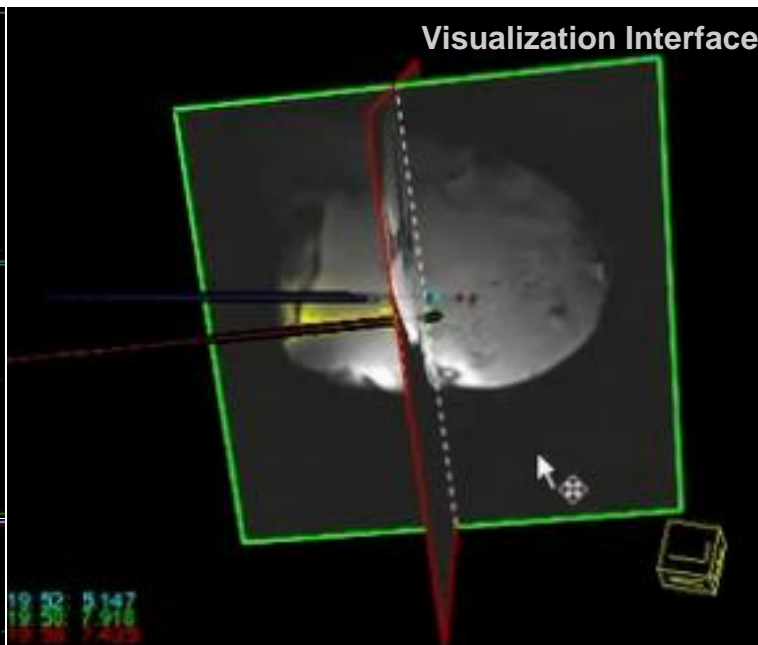
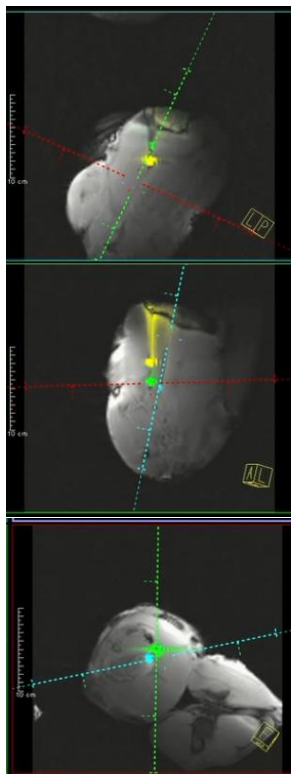
Novel developments

Active MR Tracker



Real-Time Active-Tracking of Metallic Needles during MR-Guided Radiation Therapy

Gynecologic Cancer InterGroup
Cervix Cancer Research Network



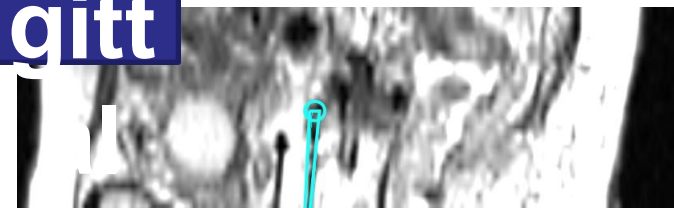
Simultaneous navigation of two needles in animal tissue

- ✓ **Speed** 40 updates/second
- ✓ **Resolution** 0.6 mm × 0.6 mm × 0.6 mm

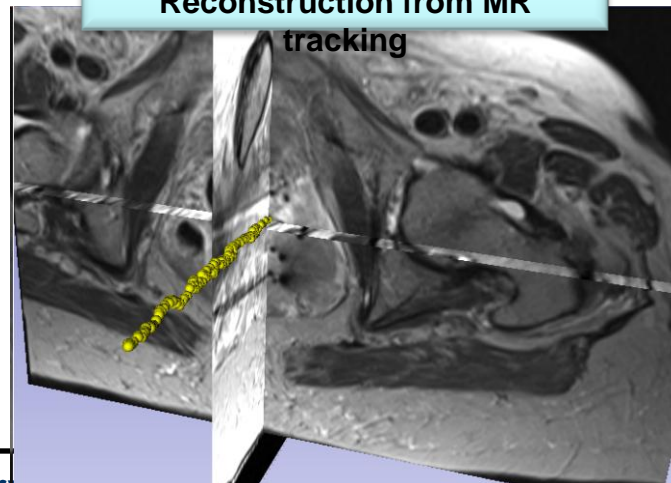
Cervix Cancer Education Symposium, January 2016, Bangkok, Thailand

