

Brachytherapy for Prostate and Gynecologic Cancers: Moving the Needle

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Objectives

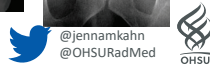
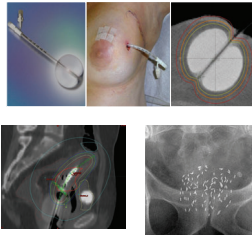
- Review and understand the advances and modernization of brachytherapy treatment in gynecologic cancers
- Review the indications for HDR brachytherapy in prostate cancers
- Understand the modality and indications of brachytherapy as a role in gynecologic and prostate cancer radiation therapy



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Types of Radiation Therapy

- Linear Accelerator: External Beam Radiation Therapy
- Brachytherapy: Internal Radiation



3

What is Brachytherapy?

- Internal Radiation Therapy
- Radioactive source is placed inside or next to an area requiring treatment
- Giving a higher dose of radiation to a tumor while sparing or reducing radiation exposure to other organs



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Historical Perspective

1901
Brachytherapy first used for cancer

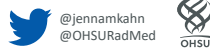
1920s
57 of 199 cases cured by Radium alone

1903
Brachyther used for gyn cancers

1901: Radium in the treatment of cancer. LINDSAY'S OF THE CERVIX UTERI. BY SIR RICHARD THORNTON. LONDON: H. K. LEWIS, 1901.

1903: Radium in the treatment of cancer. LINDSAY'S OF THE CERVIX UTERI. BY SIR RICHARD THORNTON. LONDON: H. K. LEWIS, 1903.

1920s: 57 of 199 cases cured by Radium alone. Radium in the treatment of cancer. LINDSAY'S OF THE CERVIX UTERI. BY SIR RICHARD THORNTON. LONDON: H. K. LEWIS, 1920s.



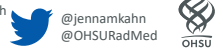
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Low Dose Rate vs High Dose Rate

- 66Seeds⁹⁹
- Dose given off from a decaying source placed inside a patient
- Usually seeds left in patient to decay over time
- Depending on source can take up to 6 months to deliver dose
- Dose given off quickly from a temporary source
- Applicator placed and source comes through an afterloader
- Treatment takes minutes
- No radiation left in patient

¹⁹² Ir	1.03 MeV	1626 yrs	8.25R.cm ² /mg.h
¹³⁷ Cs	662 keV	30 yrs	3.28R.cm ² /mg.h
¹⁰⁶ Co	1.25 MeV	5 years	13.1R.cm ² /mg.h
¹⁹² Ir	360 keV	74 days	4.69R.cm ² /mg.h
¹²⁵ I	59 keV	32 days	
¹⁷¹ Yb	28 keV	60 days	1.45R.cm ² /mg.h
^{119m} Sn	23 keV	17 days	1.48R.cm ² /mg.h
¹¹³ Cs	30 keV	10 days	

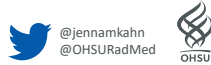
Dose Rates:
LDR: 0.3-2 Gy/h
10 Gy/day
HDR: >12 Gy/h
10 Gy/min



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Indications for Brachytherapy in Cancer

- Cervical Cancer
 - Definitive
 - Standard of Care Chemo-XRT
 - Adjuvant tx for early stage
- Endometrial Cancer
 - Adjuvant therapy after surgery to prevent recurrence at the vaginal cuff
 - Definitive early stage
- Vaginal Cancer
 - Concurrent chemo EBRT + brachy
- Prostate Cancer
 - Monotherapy
 - Boost Treatment for high risk



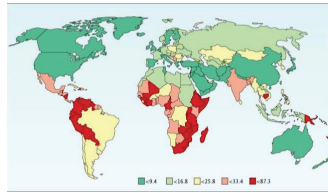
Gynecologic Cancers



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Cervical Cancer

- 4th most common cancer in women worldwide
- Leading cause of cancer death in women in many countries



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Cervical Cancer Treatment Overview

- Early stages (IA1-IB1): LEEP/CKC, Trachelectomy, Hysterectomy
- Advanced Stage (IB2-IVA): Chemotherapy and Radiation Therapy

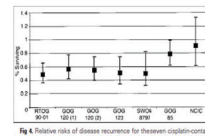
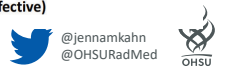
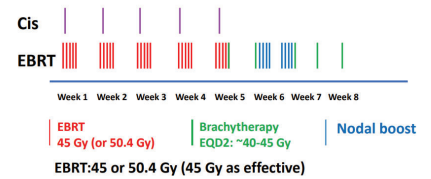
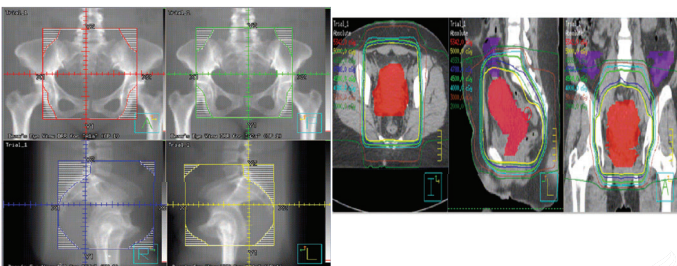


Fig 4. Relative risk of disease recurrence for cisplatin-containing arms of six recent randomized clinical trials in patients with locally advanced cervical carcinoma (RTDC; Radiation Therapy Oncology Group; GOG; Gynecologic Oncology Group; SWOG; Southwest Oncology Group; NCIC; National Institute of Cancer Canada).



