Optimizing Safety and Efficiency in Brachytherapy: Perspective from an Experienced Brachytherapy Physician

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Disclosures

- I have nothing to disclose.

Objectives

- Deliver safe and effective brachytherapy
- Understand brachytherapy workflow and how to leverage brachytherapy techniques
- Understand how imaging facilitates improve tumor delineation
- Understand importance of collaboration with your physics team

Objective Statement

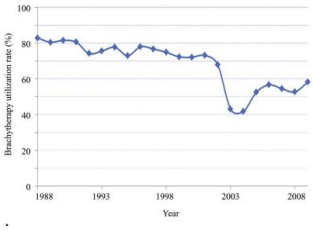
- *Technology has enabled physicians to better delineate target volumes for planning in brachytherapy. It is well-recognized that precise targeting of the tumor volume is a key prognostic factor in achieving local control in cervical cancer and can help spare organs at risk. Use of various imaging modalities are dependent on the resources available at one's institution. Additionally, equipment and implant techniques can influence the quality of the implant and ideal dosing to effectively treat the patient's disease. It is important to consider the extent of the gross tumor volume (GTV) at diagnosis and then compare that to imaging prior to brachytherapy. The high risk CTV (HR CTV) is defined with the intent to deliver a sufficient dose to eradicate all residual macroscopic disease. Intermediate risk CTV (IR CTV) should encompass any microscopic disease. The experienced physician takes into account anatomic structures which also facilitates protecting organs at risk including the bladder, rectum, and sigmoid. In doing so, the physician will work to limit the D_2 cc to the bladder, rectum, and sigmoid. Safety considerations in planning and treatment delivery will benefit the patient and will produce better outcomes. Correct handling and respect for radioactive sources not only protects the patient but all of the staff caring for the patient.*

Global Statistics: Cervical Cancer

- **2nd most common cancer in the developing world**
- **~500,000 new cases/yr worldwide**
- **288,000 deaths/yr**

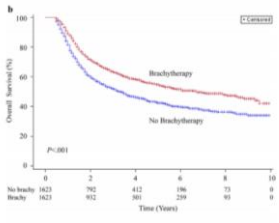
Age-Standardized Incidence Rates of Cervical Cancer per 100,000.

Brachytherapy utilization for cervical cancer



Han et al, IJROBP 2013

Overall survival by brachytherapy utilization



Han et al, IJROBP 2013

Decline in Brachytherapy use leads to….

Concerns

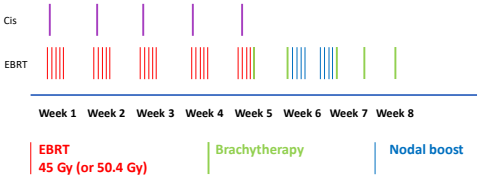
- Lack of skills
- Increase in complications
- Lack of routine
- Workflow inconsistencies
- Decrease in survival for patients

High Dose Rate (HDR) Brachytherapy

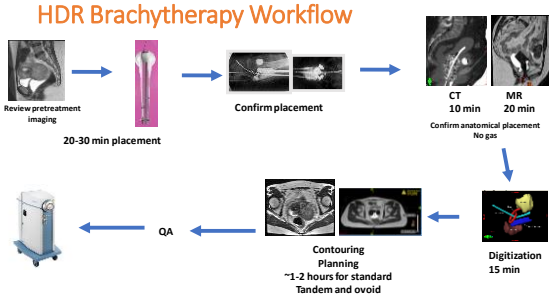
Benefits of HDR

- Outpatient procedure/ convenience
- Optimization (vs LDR)
- Stable applicator position throughout treatment
- Decreased risks of PE

Treatment Sequencing



HDR Brachytherapy Workflow



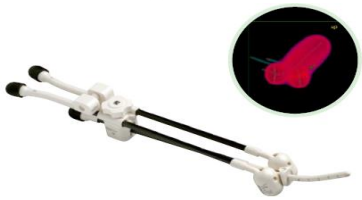
Brachytherapy Tools

- Choosing the right device
- Utilizing imaging
  - MRI before therapy to understand extent of disease
  - MRI before brachytherapy implant ideal for tumor delineation
  - PET CT

