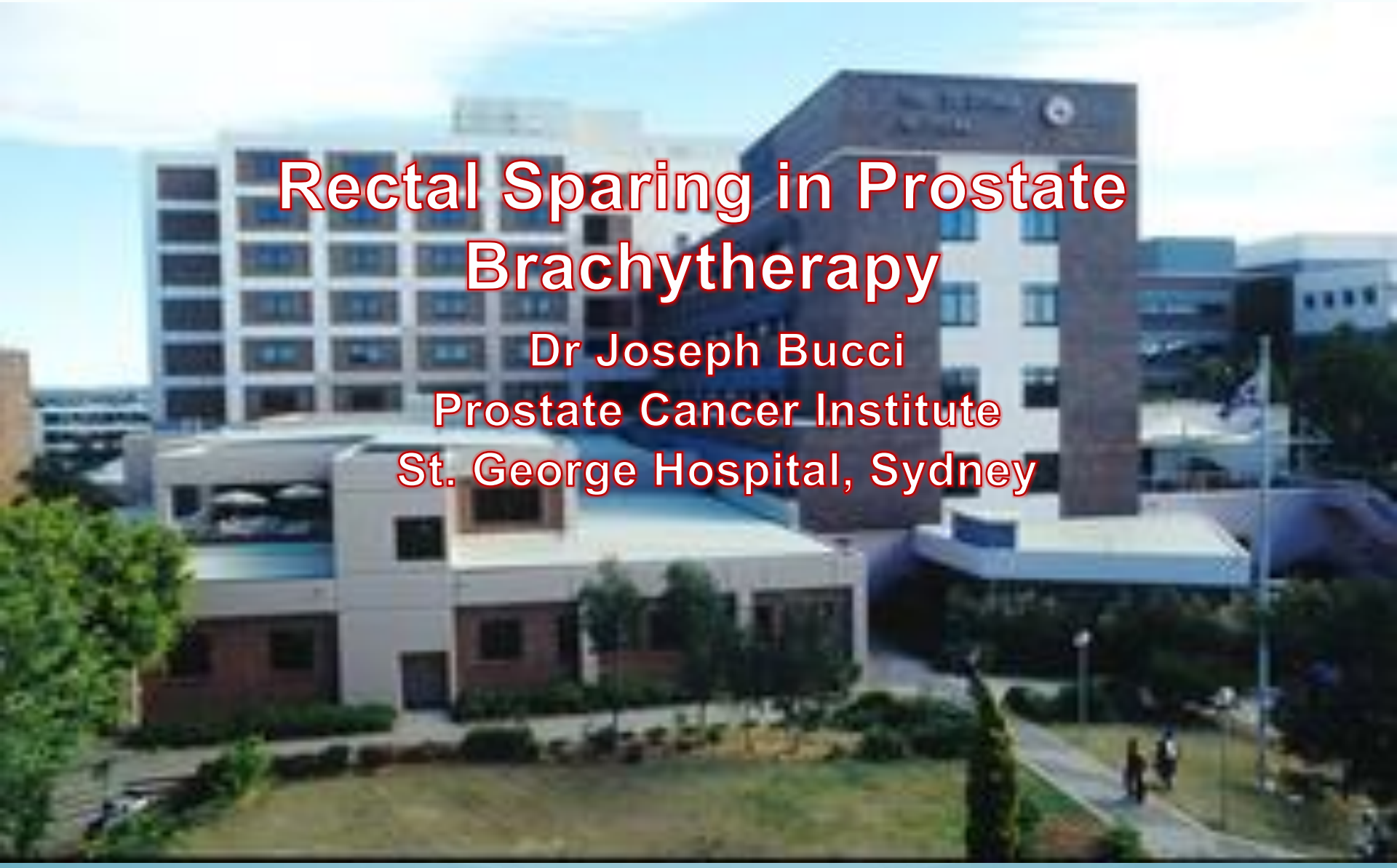

Rectal Sparing in Prostate Brachytherapy

Dr Joseph Bucci
Prostate Cancer Institute
St. George Hospital, Sydney

Rectal Sparing in Prostate Brachytherapy

- Numerous RCTs of dose escalation have shown improved tumour control outcomes
  - BUT, late toxicity increased
- Brachytherapy lowers proctitis risk,
  - BUT serious rectal complications can occur
- The acute form generally occurs within 6 weeks of implantation and occurs in approximately 30-35% of patients undergoing BT