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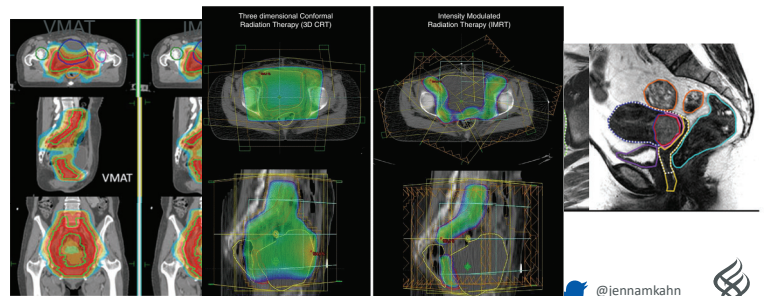
3D Conformal Radiation Therapy



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Hague et al Int Journal of Cancer and Oncology 2016

IMRT/VMAT for Cervical Cancer

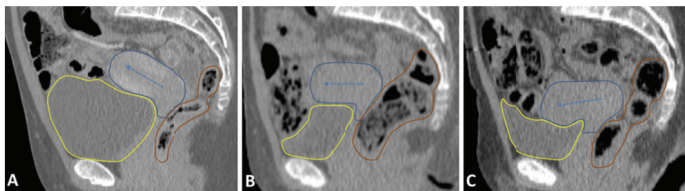


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Deng et al Journal of Applied Clinical Medical Physics 2016

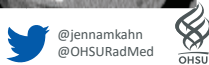
Lim et al 2011 IJROBP

Organ Motion during Treatment



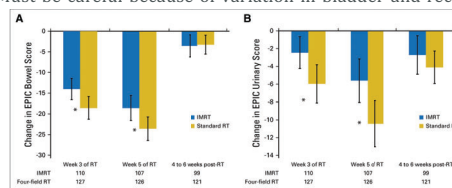
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Sun et al 2016 Cancer/Radiotherapie



Post-op GYN: IMRT vs 4 Field 3D

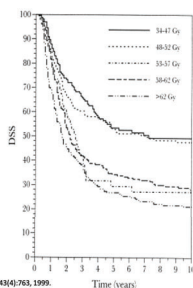
- Showed reduced gastrointestinal and genitourinary toxicity with IMRT compared with 4-field approach
- Must be careful because of variation in bladder and rectal position



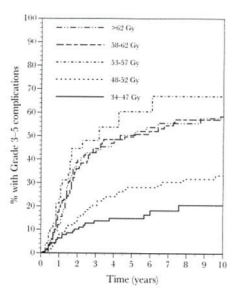
Klopp et al JCO 2018



External Beam is not Enough

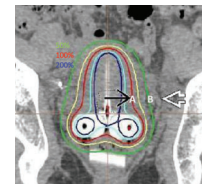
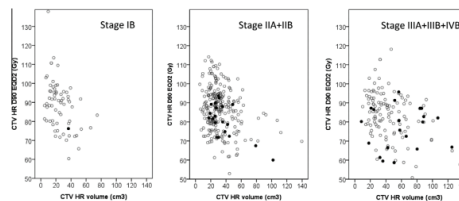


Logsdon and Eifel IJROBP 43(4):763, 1999.



Why does brachytherapy work?

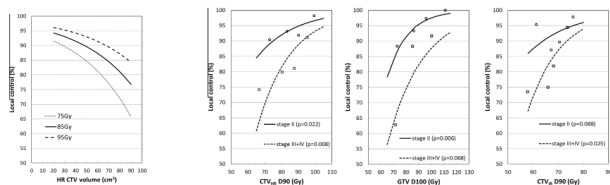
Local failures according to stage as a function of CTV volume and dose



Tanderup et al 2016 Radiation Oncology
Dyk et al IJROBP 2014



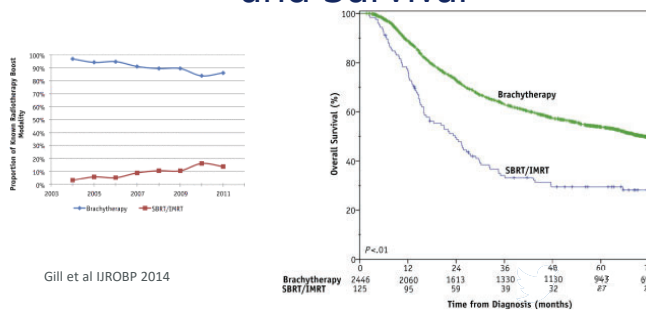
Local Control Increase with Higher Doses



Tanderup et al 2016 Radiation Oncology



Brachytherapy Declining Utilization and Survival

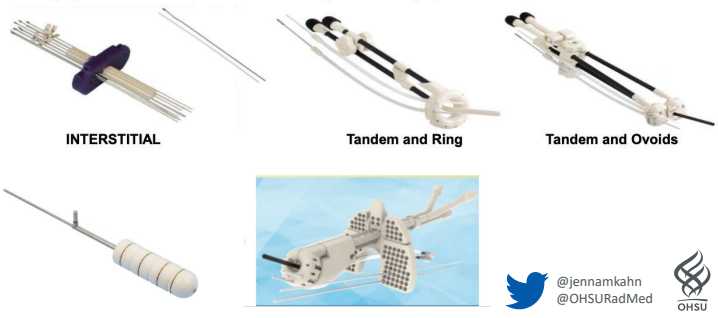


Gill et al IJROBP 2014

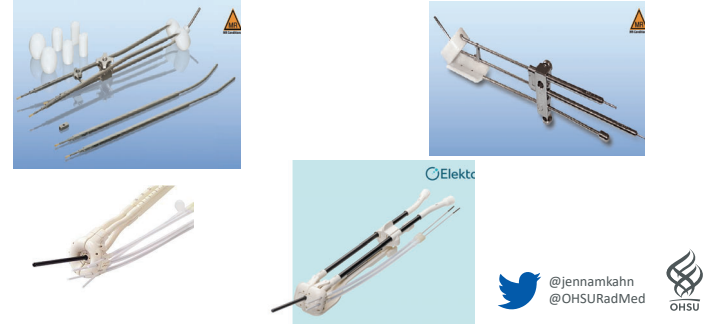
Brachytherapy SBRT/IMRT



Brachytherapy Applicators

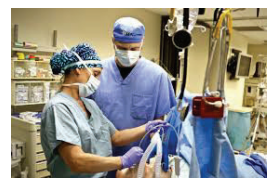


Tandem and Ovoids/Ring



Insertion – Practice Patterns

- Most (97%) of respondents' patients receive anesthesia:
 - General (46%)
 - Spinal (27%)
 - Intravenous conscious sedation (28%)
 - and/or oral pain medication (14%)

