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Cervix Cancer Research Network


# Brachytherapy -- from the Basics to GEC-ESTRO

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Professor and Chairman
Loyola University Chicago

Cervix Cancer Education Symposium, February 2018

# OBJECTIVES

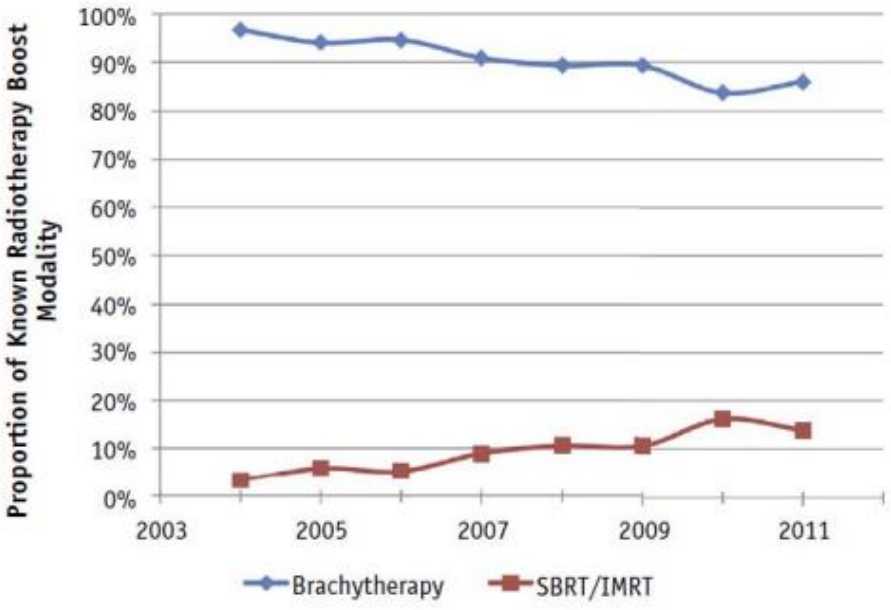
1. Review the history of Brachytherapy in Cervical Cancer.
2. Review current State of The Art Treatments.

# Is Brachytherapy Necessary?

1. **Fletcher et al, J Radiol Electrol, 1975** Tumor Control probability correlated with RT dose and cervix ca volume

2. **Montana et al Cancer, 1986** Local control with external beam alone 40%

3. **Lanciano JROBP, 1991-** External beam alone 4 year LC 45% and 4 year survival 19% compared to 67% and 46%



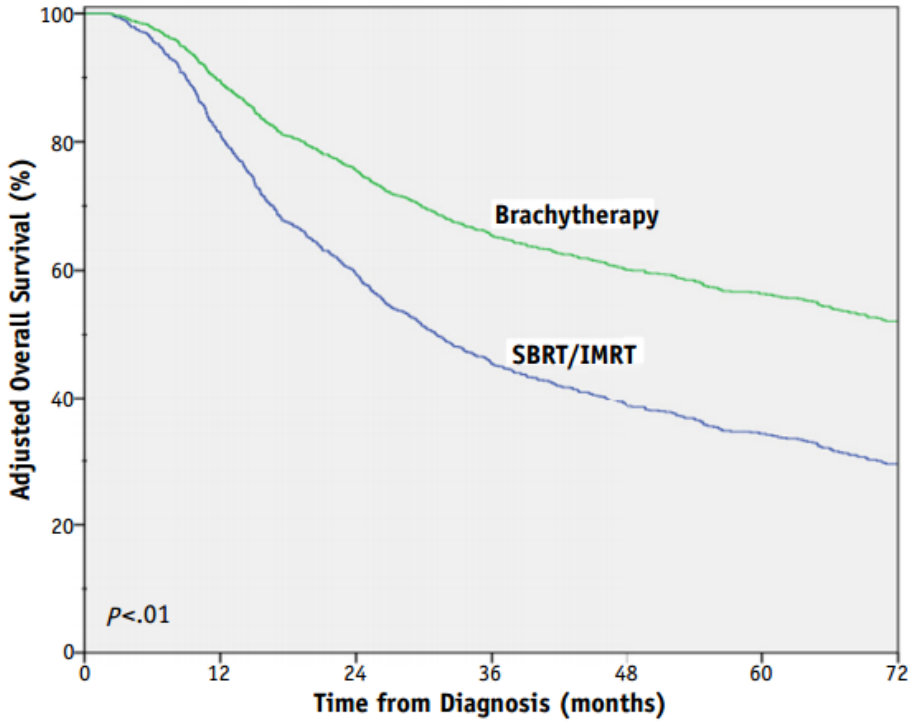




**Fig. 3.** Adjusted overall survival estimate, stratified by boost modality and corrected for significant variables on multivariable Cox proportional hazard model analysis (age, Charlson/Deyo score, stage, and chemotherapy utilization). IMRT = intensity modulated radiation therapy; SBRT = stereotactic body radiation therapy.

Gill, et al. IJROBP 2014 Dec 1;90(5):1083-90

# *Marie and Pierre Curie*
# *Antoine Henri Becquerel*

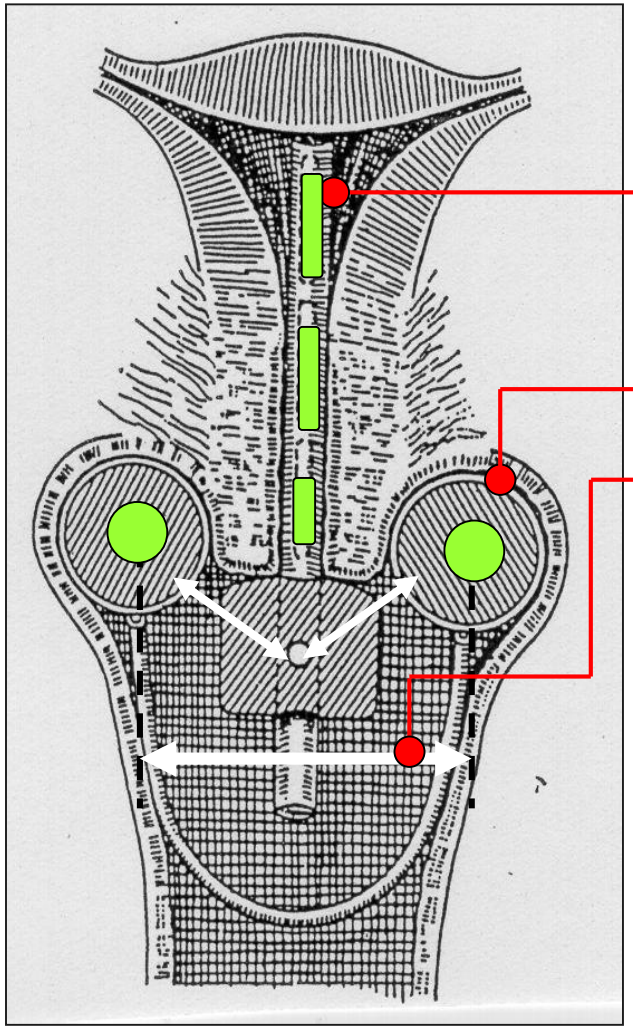
*The discovery of radioactivity, 1896 - 1898*

## Applicators for intracavitary treatments

**Manchester / Fletcher: Tandem & Ovoids**
**Stockholm: Tandem & Ring**
**Institute Gustave Roussy: Mould technique**

# Historical Paris Technique

## 1910-1920: Curie Institute, Paris, France



*GEC ESTRO Handbook of Brachytherapy*

**Applicator:**

- Rubber tandem
- Cork colpostats (paraffin coated)

→ not connected

- Distance – colpostats: not fixed

→ no fixed geometry

**$^{226}$Ra preloading**

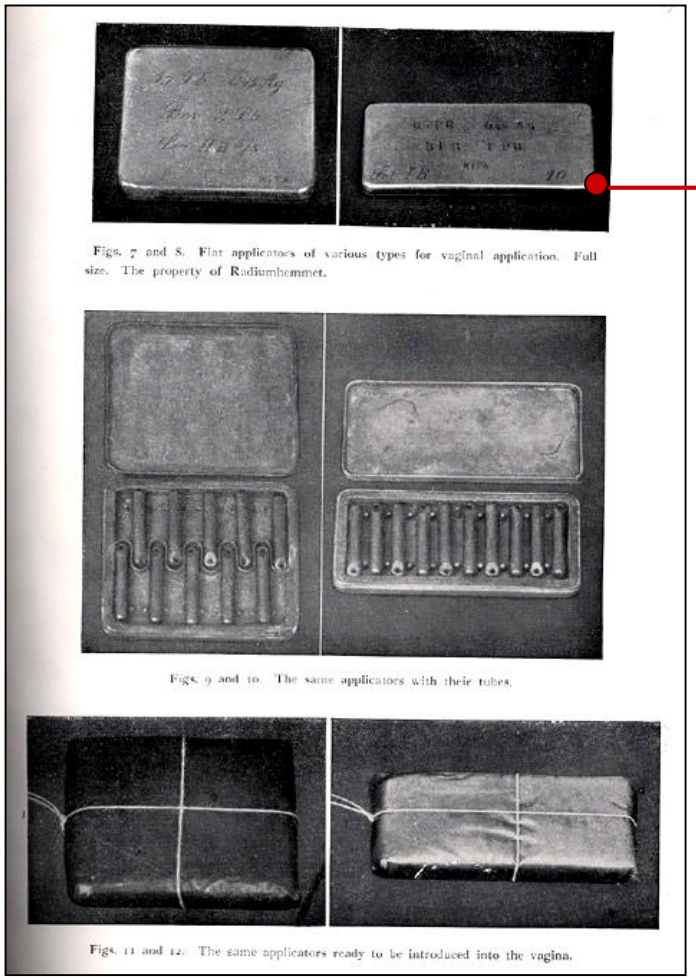
- X mg of $^{226}$Ra for Y hours

**Typical application**

- ≈ 5 days (*120 h*)
- 7000-8000 mgh

# Classical Stockholm method

## 1913-1914: Radiumhemmet, Stockholm, Sweden

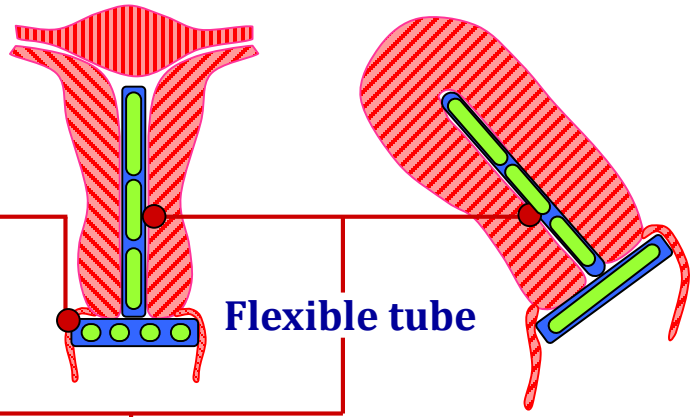


Figs. 7 and 8. Flat applicators of various types for vaginal application. Full size. The property of Radiumhemmet.

Figs. 9 and 10. The same applicators with their tubes.

Figs. 11 and 12. The same applicators ready to be introduced into the vagina.