Applicator Choice

- Tandem and ovoid
  - Increased flexibility
  - MR/CT compatible applicators
- Ring and Tandem
  - Fixed geometry
- Tandem and cylinder
- Combined IC/IS applicators
  - Vienna, Venezia, MUPIT
- Strong opinions regarding applicators; skill/knowledge probably more important than applicator choice

Fletcher CT-MR Tandem and Ovoid Applicator



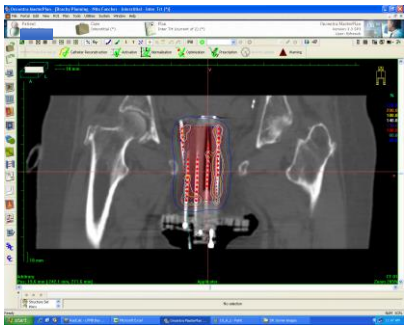
The sail is adjustable so that the tandem length can be set same as the intra-uterine sound. The set has two tandems (15 and 30 degrees) and six ovoid pairs (15/20/25/30/35/40 mm)

Tandem and Ring

Vienna CT-MR Tandem and Ring with Interstitial Capability

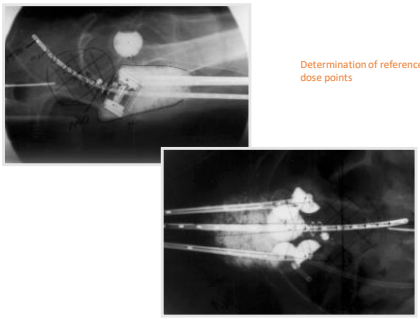
It has 9 holes in the ring which allow placement of interstitial titanium needles while the ring serves as the template. This makes it possible to achieve an asymmetric dose distribution. The 3 tandem lengths are fixed (20/40/60 mm).

Venezia applicator (Elekta)



Imaging evolution

- Historically, many institutions used orthogonal films to verify implant placement…..



Determination of reference dose points

Imaging Utilization in Brachytherapy

- CT based planning
- MRI based planning

- Results in:
  - Better tumor delineation
  - Potential for less complications
  - Improved survival

Determining Extent of Primary Tumor

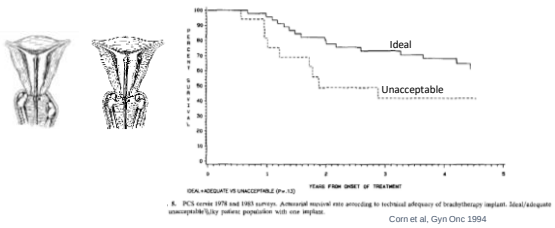
- Pelvic examination
  - Staging Accuracy: 47%
    - –Bipat et al, Gyn Onc 2003
- MRI versus CT Imaging
  - Staging Accuracy: 86%
  - MRI is superior to CT for detecting uterine body involvement/PM invasion (ACRIN 6651/GOG 183) –JCO 2006
  - MRI superior in detecting vaginal extension

Move from 2D based planning to 3D Imaging

- 124 tandem/ring insertions
- Rate of uterine perforation: 13.7% (17/124)
- Perforation in 8/98 (8.2%) when RO felt confident there was no perforation

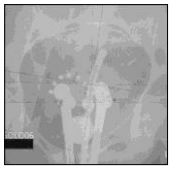
Barnes et al, IJGC 17(4)821-6, 2007

Quality of the implant matters



Corn et al, Gyn Onc 1994

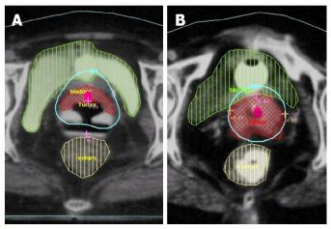
Quality matters: RTOG 0116 and 0128



- Mean f/u: 24.5 months
- Reviewed brachytherapy records
- Higher LR with unacceptable geometry
  - Displacement of ovoids relative to os **HR 2.67**
  - Unacceptable symmetry of ovoids and tandem **HR2.50**
  - Inappropriate packing placement **HR 2.06**