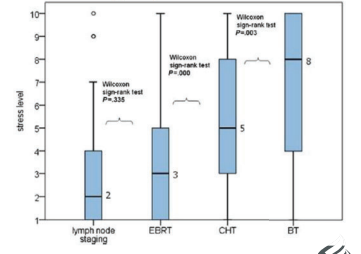


Viswanathan et al. Internat'l Practice Patterns. Red Journal 2012

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Comfort is Important

- PTSD in 41% for brachytherapy
 - Pain
 - Organizational problems
 - Immobility
- Helpful Experiences
 - Treatment team
 - Psychological support
 - Positive attitude



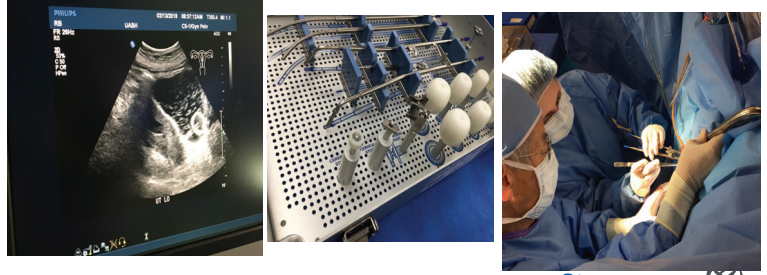
Kirchheiner et al UROBP 2014

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Goals of the Implant

- Good internal geometry
- Proper position relative to the cervix (dose to target)
- Minimize dose to organs at risk (rectum, bladder, small intestines)
- Mechanical stability
- Minimization of discomfort

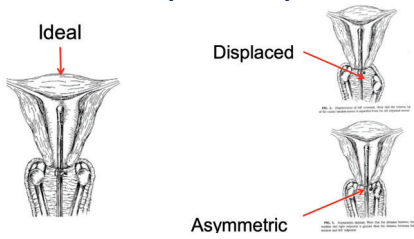
Implant



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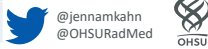
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Implant Technique Impacts Control

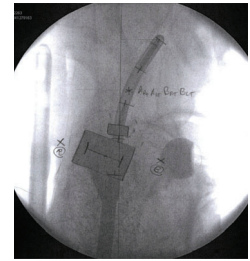
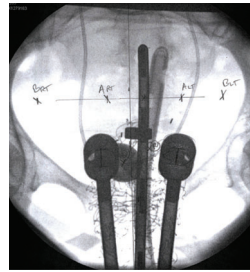


	Acceptable	Unacceptable
Local Control (5yr)	68%	35%
Overall Survival (5 yr)	61%	42%

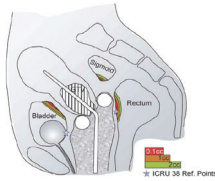
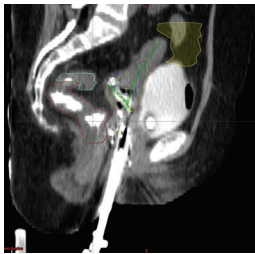
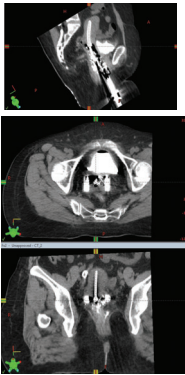
Corn et al Gyn Onc 1994



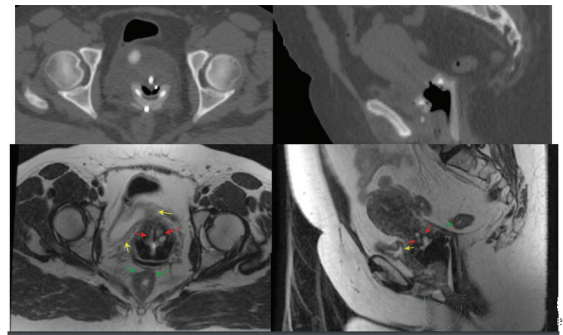
2D planning: Point A



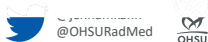
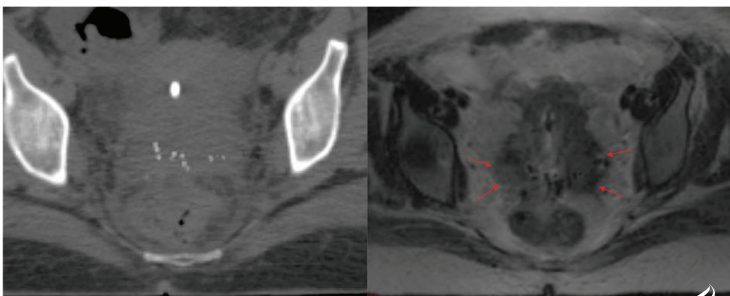
3D Planning



CT vs MRI



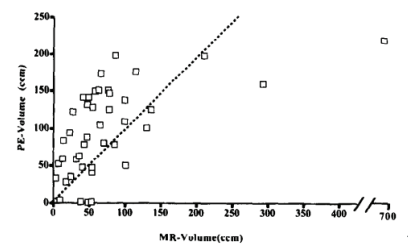
CT vs MRI



Integrating MRI

Mayr et al 1997:

- 43 patients underwent MRI
- Correlation between Exam and MR is poor and decreases with increasing size



Mayr et al IROBP 1997

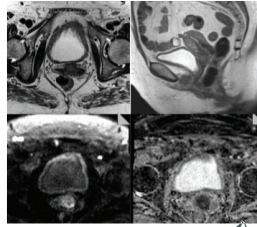
Integrating MRI

Staging

- accuracy up to 80%¹
- superior to CT and clinical examination for uterine body involvement and tumor size and evaluation of parametrial involvement^{1,2}