**Applicator:**



- Flat box (plate)
- Flexible tube
- not connected → No fixed geometry

**$^{226}$Ra preloading**

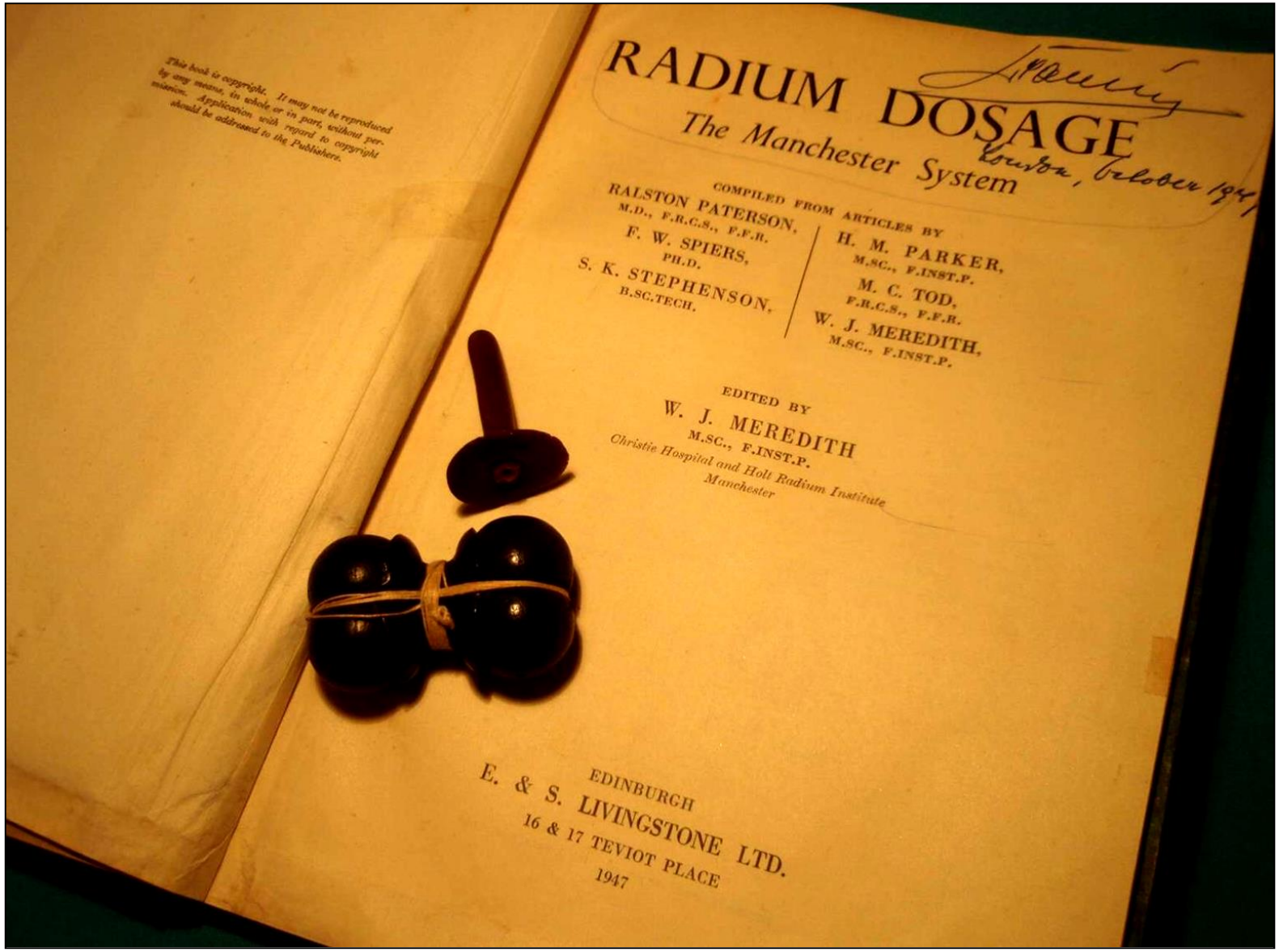
- Intrauterine tube: 30-90 mg
- Vaginal plate: 60-80 mg
- Unequal loading of uterine / vaginal $^{226}$Ra

**Typical treatment**

- 2 – 3 applications (á 20-30 h)
- ≈ 7000 mgh

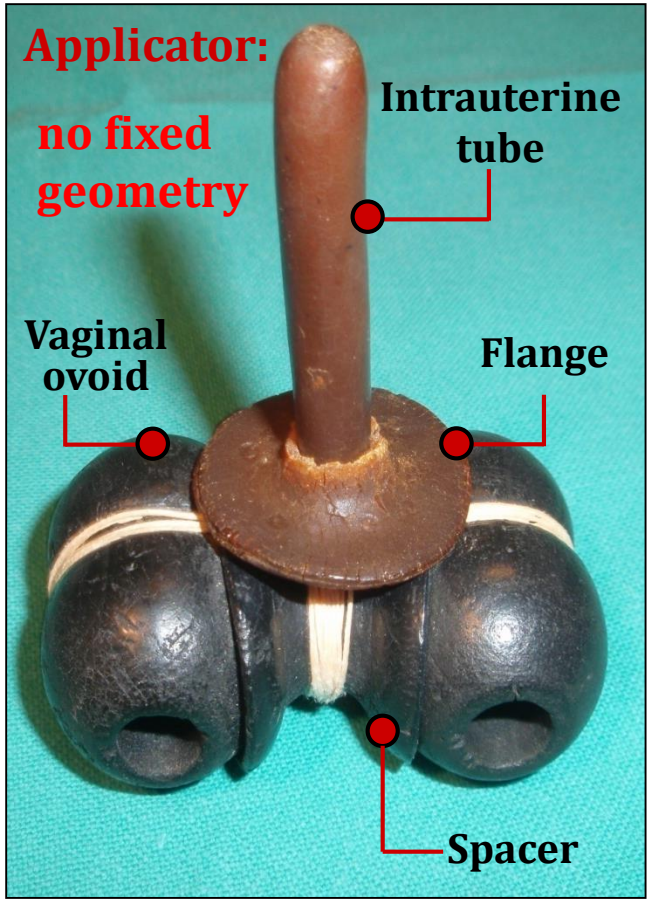
# Historical Manchester System

## 1938: Holt Radium Institute, Manchester, England



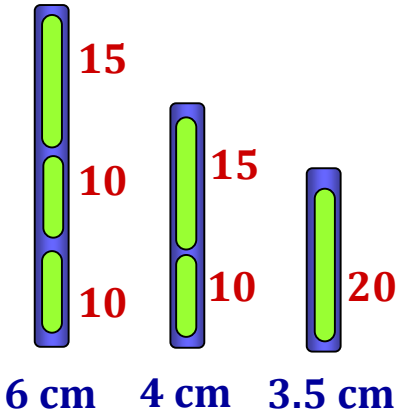
# Historical Manchester System

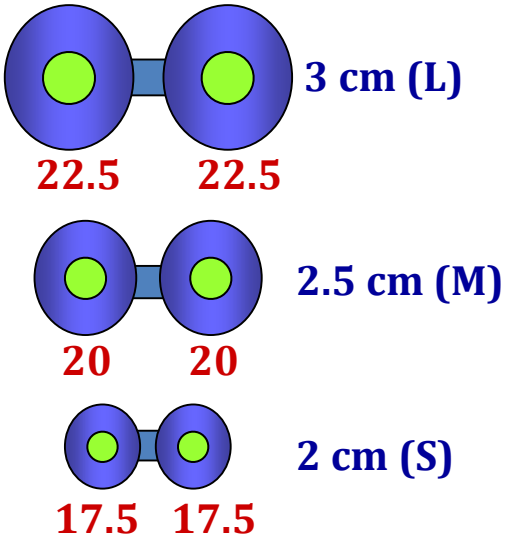
**Related to historical Paris technique**

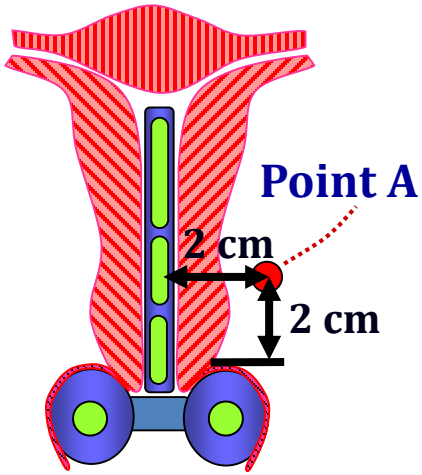



**TYPICAL TREATMENT:**
**140 hours for 7500 R at point A**
**(dose rate 53 R/h)**

**$^{226}$Ra preloading (mg):**




Given tumour volume

↓

A set of rules

- Geometry
- mg of $^{226}$Ra
- Duration

↓

Certain point A dose

*Meredith WJ, ed.. Radium dosage. The Manchester system. Edinburgh;1947.*

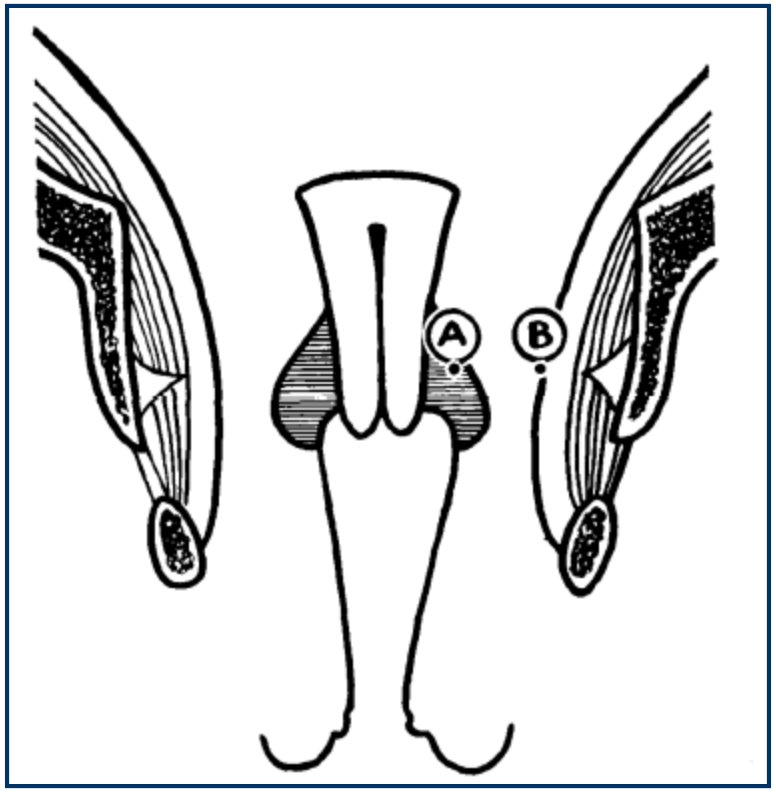
*Detailed studies of the nature and course of RT necrosis*

- **1938 hypothesis:** Necrosis secondary to damage to paracervical vessels (not direct effect on rectum/bladder)
- Definition of a “paracervical triangle”
- Definition of **Point A** as a “point of limiting tolerance”

**Point B**

*Anatomical studies of regional spread patterns:*

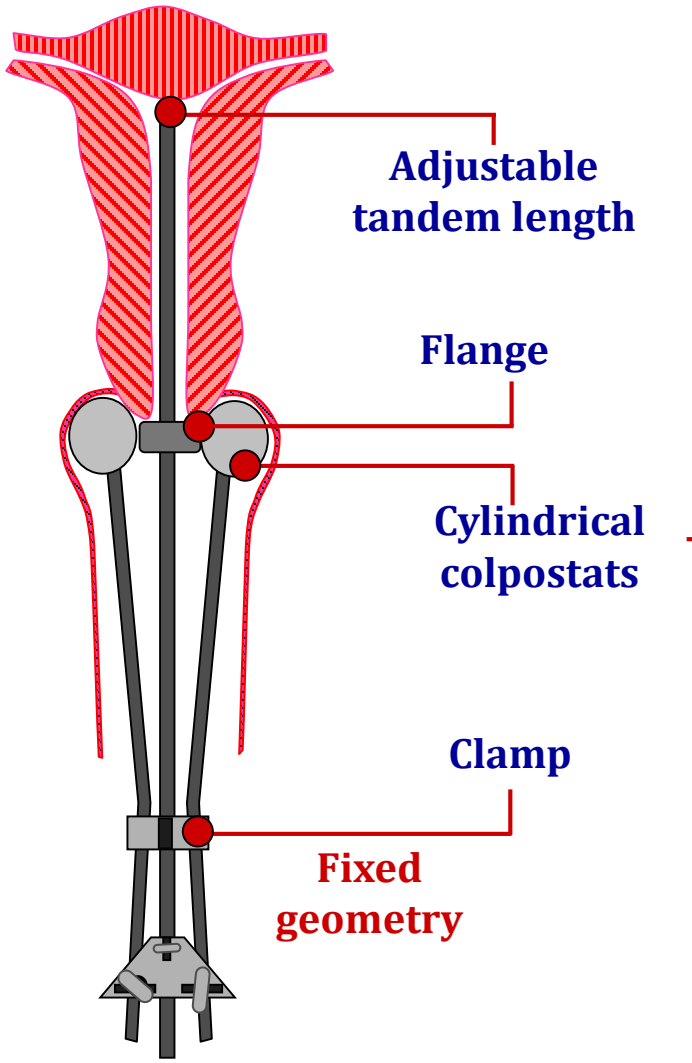
- Broad ligament lymphatics
- Obturator nodes