Viswanathan IJGC 2012

Improved tumor delineation with 3D imaging



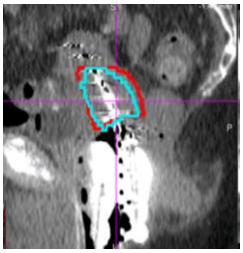
Datta et al Brachytherapy 2005

Advantages of image guided brachytherapy

- **Confirmation of applicator placement**
- **Dosimetry**
  - **HRCTV**
  - **OARs**
- **Small cervix volume vs large tumor volume**

CT contouring guidelines

- Inferiorly:
  - Ovoids: Contour tissue to level of ovoids
  - Ring: inferiorly at level of ring contour tissue inside of ring
  - Adjacent vaginal tissue if involved
- Superiorly:
  - Contour to level where uterus indents (internal os)
  - Next 1 cm as pointed cone
  - Cervix ~3 cm
- Laterally: PM extension (grey/white on CT)
- PE findings and MR at prebrachy



Viswanathan et al, IJROBP 2014

MRI Brachytherapy Guidelines

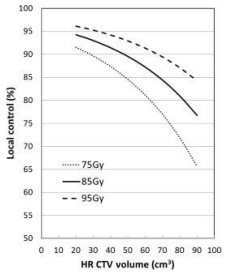
- GTV
  - Macroscopic tumor extension at time of brachytherapy
  - High signal intensity mass(es) (FSE, T2) in cervix/corpus, parametria, vagina, bladder and rectum
- High Risk-CTV
  - Includes gtv, whole cervix, and presumed extracervical tumor extension. Pathologic residual tissues as defined by palpable induration and or grey zone in parametria, uterine corpus, vagina, or rectum, and bladder are included in HR-CTV. No margins.
- Intermediate Risk-CTV
  - Encompasses HRCTV with margins added according to tumor size and regression; minima margins of 5-15 mm
  - Extensive disease: w/ good remission HR-CTV and initial tumor extension

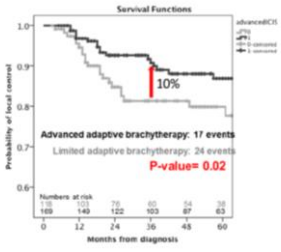
GEC-ESTRO Guidelines, Radiother Oncol 2005

Results of image guided brachytherapy

	# yr	Local control	Overall Survival	Late toxicity (Grade 3+)
STIC	2	78.5-100%	74-96%	2.6-8.9%
Pittsburgh	2	90%	82%	
Vienna	3	91%	94%	0%
Addenbrooke	3	96%	82%	11% crude (14% actuarial)
Korea	3	97%	NR	2%
Paris	4	91%	94%	0%
Australia	5	87-88%	60%	0.6-4.6%
Leuven	5	96%	65%	6%