Clinical Utility

- incorporated to guide treatment decisions and design
- Assess recurrence due alterations physical exam due to radiation changes

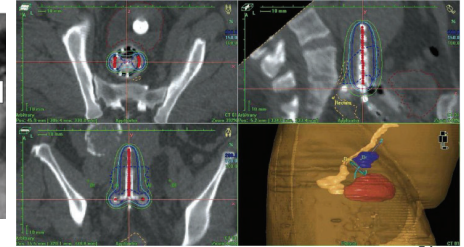
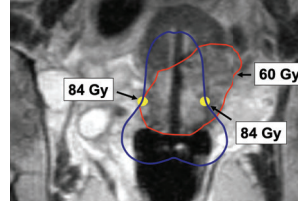


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¹ Kim et al. Uterine cervical carcinoma: comparison of CT and MR findings. Radiology. 1990 Apr;175(1):45-51

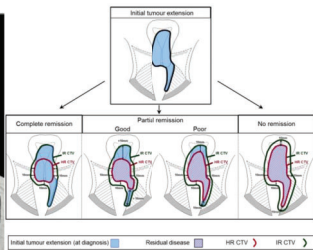
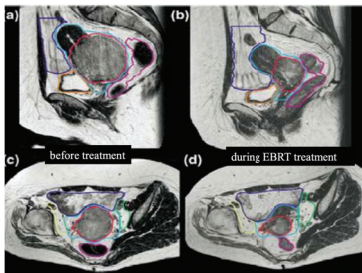
² Mitchell et al. Early invasive cervical cancer: tumor delineation by magnetic resonance imaging, computed tomography, and clinical examination, verified by pathologic results. In the ACORN 6011/GOG 183 Intergroup Study. JCO 2008 Dec 30;24(52):5207-14

3D to MRI planning



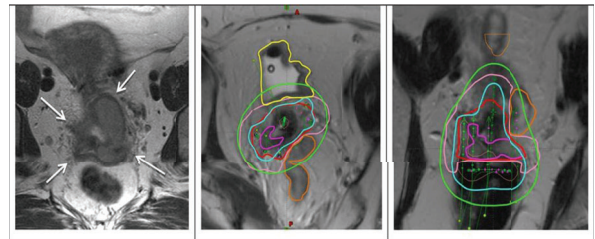
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Volumetric Planning



IGRU Report No 89
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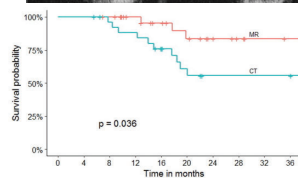
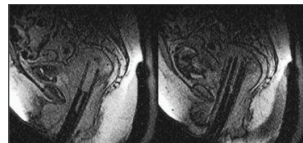
MRI Guided Brachytherapy



Tanderup et al Semin Radiat Oncol 2014
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Brachytherapy: MR guidance

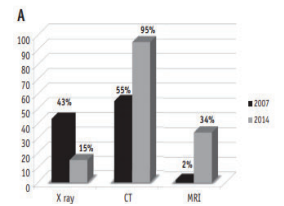
- Prospective trial of 56 patients with Stage I-IVA cervical cancer
 - 27 patients CT guided and 29 patients MR guided
 - 2 year LC: 87% vs 96%
 - 2 year OS: 56% vs 84%
 - No difference in toxicity



Viswanathan A et al. A prospective trial of real-time magnetic resonance-guided catheter placement in interstitial gynecologic brachytherapy. Brachytherapy. 2013-05-01

MRI Based Brachytherapy

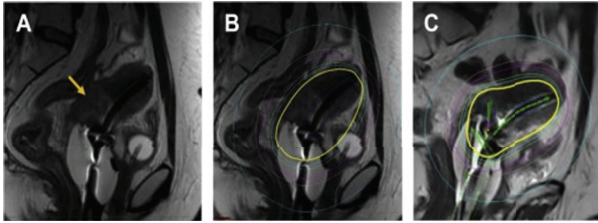
- 370 practitioners surveyed
- 95% always use CT
- 34% always use MRI



Grover et al 2016 Red Journal

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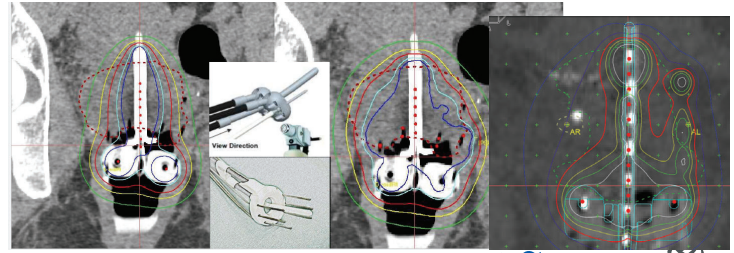
Brachytherapy with and without Interstitial Needles



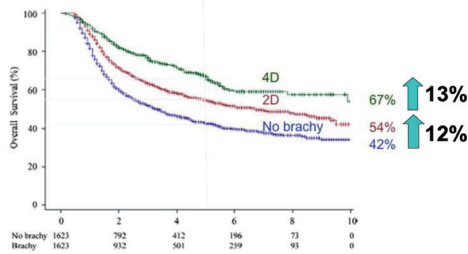
Suneja and Viswanathan 2019 Gynecologic Malignancies



Interstitial Needles improves Tumor Coverage



Survival is impacted by Advances in Brachytherapy

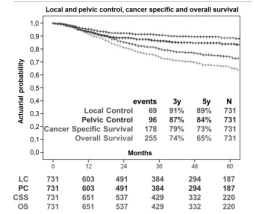


Sturdza Radiother Oncol 2016



Image Guided Brachytherapy

- Improves pelvic control and survival
- Local Control: 91%
- Pelvic Control: 87%
- Overall Survival: 74%