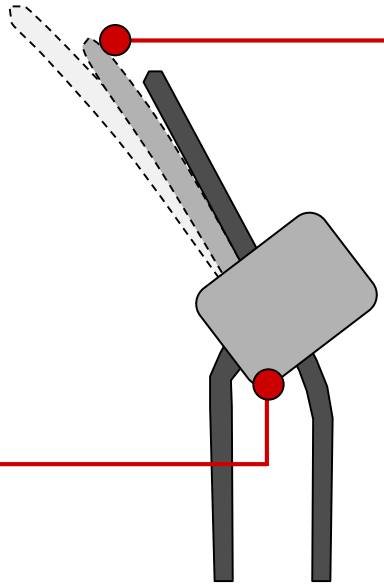


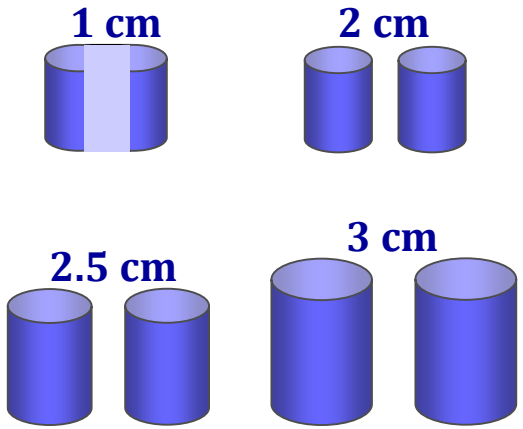

**Tod and Meredith BJR 11:809, 1938**

# Fletcher–Suit–Delclos–Horiot Technique

## 1950's: Fletcher



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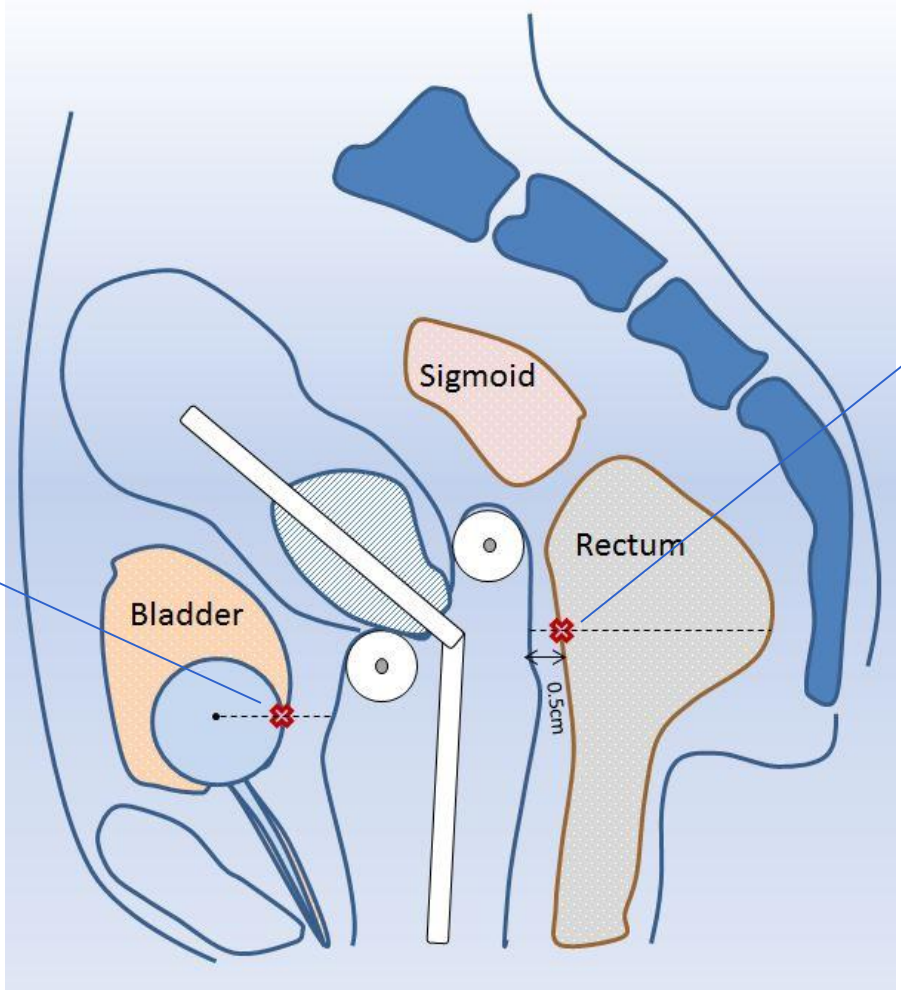
5 mm behind the post surface of the Foley balloon on a lat x-ray filled with 7 cc radiopaque fluid and pulled down against the urethra




5 mm behind the post vaginal wall between the ovoids at the inf point of the last intrauterine tandem source or mid vaginal source

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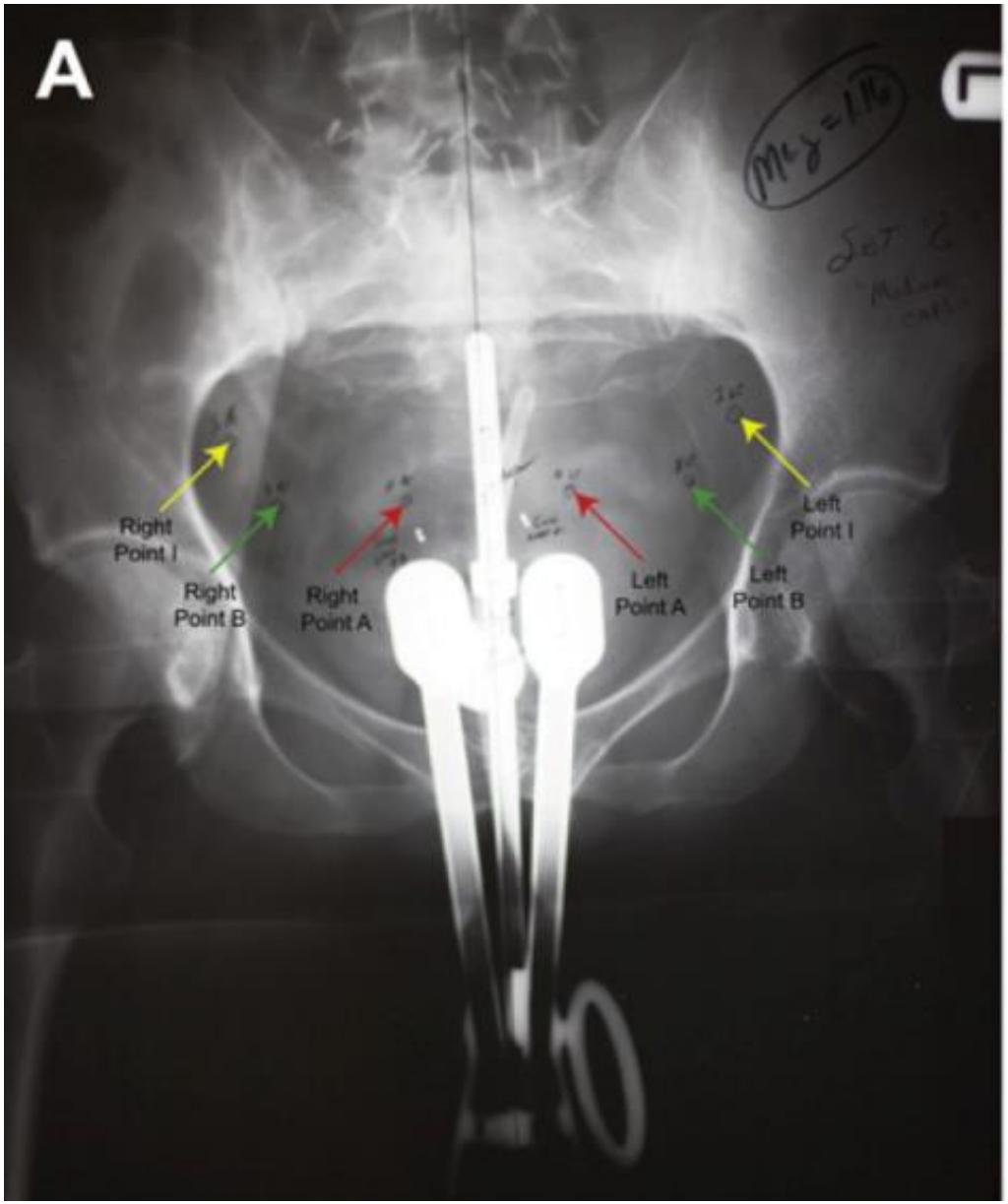
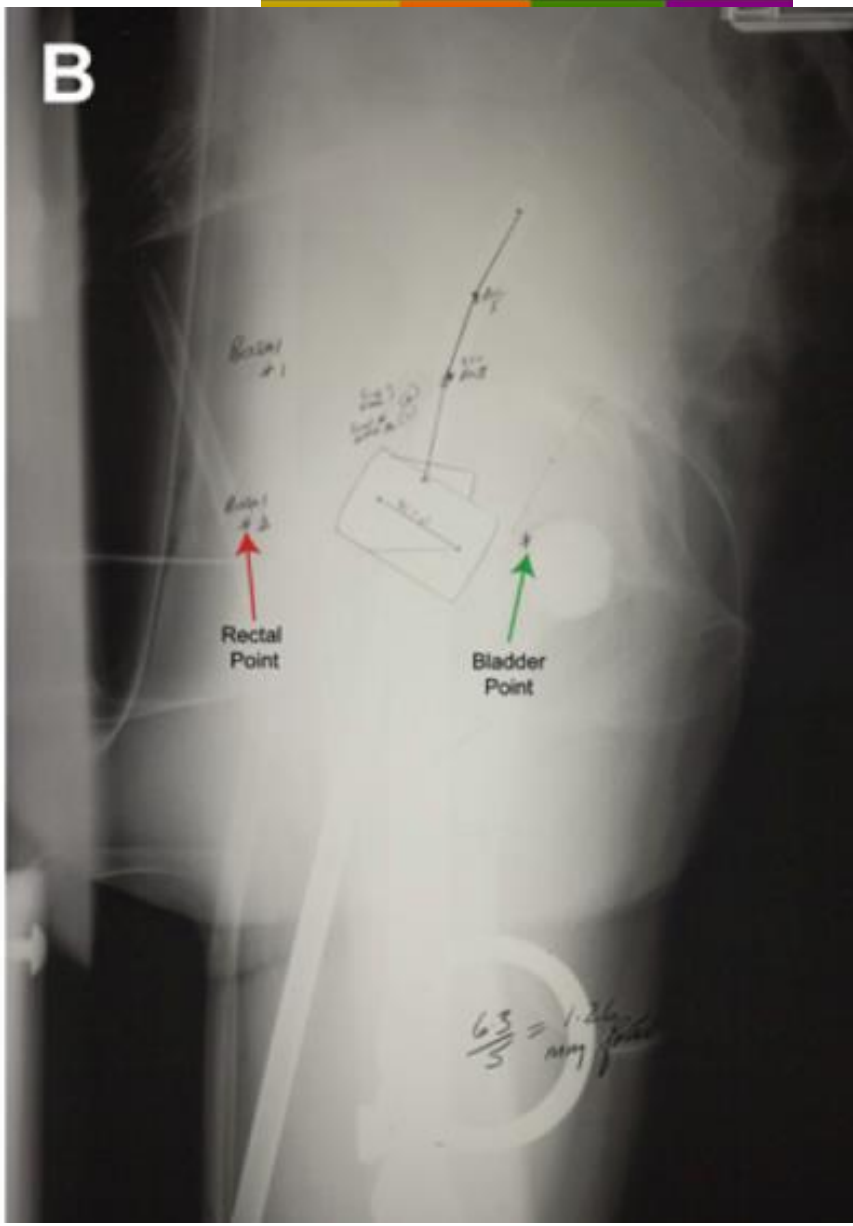
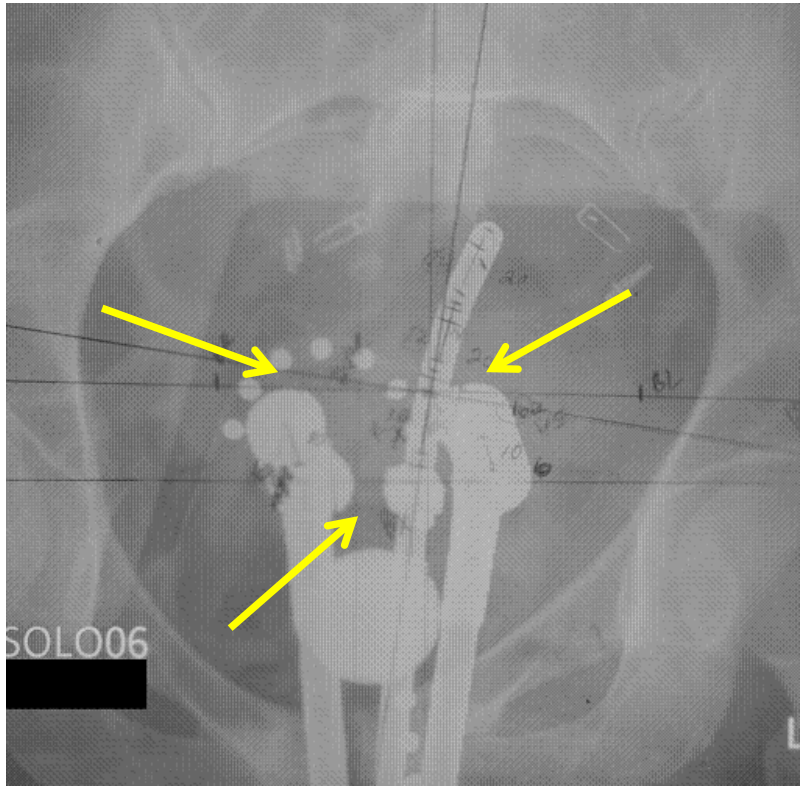