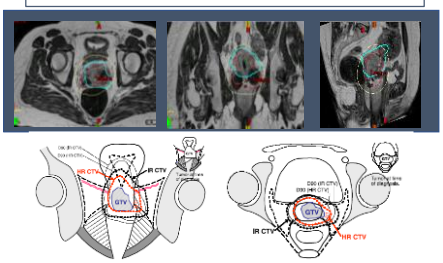
RETROEMBRACE





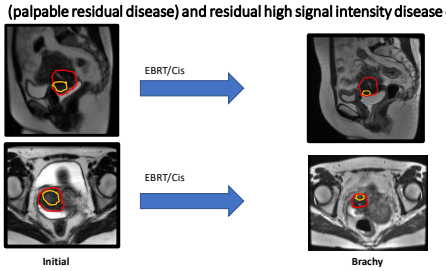
Tanderup et al, Radiother Oncol 2016

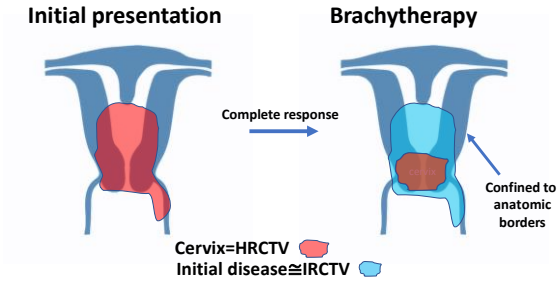
MRI for Image Guided Brachytherapy



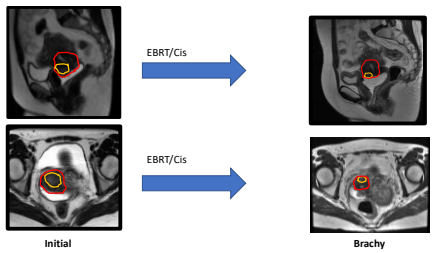
GTV_{BT}

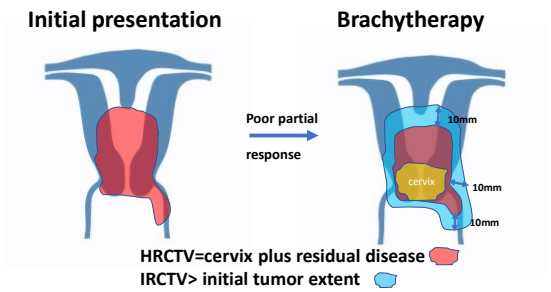
(palpable residual disease) and residual high signal intensity disease on MR

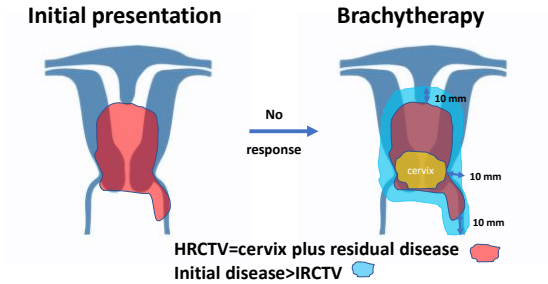




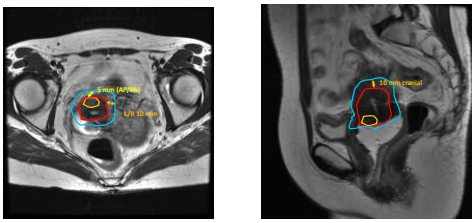
HRCTV= GTV_{BT} + cervix + grey zones





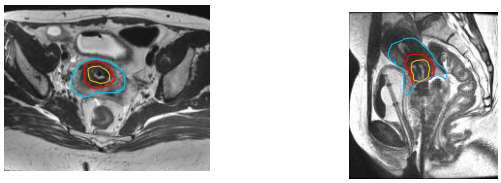


IRCTV= HRCTV + presumed adj micro disease +margin



For limited disease (tumor <4 cm): IRCTV= HRCTV + 5mm (AP/PA), 10 mm (cranially to corpus), 10 mm(R/L)
Confined by anatomic borders: pelvic wall, uterus, bladder, rectum (unless invasion noted)

IRCTV= HRCTV + presumed adj micro disease +margin



More extensive disease: IRCTV based on initial GTV
Confined by anatomic borders: pelvic wall, uterus, bladder, rectum (unless invasion noted)

SAM Question

- A patient with stage IIB cervical cancer is being prepared for high dose rate (HDR) brachytherapy after completing 45 Gy external beam radiation. What is the best imaging approach using IV contrast to target the high-risk CTV for cervical cancer brachytherapy?
  A. CT scan at diagnosis and at the time of the implant
  B. MRI before the implant only
  C. CT scan before the implant only
  D. MRI at diagnosis and at the time of the implant

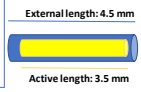
Answer

- Correct answer: D
- REFERENCE:
- Recommendations from Gynaecological (GYN) GEC-ESTRO Working Group (I): concepts and terms in 3D image based 3D treatment planning in cervix cancer brachytherapy with emphasis on MRI assessment of GTV and CTV. Radiotherapy and Oncology, Volume 74, issue 3, March 2005, pp235-245.
- Computed tomography versus magnetic resonance imaging based contouring in Cervix cancer brachytherapy: results of a prospective trial and preliminary guidelines for standardized contours. Int J Radiation Oncology Biol Phys. 2007;68(2):491-498.