Sturdza Radiother Oncol 2016

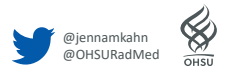
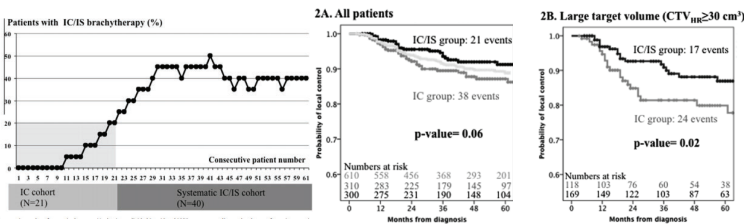
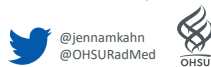


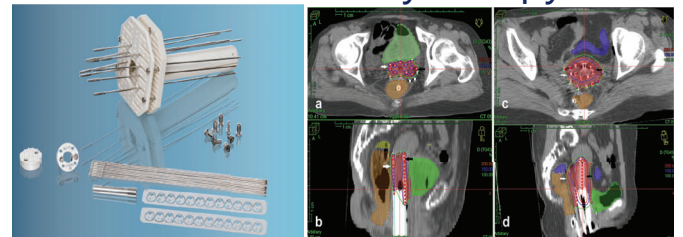
Image Guidance= More Interstitial



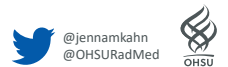
Fokdal et al 2016 Radio Oncol



Interstitial Brachytherapy

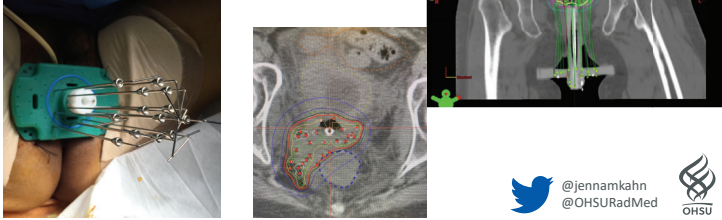


Tiwari et al Brachytherapy 2020
Tanderup et al Semin Radiat Oncol 2014



Interstitial Template

- Needles inserted under laparoscopic guidance
- Will stay in place for 3 days (2 nights)
- 5 radiation treatments, at least 6 hours apart



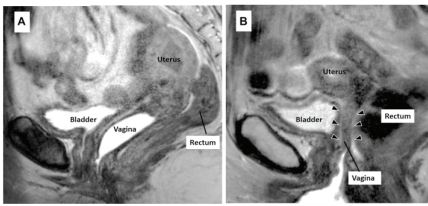
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Toxicity

- 2D planning has increased dose to vagina, sigmoid, bladder, and rectum
- This matters because increasing dose to these organs has higher rates of rectal and vaginal toxicity



Mazeron et al 2016 Radiat Oncol
Kirchheiner et al Radiat Oncol 2016

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Brachytherapy: 2D vs 3D

- Prospective clinical trial with 705 patients
 - Group 1: Brachytherapy (BT), surgery
 - Group 2: EBRT, BT, surgery
 - Group 3: EBRT, BT
- 3D less Grade 3-4 toxicity than 2D planning
 - (22.7% (2D) vs 2.6% (3D))
- Improved local relapse-free survival at 24 months compared to 2D imaging (78.5% vs. 73.9%)

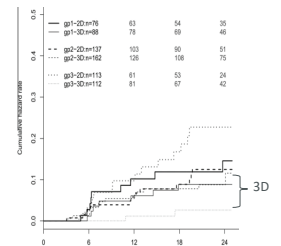


Fig 2. Cumulative toxicity hazard curves according to regimen group and RT planning method.

Charra-Brunaud et al 2012 STIC Radioth Oncol

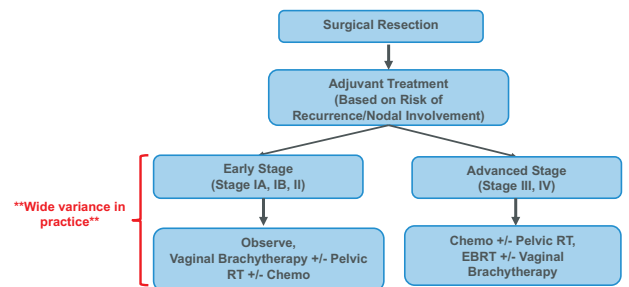
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Endometrial Cancer

- Most common gynecologic cancer in US
- 4th most common malignancy in women

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Endometrial Cancer Treatment Overview



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Whole Pelvis and Vaginal Brachy

- GOG 99 and PORTEC 1
- WPRT vs Observation
- RT in early stage intermediate risk endometrial cancer decreases the risk of recurrence in the High Intermediate Risk groups
- PORTEC 2
- WPRT vs Brachytherapy
- Brachytherapy should be the treatment of choice for patients with intermediate risk endometrial cancer

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Treatment for Grade and Invasion

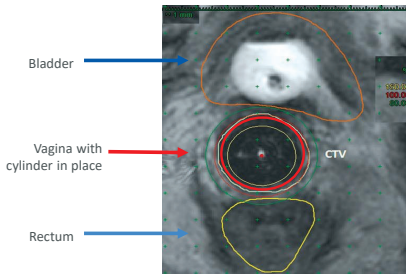
Stage	Grade 1	Grade 2	Grade 3
IA non invasive	Obs	Obs or VB*	VB
IA invasive	Obs or VB*	VB	VB
IB	VB	VB	WPRT