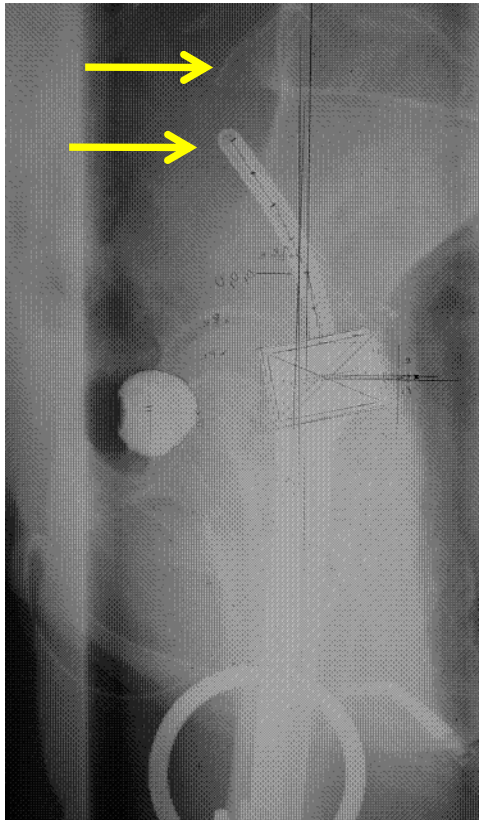
# RTOG O116/0128 Brachy Quality

- Asymmetry of ovoids
- Displaced ovoids
- Inappropriate packing

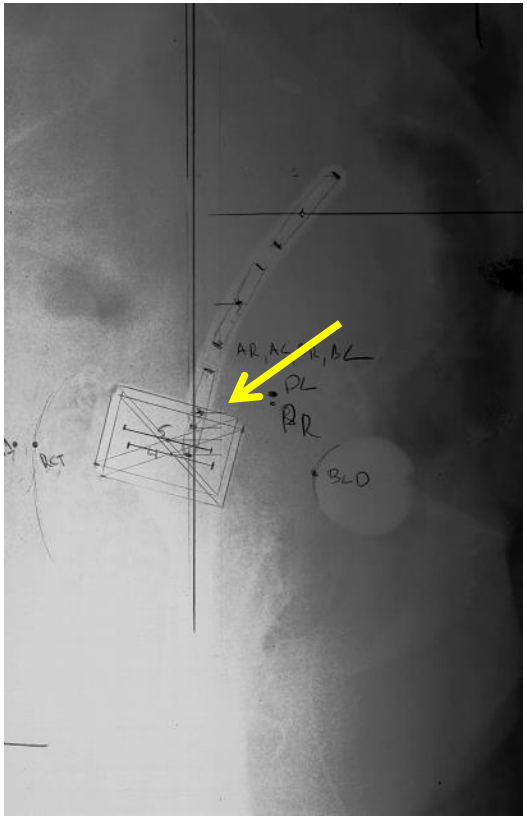


# Unacceptable Tandem

## Midline on lateral film



## Bisecting ovoids



# Local Recurrence

| Parameter* | HR† (95% C.I.) | p-value |
|---|---|---|
| Symmetry of Ovoids to Tandem | 2.61 (1.05, 6.45) | 0.039 |
| Displacement of Ovoids in Relation to Cervical Os | 2.54 (1.11, 5.80) | 0.027 |
| Position of Tandem in Mid-Pelvis on Lateral Film | 1.01 (0.43, 2.37) | 0.98 |
| Tandem Bisecting Ovoids on Lateral Film | 0.68 (0.27, 1.67) | 0.39 |
| Appropriateness of Packing | 1.66 (0.73, 3.77) | 0.23 |

*Model included pelvic/iliac, para-aortic node positive, FIGO stage

†This represents the HR of unacceptable/not evaluated scores compared to acceptable scores

# Disease-Free Survival

| Parameter* | HR† (95% C.I.) | p-value |
|---|---|---|
| Symmetry of Ovoids to Tandem | 1.43 (0.73, 2.80) | 0.29 |
| Displacement of Ovoids in Relation to Cervical Os | 2.12 (1.16, 3.89) | 0.02 |
| Position of Tandem in Mid-Pelvis on Lateral Film | 1.15 (0.63, 2.09) | 0.65 |
| Tandem Bisecting Ovoids on Lateral Film | 0.79 (0.42, 1.48) | 0.47 |
| Appropriateness of Packing | 1.95 (1.08, 3.55) | 0.028 |

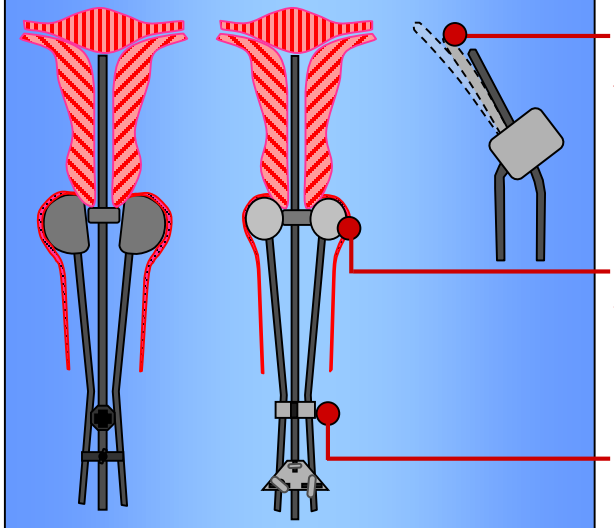
*Model included pelvic/iliac, para-aortic node positive, and FIGO stage

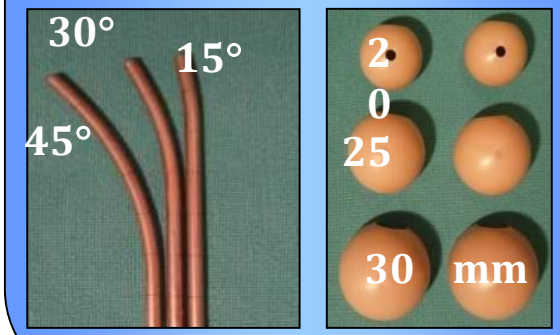
†This represents the HR of unacceptable/not evaluated scores compared to acceptable scores

# Modern Intracavitary Techniques

## *Applicators:* mimicking historical geometries

### Manchester / Fletcher style





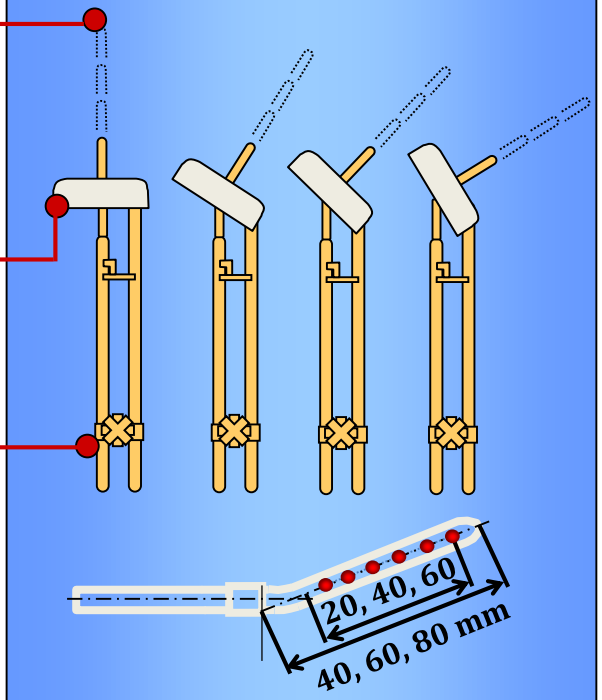


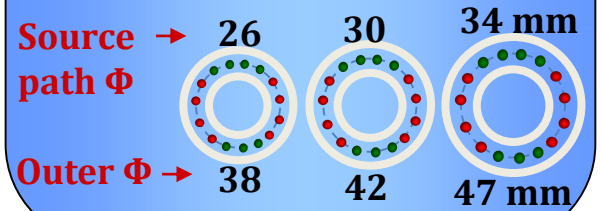


### Common features:

- Uterine Tandem: various lengths, angles or curvatures
- Ovoids, cylinders, rings various outer & source path diameters
- Clamp