Rectal Sparing in Prostate Brachytherapy

- Problem
- Patient selection
- Planning
- Technique
- Spacers
- Quality assurance
- New and Novel developments

Rectal Sparing in Prostate Brachytherapy

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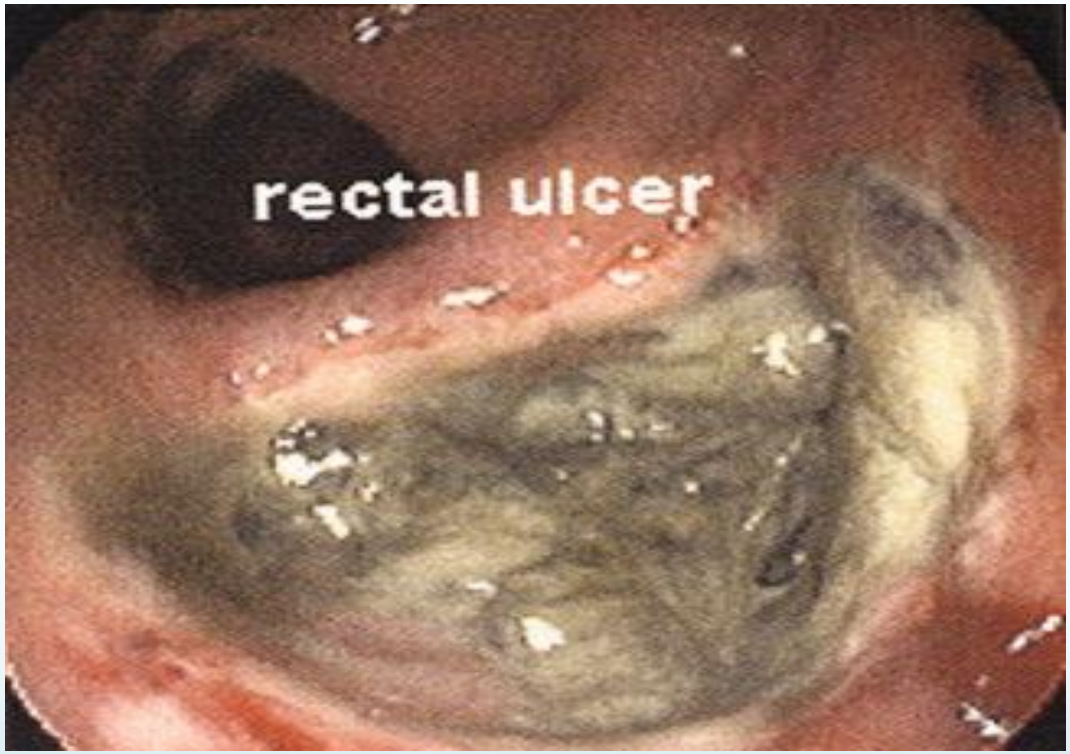
Beware Brachytherapy toxicity!!!
2. Sydney Funnel-Web