*VB if MMI, LVSI, or >60

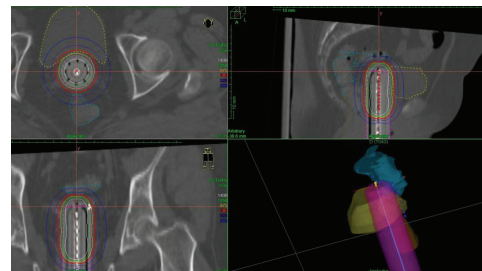


Endometrial Cancer

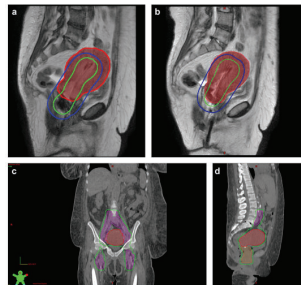
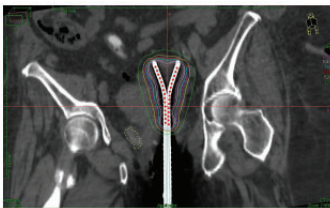
- Early Stage VBT



Vaginal Cuff Brachytherapy



Inoperable Endometrial Cancer

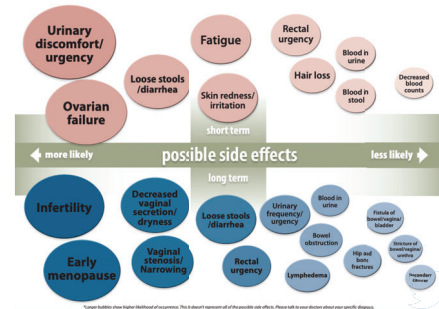


EBRT (Gy)	HDR total dose (Gy)	HDR dose fractionation	EQD ₂ (Gy)
45	19.5	6.5 Gy x 3	71.1
45	18.9	6.3 Gy x 3	69.9
45	20.8	5.2 Gy x 4	70.6
45	25	5 Gy x 5	75
45	17	8.5 Gy x 2	70.5
50.4	12	6.0 Gy x 2	65.6
50.4	22.5	3.75 Gy x 6	75.3



Schwarz 2015 Brachytherapy

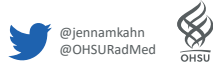
Radiation Therapy Side Effects



Prostate Cancer

Risk Groups

- Very Low Risk
 - All the following: T1c, Gleason 6, PSA < 10, < 3 positive cores, <=50% in any 1 core, PSA density<0.15 ng/ml
- Low Risk: PSA <=10 ng/ml, Gleason <=6, T1c-T2a
- Intermediate Risk: PSA 10-20 ng/ml, Gleason 7, T2b-T2c
- High Risk: T3a or Gleason score 8-10 or PSA> 20
- Very High Risk: T3b -T4, Primary Gleason pattern 5 or > 4 cores with Gleason 8-10

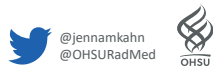


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Low Risk Prostate Cancer

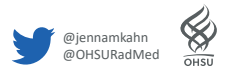
- Active Surveillance**
- Radical Prostatectomy
- External Beam Radiation Therapy
- Stereotactic Body Radiation Therapy
- Brachytherapy



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Intermediate Risk Prostate Cancer

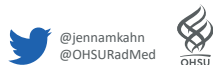
- Radical Prostatectomy
- Brachytherapy
- EBRT +/- ADT
- EBRT + Brachytherapy
- SBRT



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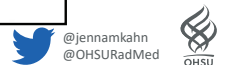
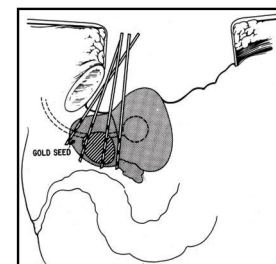
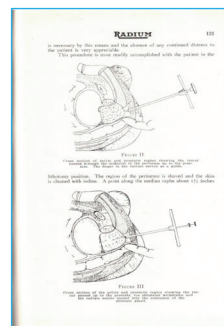
High Risk Prostate Cancer

- Radical Prostatectomy
- EBRT + ADT
- EBRT + ADT + Brachytherapy
- SBRT*

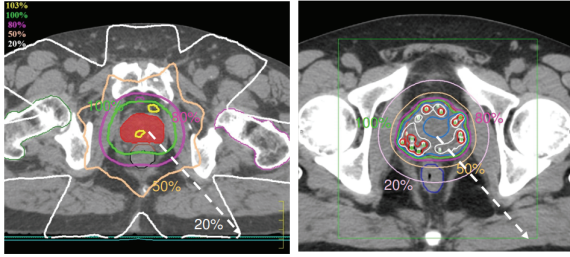


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1920s and 1930's Prostate Implants



EBRT vs Brachytherapy

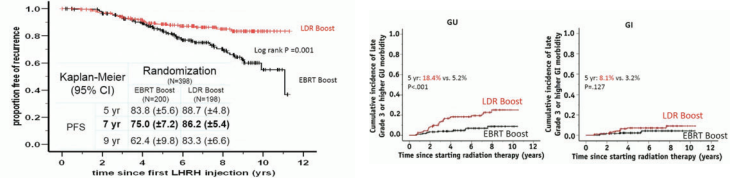


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ASCENDE-RT: EBRT + Brachy



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Great Outcomes Monotherapy

Monotherapy Brachytherapy = Surgery

- Close to 80% of men 4-5 years after LDR prostate brachytherapy will achieve a PSA of <0.2
- PSA <0.2 is associated with 97-99% freedom from prostate cancer recurrence at 10-15 years

Table 1 Summary of Results from a Series of Publications on HDR as Monotherapy with a Follow-Up >3 Years Unless the Study was Conducted as Part of a Comparative Cohort Study