### Stockholm style



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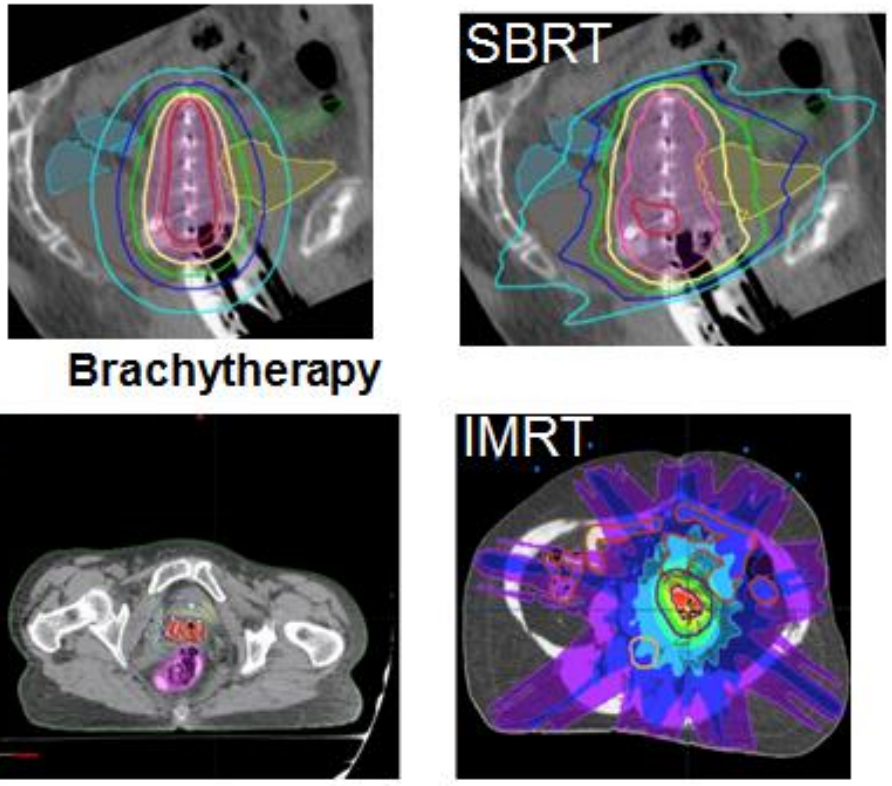


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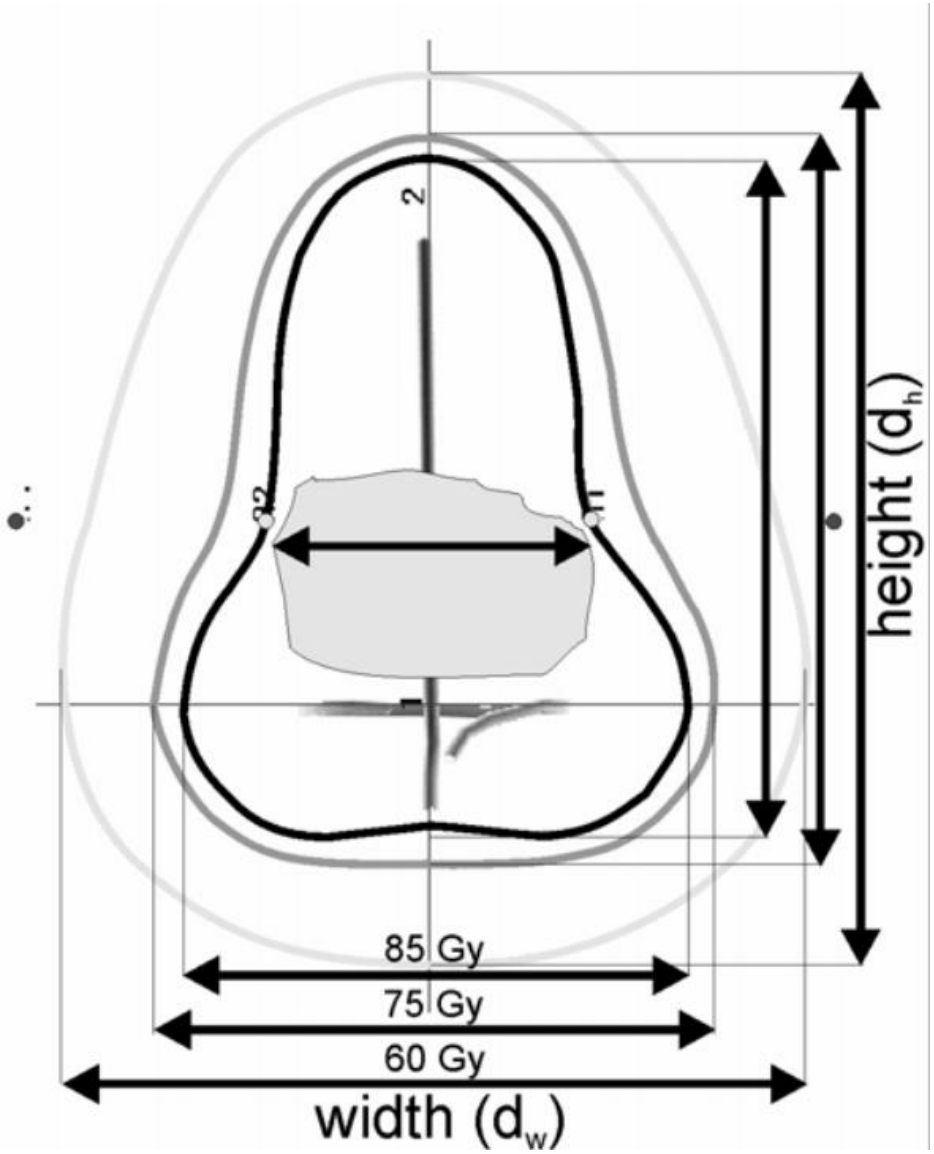

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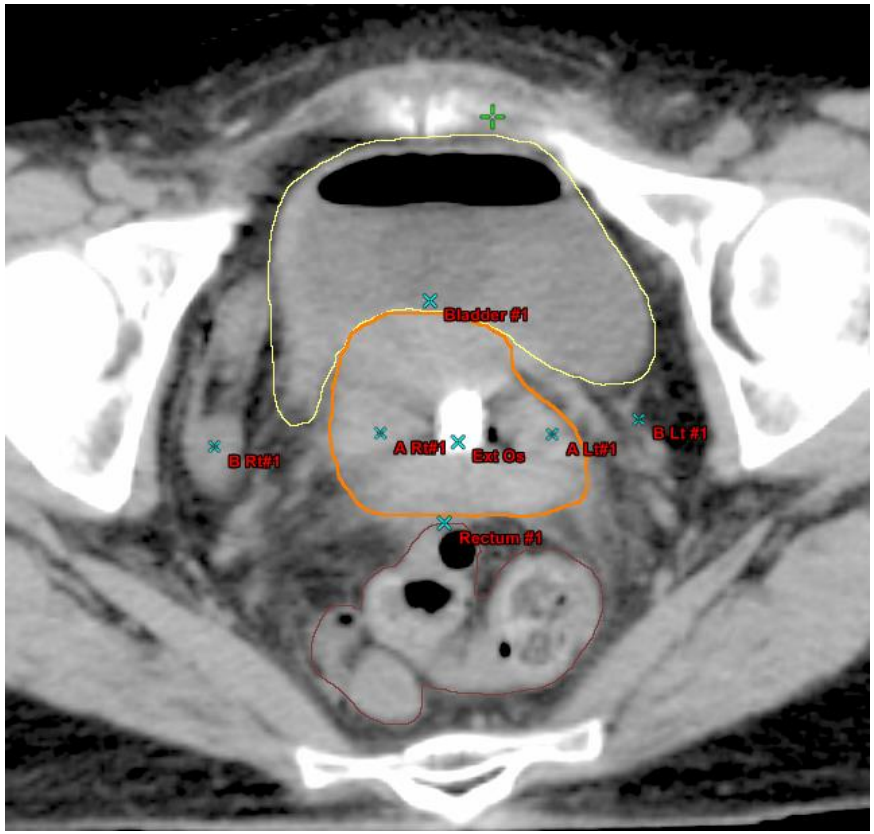