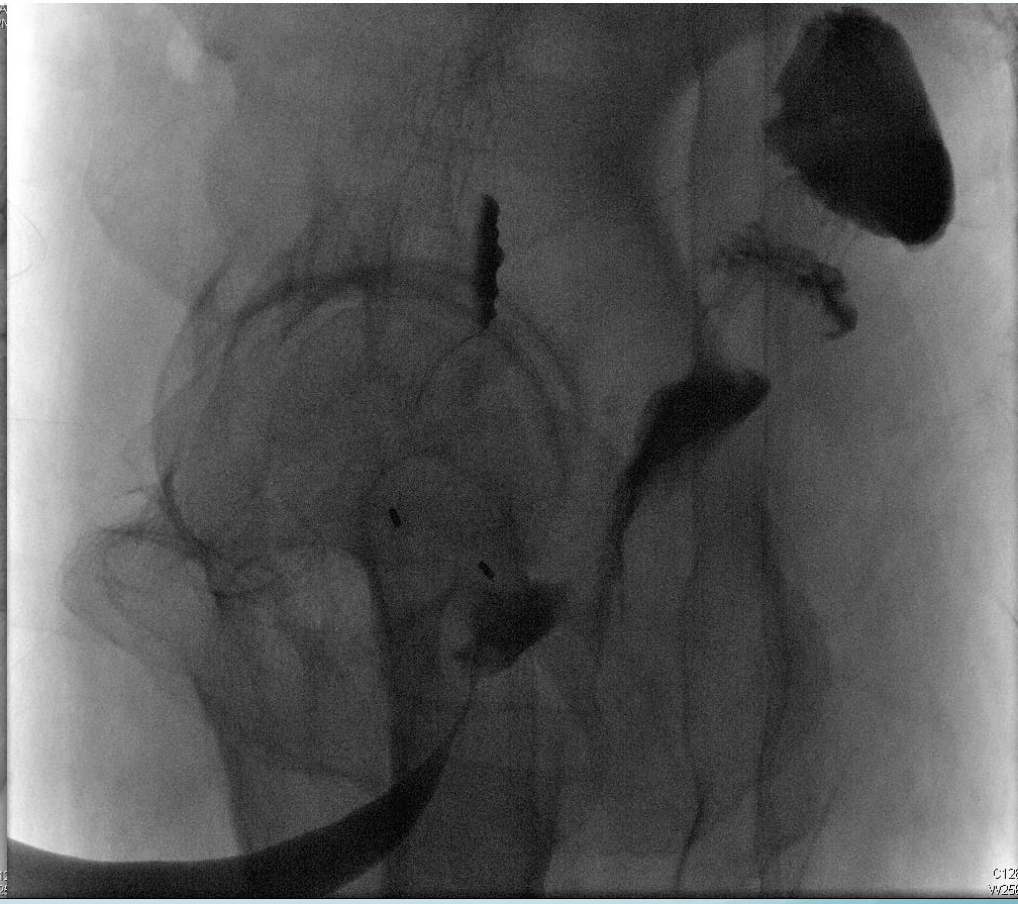
Brachytherapy Rectal Toxicity - Problem

Brachytherapy Rectal Toxicity - Problem



Cancer
Volume 115, Issue 9, pages 1827-1839, 26 FEB 2009 DOI: 10.1002/cncr.24223
http://onlinelibrary.wiley.com/doi/10.1002/cncr.24223/full#fig2

Brachytherapy Rectal Toxicity - Problem



Brachytherapy Rectal Toxicity - Problem

- Rare but major late rectal complication is the development of **rectal fistula**
  - Early series varied from <1%- 7%. Recent series, rates are 0%-1%
- Rectal bleeding prompts a colonoscopy and a reflex biopsy of the radiation-scarred anterior rectal wall
- Elliott et al. Medical malpractice of prostate brachytherapy. Brachytherapy 2004
  - 13 Brachytherapy-related medical malpractice cases, 11 because of a prostatic-rectal fistula - beware
- **Recommend avoidance of anterior rectal wall biopsy for the investigation of rectal bleeding after prostate brachytherapy**