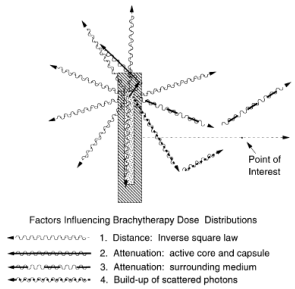
Working as a team with Physics

Radioactive Sources: Iridium^{192}

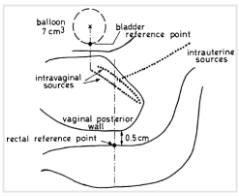
- Half life is 73.8 days
  - Produced by bombarding Iridium^{191} with thermal neutrons in a nuclear reactor
  - HDR source replaced every 90 days
- X & Gamma rays 0.063 to 1.4 MeV
  - Average energy: 0.397 MeV
- Manufactured as seeds and ribbons
- Γ = 4.60 R-cm^2/mCi-hr



Basic Principles



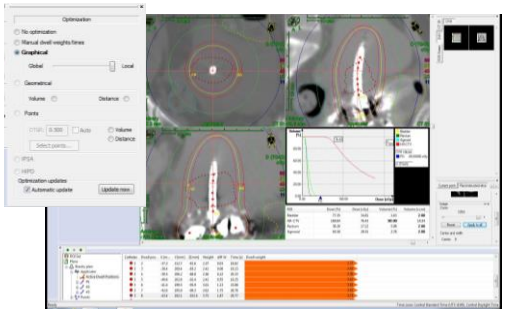
Normal Tissue Dose Points (ICRU)



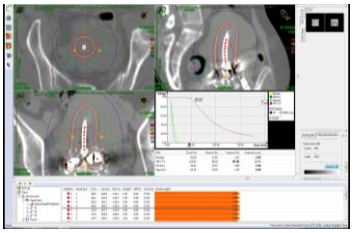
- Bladder
  - ICRU Bladder pt<75 Gy
- Rectum
  - ICRU Rectal pt<70 Gy
- Vagina:
  - Upper: 120-140 Gy
  - Lower: 90 Gy

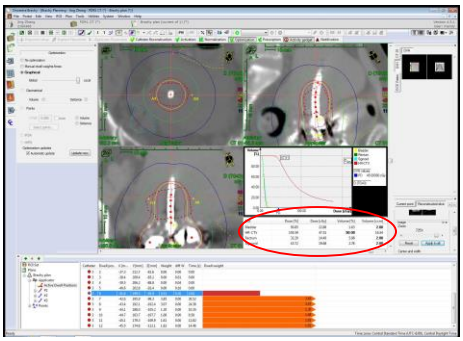
Manual optimization

- Times entered manually with weighting considerations
- Iterative process



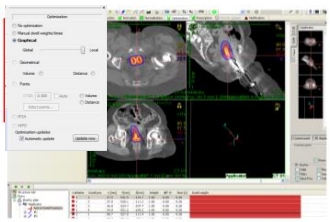
Graphical optimization



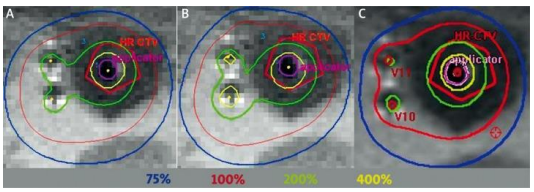


Inverse optimization

- Inverse optimization
  - HIPO (hybrid inverse planning and optimization)- preserves typical dose distribution and keeps high dose regions within target
  - IPSA (UCSF)-no specific tools to control spatial dose distribution
- What happens to my pear?
  - Pear: concentrated doses within the uterus with sparing of adjacent OARs
- Concern:
  - **Blow up dwell times/needles**