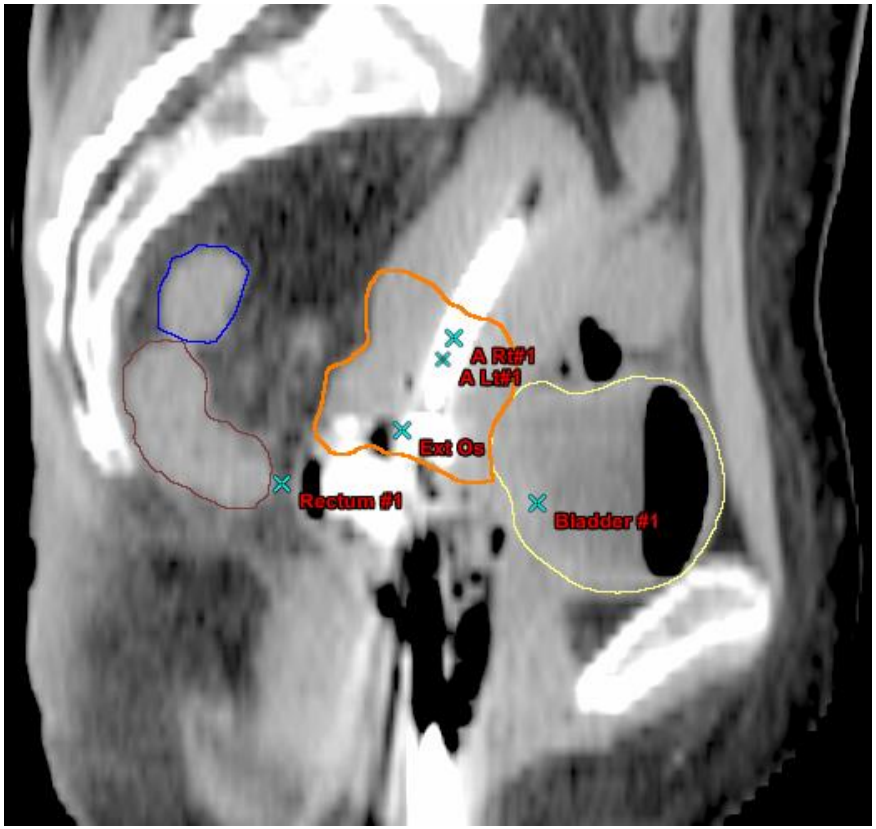


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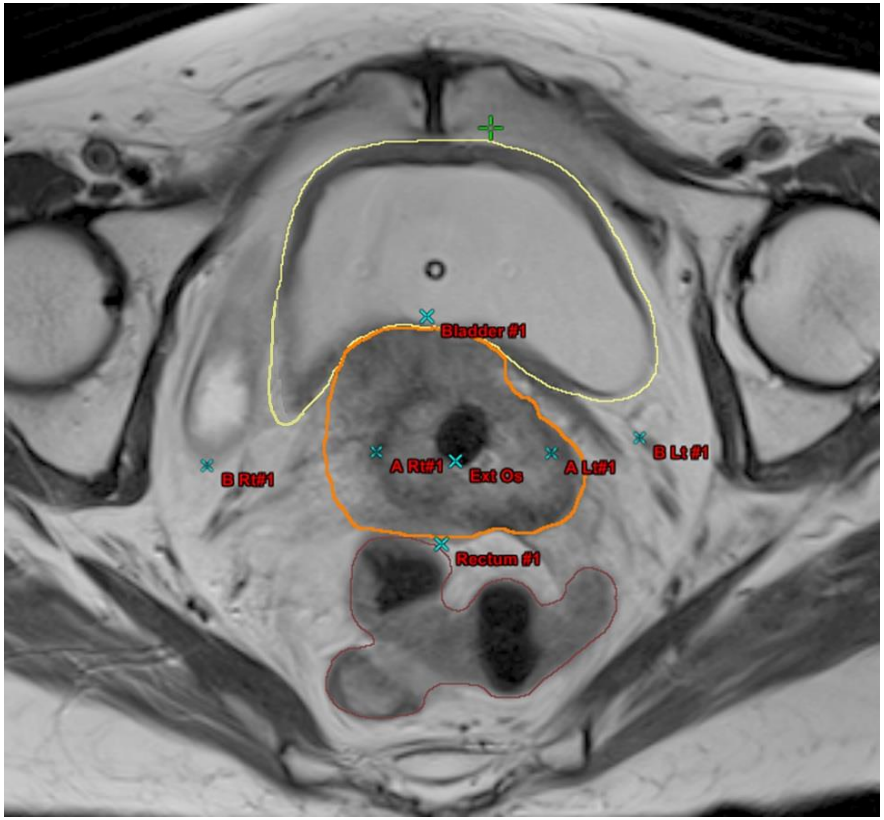
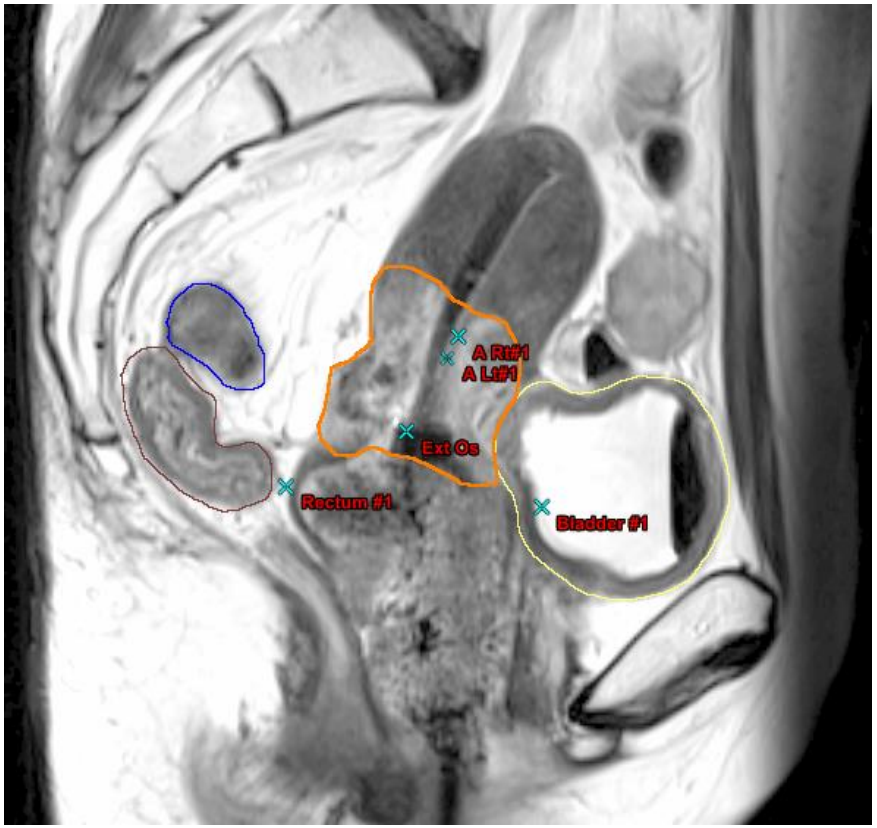
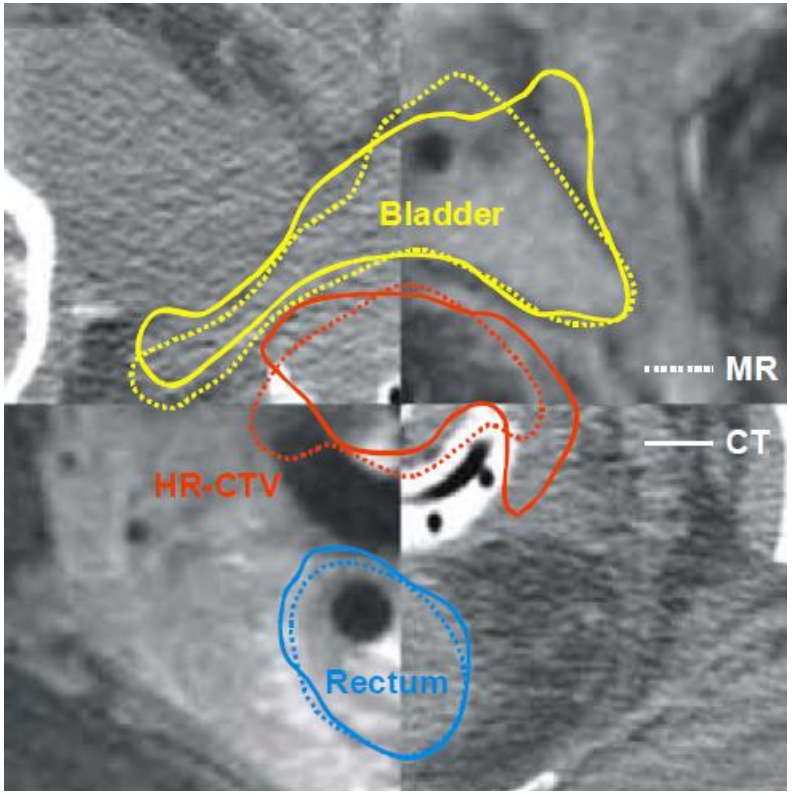



vs.


10 patients who were contoured and planned on both MRI and CT planning according to GEC-ESTRO

CT overestimated the width of the high risk CTV (HR CTV) leading to an increased volume receiving the prescription dose (V100) as well as minimum dose to 100% (D100) and 90% (D90) of the target volume

There were no differences in dose to the organs at risk with MRI versus CT planning

**Viswanathan et al, IJROBP, 2007**

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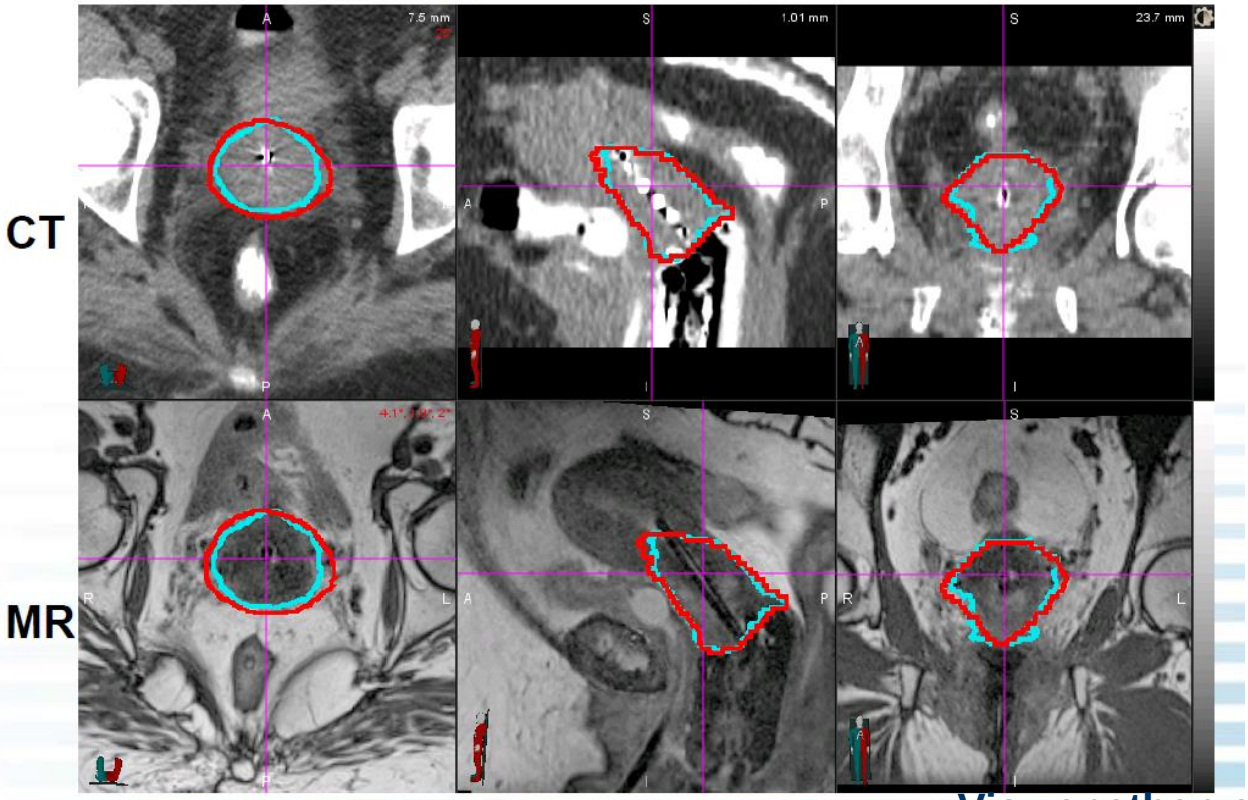
# No parametrial extension
# Complete response




**Viswanathan et al, IJROBP, 2007**

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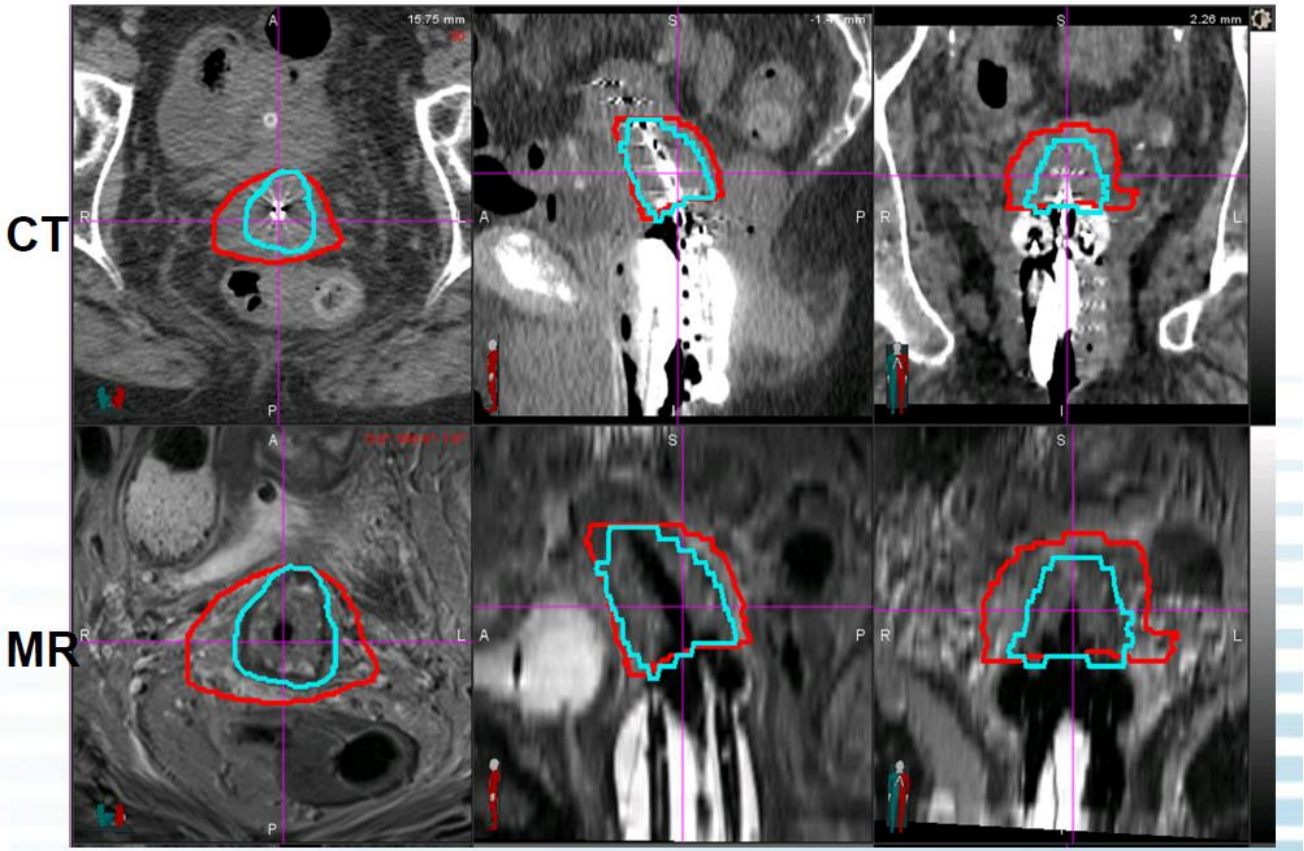
## Parametrial extension, good response
## CT (red) vs. MR (blue)