First

Real-time MR-
Tracking in
a Human



Needle Trajectory
Reconstruction from MR
tracking



Imaging Protocol



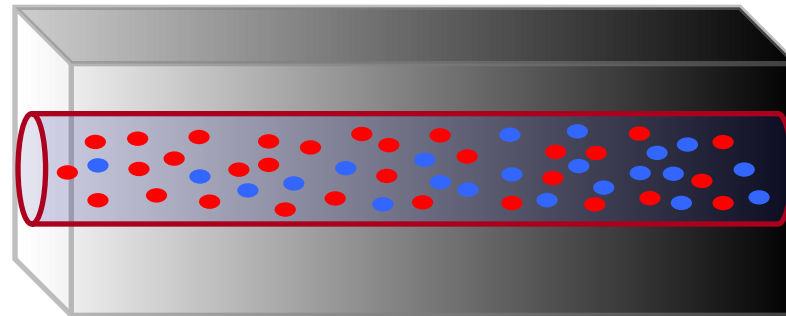
- 3 Tesla in AMIGO at BWH
- T₂-weighted turbo-spin-echo (TSE)
- Diffusion-weighted
- Pre and post-contrast enhanced T1-weighted
- Multi-echo gradient-echo for T₂* mapping (TE= 3, 9, 18, 27, 36, 45ms) over multiple O₂ levels

BOLD & T_2^* Mapping

Endogenous deoxyhemoglobin (Hb)

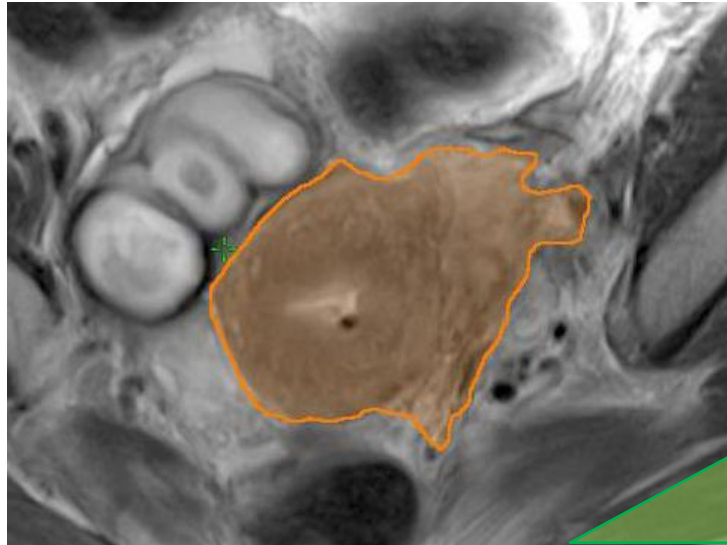
- $\downarrow T_2^*$
- \downarrow MR signal

● HbO_2
● Hb (paramagnetic)

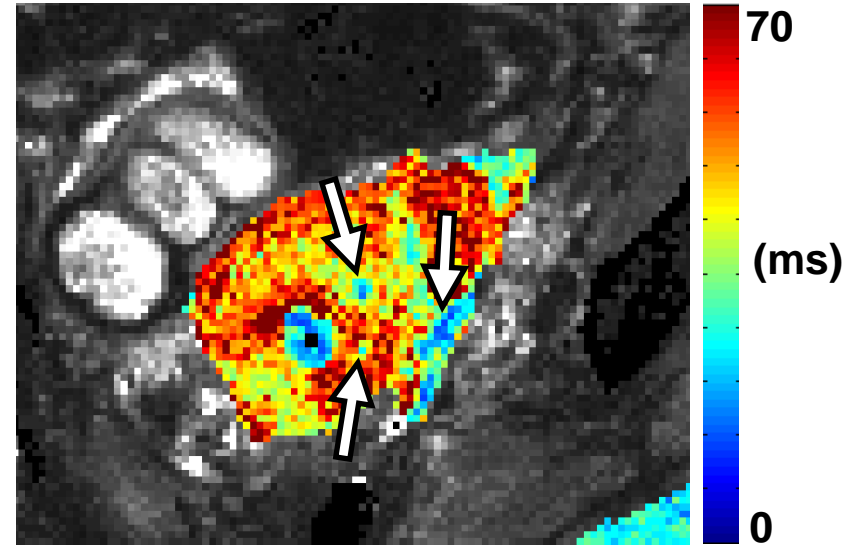


- Single T_2^* -weighted measurement \Rightarrow BOLD
- Multiple measurements & exponential fit $\Rightarrow T_2^*$ map

T₂* Mapping



**Residual tumor &
muscle contours on
T₂-TSE**



**T₂* map with color
overlay within tumor and
muscle contours**

Ciris PA, Damato AL, Schmidt EJ, Viswanathan AN.
Preliminary Study of Oxygenation Assessment in
Residual Cervical Cancer after External Beam
Radiation using Blood Oxygenation Level Dependent
(BOLD) MRI. American Brachytherapy Society, Gyn

Plans, Trials and the Future

**Resources: Ultrasound for planning
HPV stratification/Dose escalate lg residual
High Tech: MR Radiomics
EM-Tracking for identification of catheters
Robotic insertion**

An aerial photograph of a vast, arid landscape. The terrain is characterized by a complex network of deep, winding cracks and ridges, creating a textured, almost cellular appearance. The colors range from light tan and beige to deep, dark brown and black, suggesting different mineral compositions or perhaps the presence of dried mud and salt. The overall effect is one of extreme dryness and geological complexity. In the lower right quadrant, the words "Thank You" are superimposed in a bold, black, sans-serif font, set against a semi-transparent yellow rectangular background.

Thank You