Author	Year	N	med FU	Risk	HDR Dose/tx	BED (t, s)	#imp	Interval	MFFS L %	bFFS 1%	bFFS H %	late GU G3 %	late GI G3 %
Hausman ¹¹	2016	448	6.5	L + I	42-43.5/6	238-254	2	1 wk	99	95	91	4.7	0
Hoskin ¹²	2017	106	9	I + H	21/5/3	252	1				93	11	1
		138	5.25		26/2	251	1				93	2	0
		50	4.1		15/20/1	250/287	1				94	2	0
Jawad ¹³	2016	319	5.5	L + I	38/4	279	1				97	0	0
		79	3.5		24/2	216	1-2	6h-2wk			97	0	0
		98	2.9		27/2	270	1-2	6h-2wk			90	0	0
Kabalin ¹⁴	2015	77	4.7	I	45/2	455	3	1 wk			97	1	0
Mak ¹⁵	2010	301	8	L + I + H	45/6	270	2	4 wk			88	0	0.5
Martinez ¹⁶	2010	248	4.8	L + I	43/6	238	2	1 wk			88	9	0.5
					38/4	279	1				91	9	
Morton ¹⁷	2017	87	1.7	L + I	18/1	260	1				Not reported	0.8	0
		83	1.7		26/2	251	2	1 wk			90	0	0
Prada ¹⁸	2017	190	6.2	I	43.5/6	254	2	1 wk			90	0	0
	2016	60	6	I	18/1	260	1				96	0	0
Shroff ¹⁹	2018	490	4.7	L + I + H	34.5/3	299	3	3 wk	96	96	92	1	0
Yoshida ²⁰	2016	190	7.6	I + H	45/6	240	1				93	81	1
					54/9	270	1				93	81	1
					45.5/7	242	1				95	93	0
Zamboglou ²¹	2013	492	9-7.7	L + I + H	38/4	279	1				93	93	0

Abbreviations: FU = follow-up time; L = low-risk prostate cancer; I = intermediate-risk prostate cancer; H = high-risk prostate cancer; med FU = median follow-up in years; N = number of patients; time/imp = time between implants; tx = toxicity.

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Crook et al Radiat Oncol 2020

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Prostate Brachytherapy

- Highly Effective Treatment for Prostate Cancer
 - Can be used as monotherapy for low or favorable intermediate risk prostate cancer
 - Boost for unfavorable intermediate or high risk prostate cancer
 - Salvage treatment for prior EBRT
- Concern around toxicity
 - How can we use modern imaging to reduce brachytherapy toxicity and still maintain high cure rates?

Who are Candidates for brachytherapy?

- Good KPS
- Urinary symptoms: favorable AUA
- Anatomy: Gland Size, ureteral position, bladder and rectum proximity

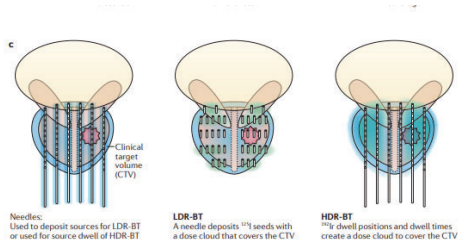
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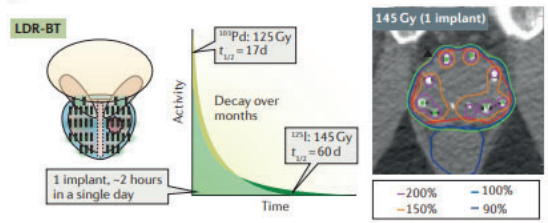
LDR vs HDR



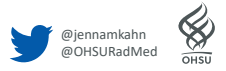
Zaorsky et al 2017 Nat Reviews Urology



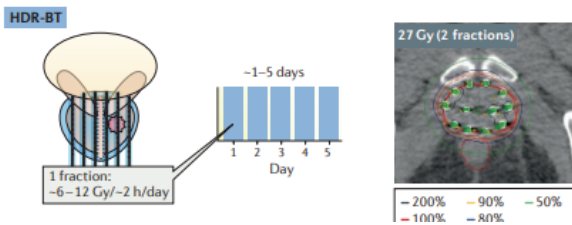
Low Dose Rate



Zaorsky et al 2017 Nat Reviews Urology



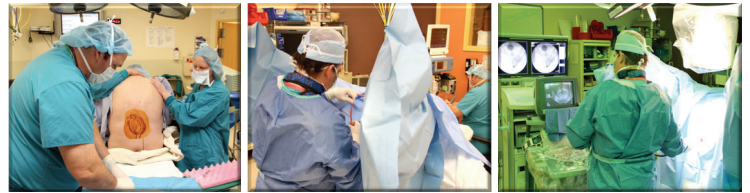
High Dose Rate



Zaorsky et al 2017 Nat Reviews Urology



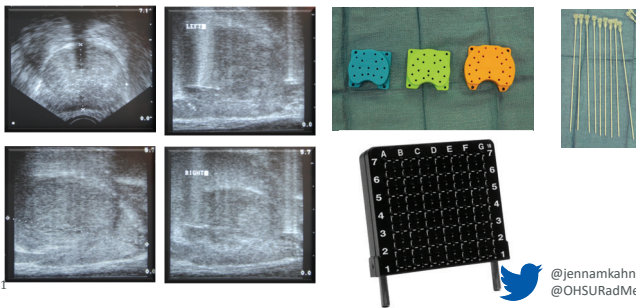
Brachytherapy Procedure



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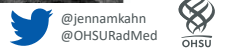
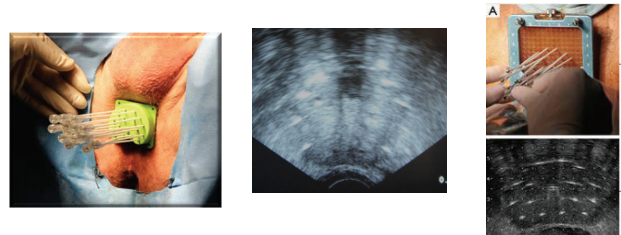


Implant



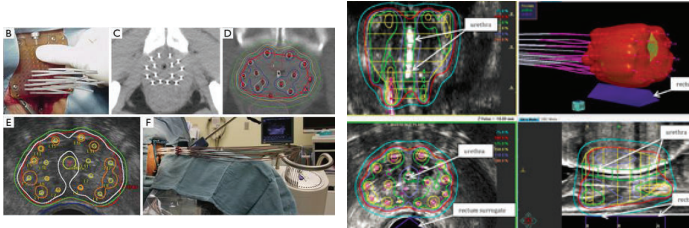
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Implant