Viswanathan et al, IJROBP, 2014

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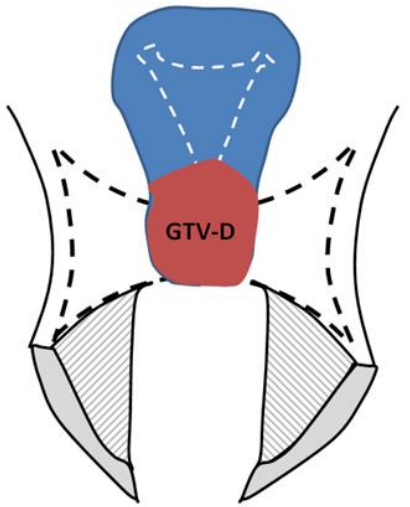
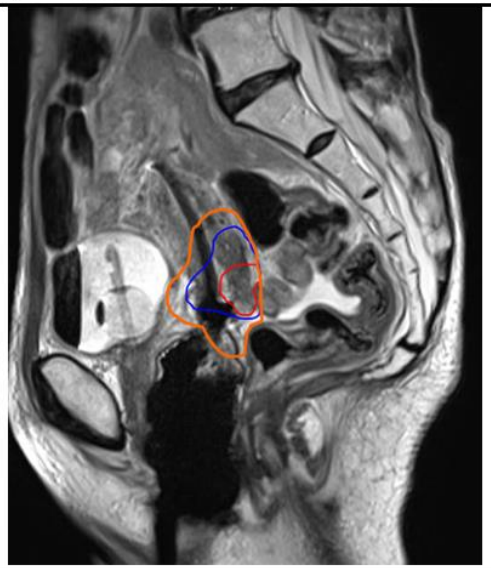
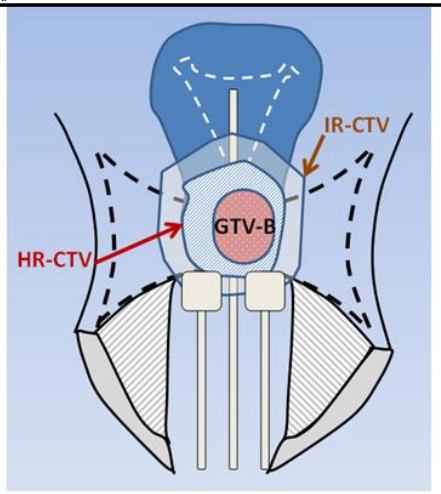
| Volume | Definition | Sagittal MRI† Volume Example | Coronal Diagram |
|---|---|---|---|
| GTV-D†† | **Gross Tumor Volume at diagnosis** based on visualization, palpation and T2 MRI |  |   |
| IR-CTV# | **Intermediate Risk Clinical Target Volume** includes 5-15mm margin around HR-CTV and includes initial sites of involvement<br><br>Note: Safety margin based on tumor size, location, spread, regression and/or treatment technique |  |   |

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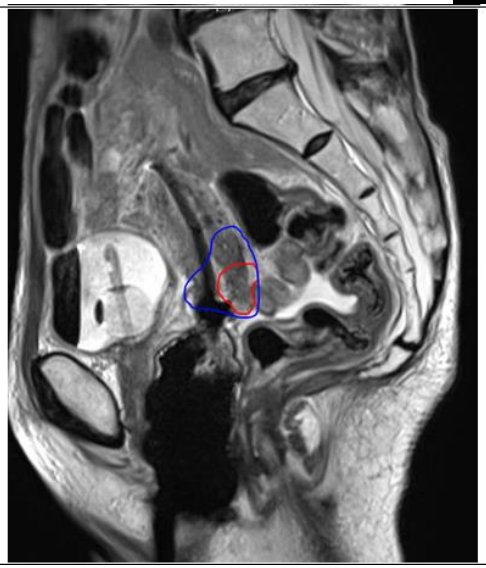
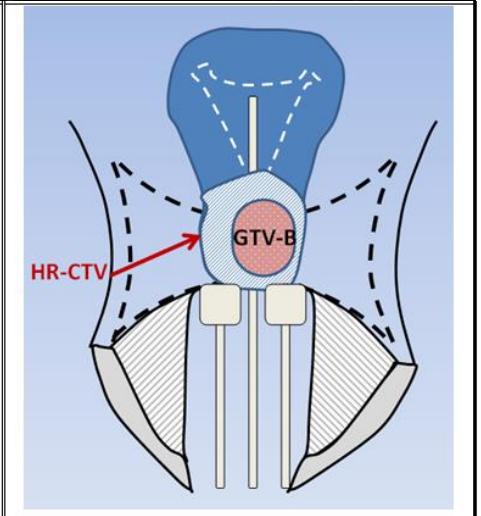
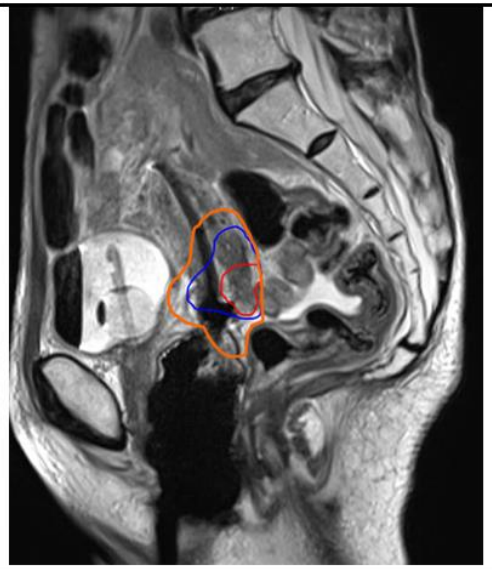
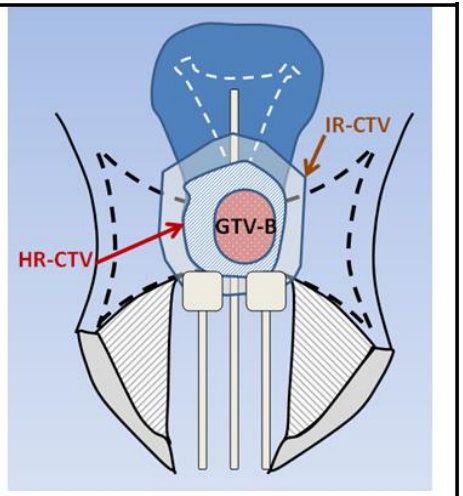
| | | | |
|---|---|---|---|
| HR-CTV-B¶ | **High Risk Clinical Target Volume at brachytherapy** includes GTV-B, entire cervix and "gray zones" on MRI T2 sequence |  |  |
| IR-CTV# | **Intermediate Risk Clinical Target Volume** includes 5-15mm margin around HR-CTV and includes initial sites of involvement<br><br>Note: Safety margin based on tumor size, location, spread, regression and/or treatment technique |  |  |

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**Potter et al. Radiotherapy and Oncology 2006**

Concepts and terms in 3D image-based treatment planning in cervix cancer brachytherapy—3D dose volume parameters and aspects of 3D image-based anatomy, radiation physics, radiobiology

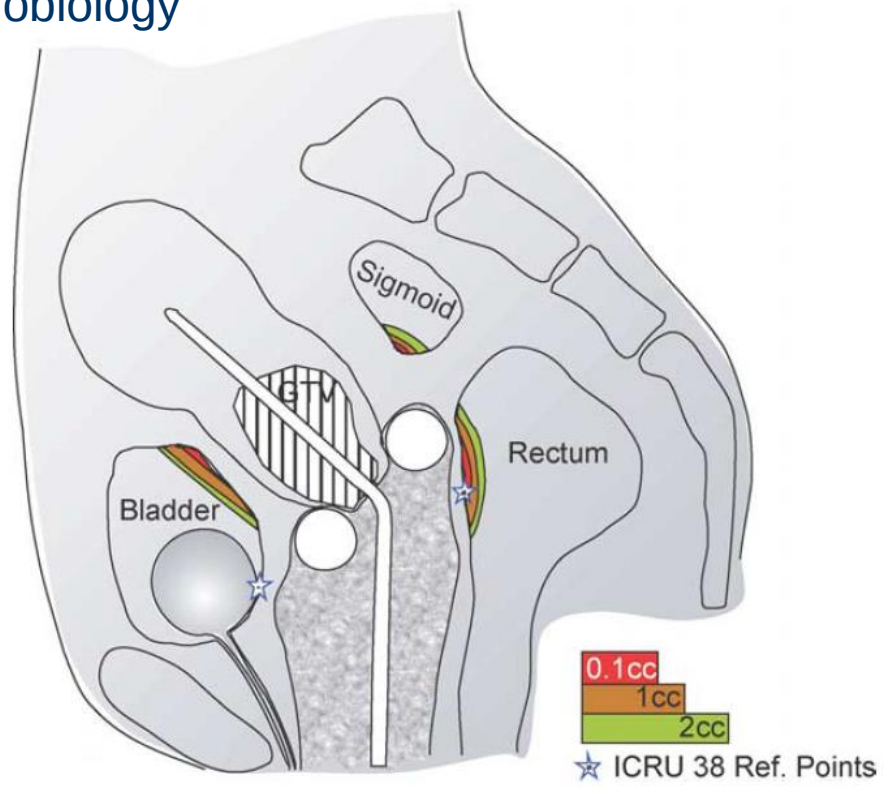


Fig. 6. Schematic anatomical diagram (sagittal view) indicating the most irradiated tissue volumes adjacent to the applicator for rectum, sigmoid and bladder: 0.1, 1, and 2 $cm^3$ (identical patient as in Figs. 1 and 2, dose volume parameters for this schematic patient example can be taken from Fig. 5).

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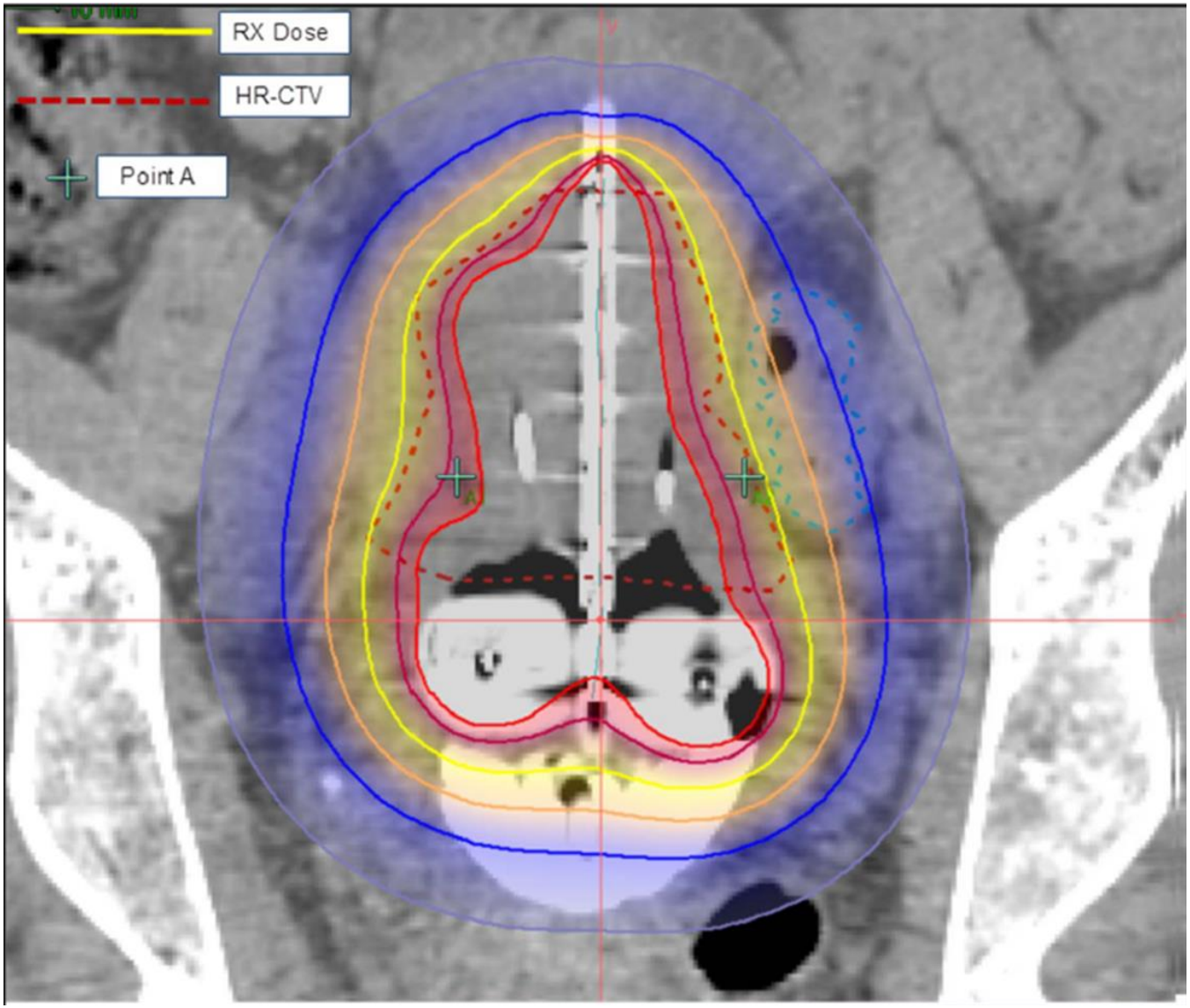