Manual **IPSA** **HIPO**



Sapru et al, J Contemporary brachy

Dose: 45 Gy Pelvis EQD2

Fx #	Dose	EQD2 Tumor	EQD2 Normal tissue (90% PD)	EQD2 Normal tissue (70% of PD)
4	7 Gy	83.9 Gy	90.1 Gy	74.2 Gy
5	6 Gy	84.3 Gy	88.6 Gy	73.4 Gy
6	5 Gy	81.8 Gy	83.7 Gy	70.5 Gy
5	5.5 Gy	79.8 Gy	82.6 Gy	69.6 Gy

GEC ESTRO: Planning target goals

	D90 HRCTV EQD2	D98 HRCTV EQD2	D98 GTV EQD2	D98 IRCTV EQD2	Point A EQD2
Planning goals	>90 Gy <95 Gy	>75 Gy	>95 Gy	> 60 Gy	> 65 Gy
Upper limit	> 85 Gy	-	>90 Gy	-	-

GEC ESTRO: OAR planning goals

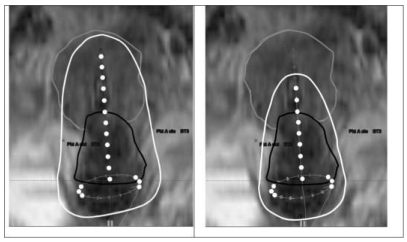
	Bladder D2cc EQD2	Rectum D2cc EQD2	Sigmoid D2cc EQD2	RV point EQD2
Planning goal	<80 Gy	<65 Gy	<70 Gy	<65 GY
Upper limit	<90 Gy	<75 Gy	<75 Gy	<75 Gy

Vaginal dose constraints

	Aim	Primary
ICRU recto-vaginal point dose	<65 Gy EQED2 (EBRT+BT)	Primary
Ratio of vaginal TRAK and total TRAK	<30-40%	Secondary
Vaginal lateral dose points at 5 mm	<85 Gy EQD2 (EBRT+BT)	Secondary
Visual inspection of the 140% isodose	Intruding as little as possible into vaginal tissue; located within applicator	Secondary

EMBRACE protocol

Uterine dose with MR guided brachy



Sapru et al, Radiotherapy and Oncology April 2013

SAM Question

- After a HDR brachytherapy treatment has been delivered and the source retracts, the physician and physics staff enter the room and perform which procedure first?
  - A. Patient identification.
  - B. Immediate removal of the implant device.
  - C. Radiation survey of the patient.
  - D. Chart completion noting dose delivered and source activity.

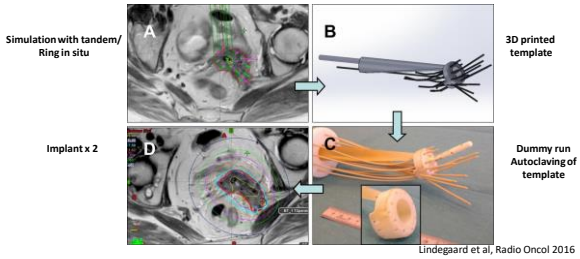
- Correct answer: C
- REFERENC: NRC's 10CFR Part 35

What's next….

3D Printed templates for GYN brachytherapy

- **Patient specific**
  - **Small vaginal dimensions can be accommodated**
  - **Angled catheters**
- **Second copy of template outside for guidance**
  - **Color coded holes for easier guidance**
- **Optimal dose distributions for large complicated implants**
  - **Uterosacral disease**
  - **Lateral parametrial disease**
- **Commercialization possible**
  - **Produced in house vs 3D printing company**

3D printed templates for GYN brachy



Lindegaard et al, Radio Oncol 2016

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