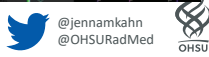


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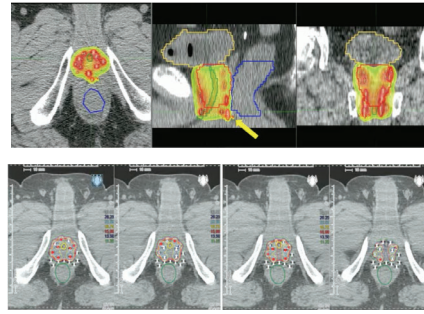
Planning



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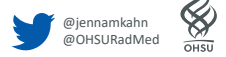


LDR vs HDR

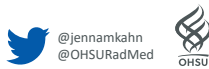
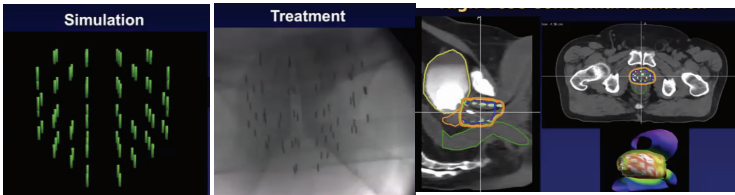


Low Dose Rate

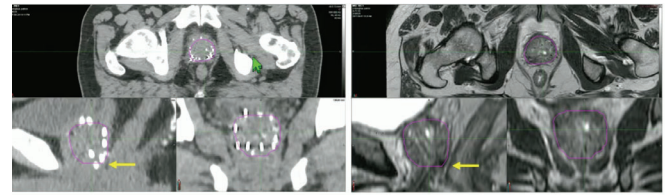
High Dose Rate



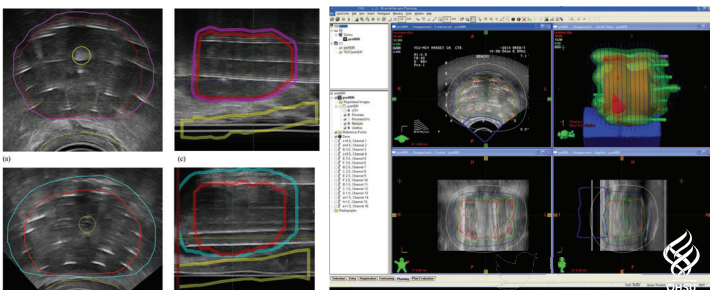
LDR brachytherapy



Imaging in Prostate Brachytherapy



Implant-Ultrasound based planning

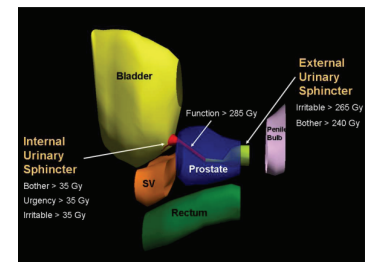


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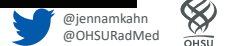


Why is improvement of imaging important?

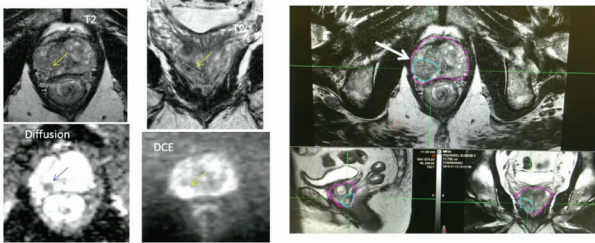
- Urinary Toxicity



Boyce-Fappiano et al 2020 Brachytherapy



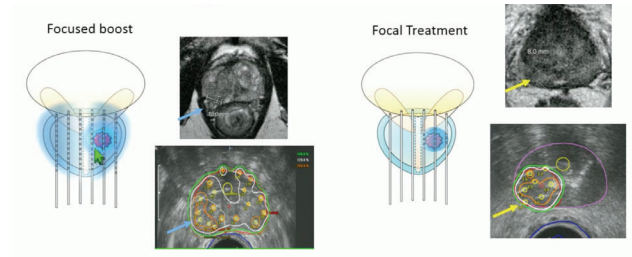
MRI in Prostate Cancer



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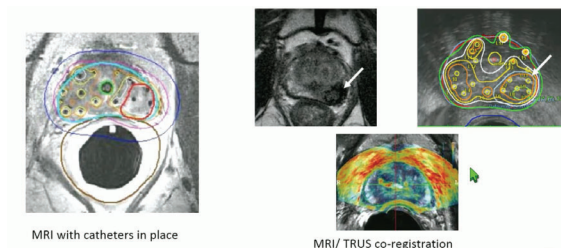
Boosting a Nodule



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MRI based planning



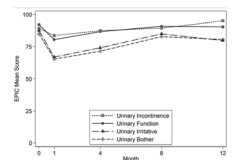
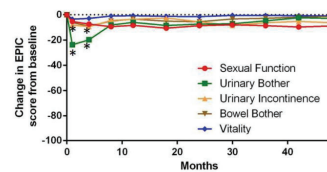
MRI with catheters in place

MRI/ TRUS co-registration

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Side Effects from Brachytherapy



Anderson Urology 2008
Thaker 2016

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Prostate Brachytherapy

- Can be utilized as monotherapy
- Can be utilized as a boost for higher risk
- Integrating more imaging modalities such as MRI helps to dose escalate

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Conclusions

- Gynecologic malignancies such as cervical cancer increase control and survival with improved imaging techniques
- Using imaging techniques helps to guide brachytherapy placement and accuracy of treatment

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OHSU Brachytherapy Program

- Started August 2020
- Hybrid and Interstitial Brachytherapy Program started Nov 2020
- Prostate HDR Brachytherapy: Starting May 2021
- Marquam Hill: Kohler Pavilion



Thank you

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Questions?