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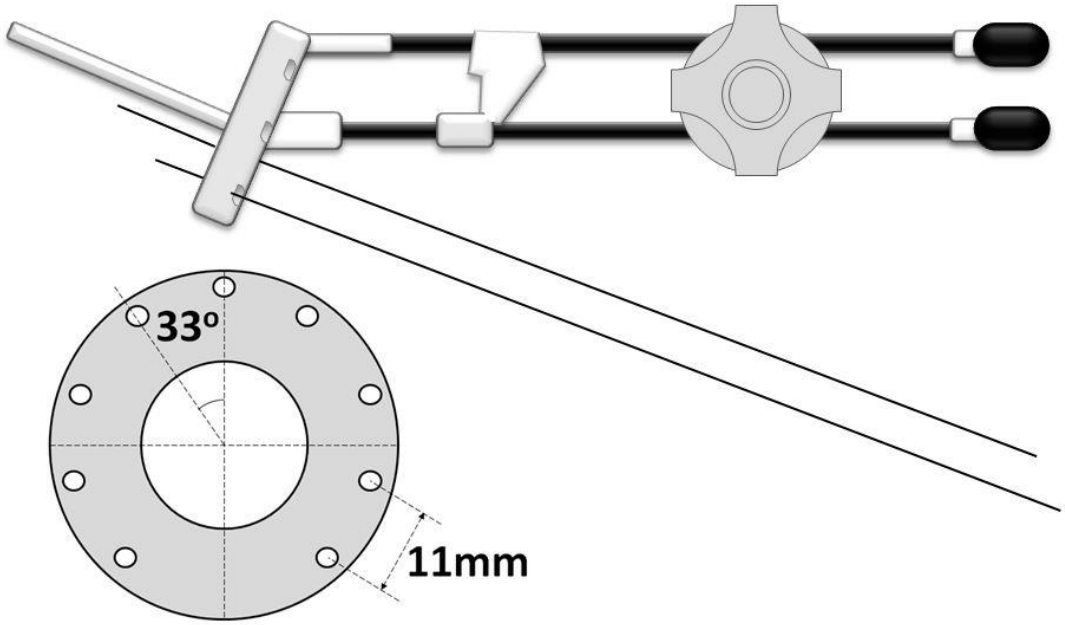
# Vienna Applicator



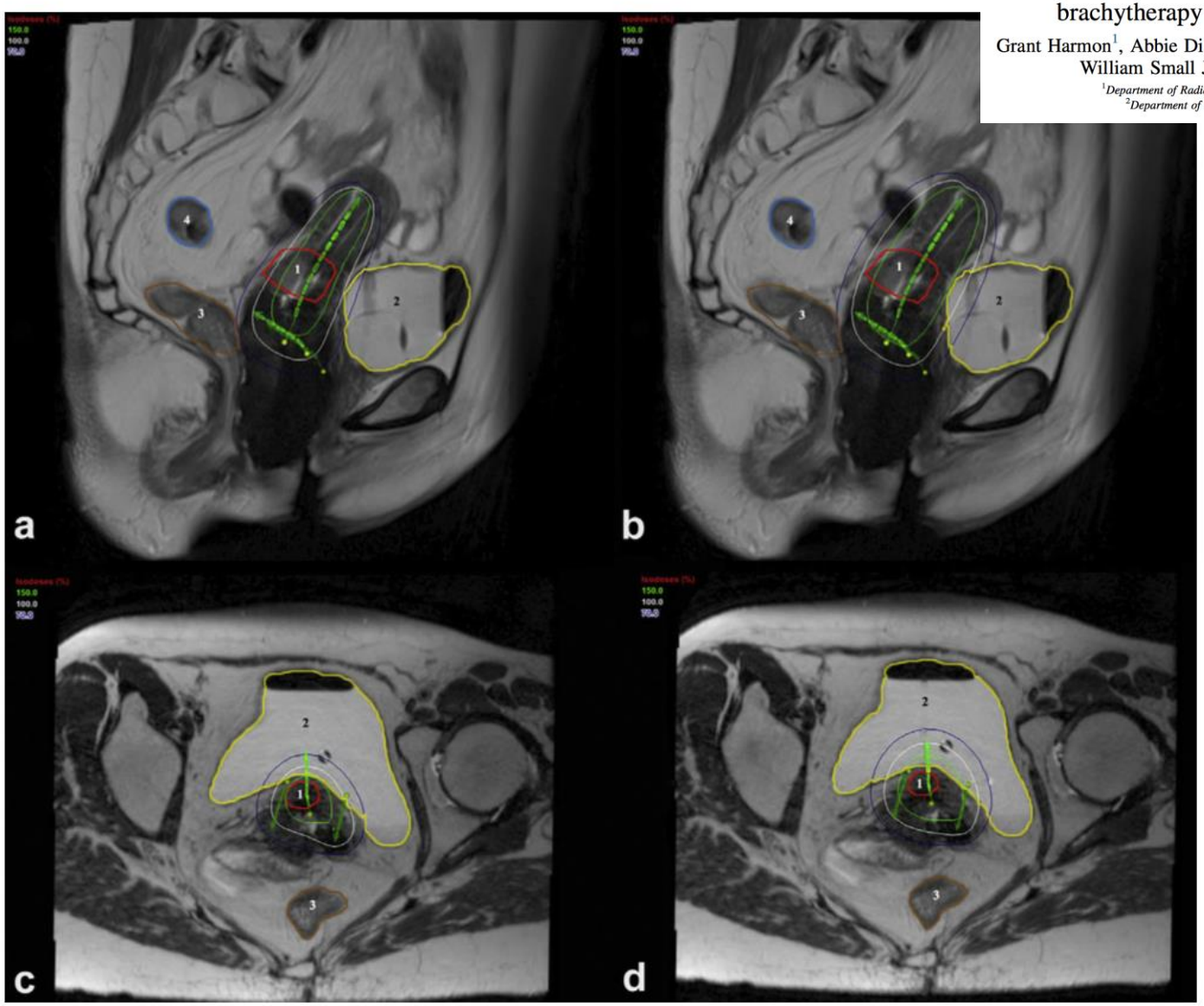

- MRI compatible for 1.5 and 3T
- Combined Intracavitary/Interstitial
- Modification of Tandem and Ring
- Validated to  provide prescription dose up to 15 mm lateral to classic point A
- Clinically validated for average dosimetric gain for D90 HR-CTV of 9 Gy α/β=10

**Kirisits et al., IJROBP, 2006**

# Point A vs. HR-CTV $D_{90}$ in MRI-based cervical brachytherapy of small and large lesions

Grant Harmon[1], Abbie Diak[1], Steven M. Shea[2], Joseph H. Yacoub[2], William Small Jr.[1], Matthew M. Harkenrider[1,*]

[1]Department of Radiation Oncology, Loyola University, Chicago, IL
[2]Department of Radiology, Loyola University, Chicago, IL



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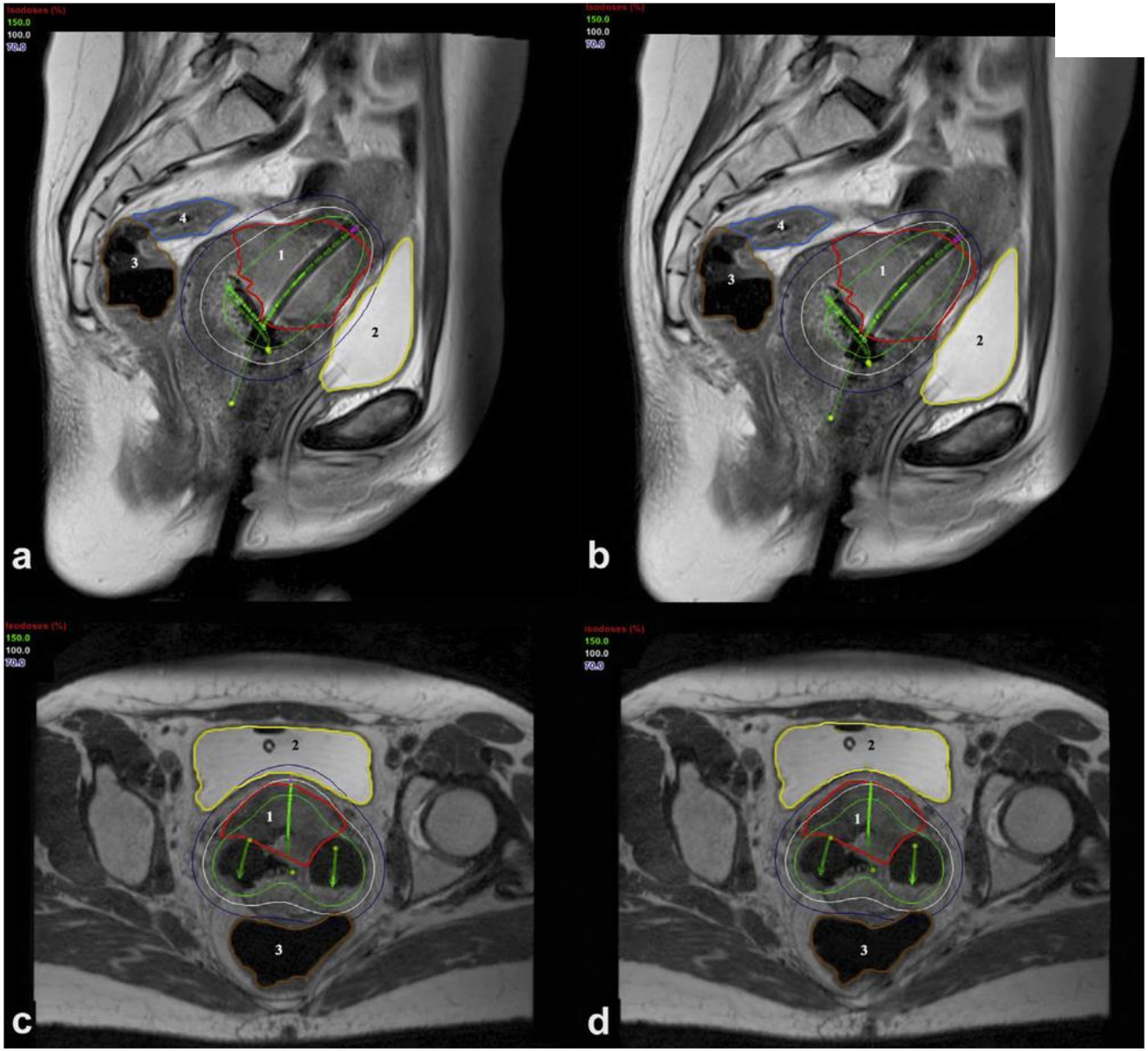

# CONCLUSIONS

1. Brachytherapy is a critical component of the treatment of cervical cancer.

2.Current State of the art therapy involves image guided therapy.