Rectal Sparing in Prostate Brachytherapy

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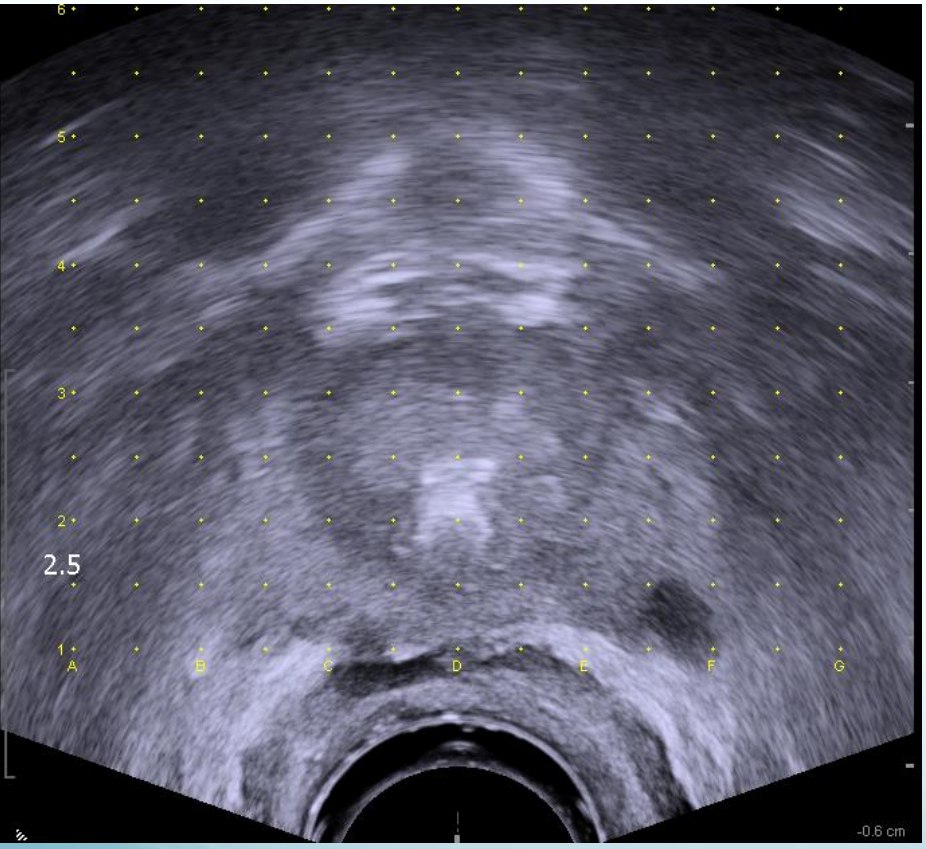
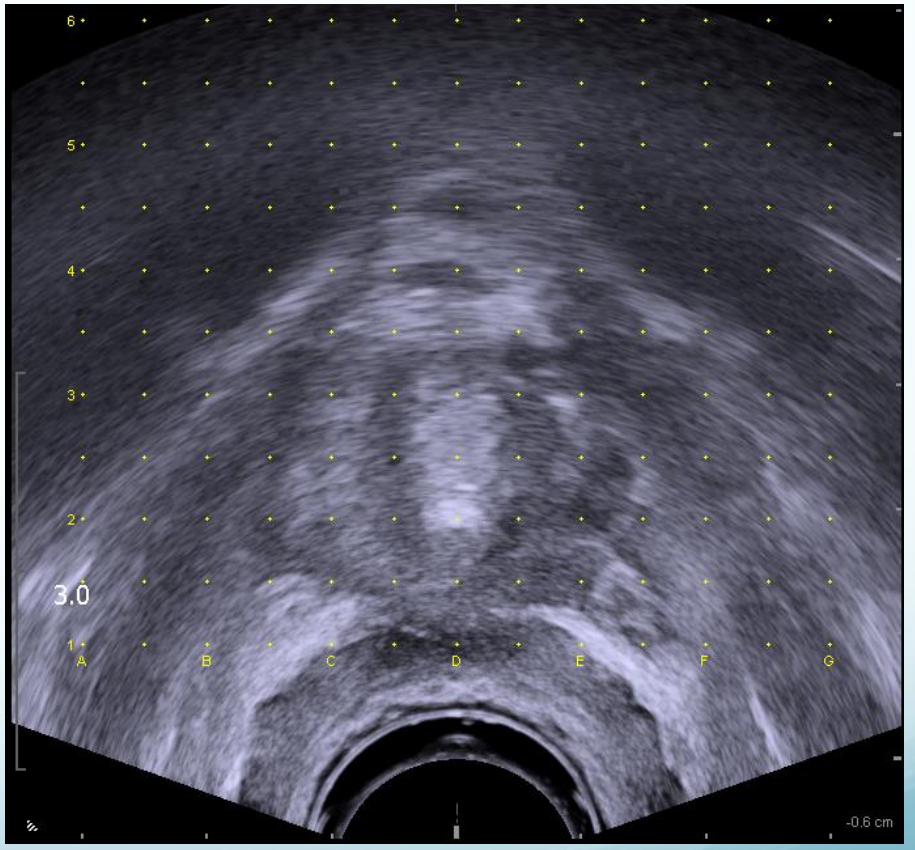
Rectal Toxicity - Patient selection

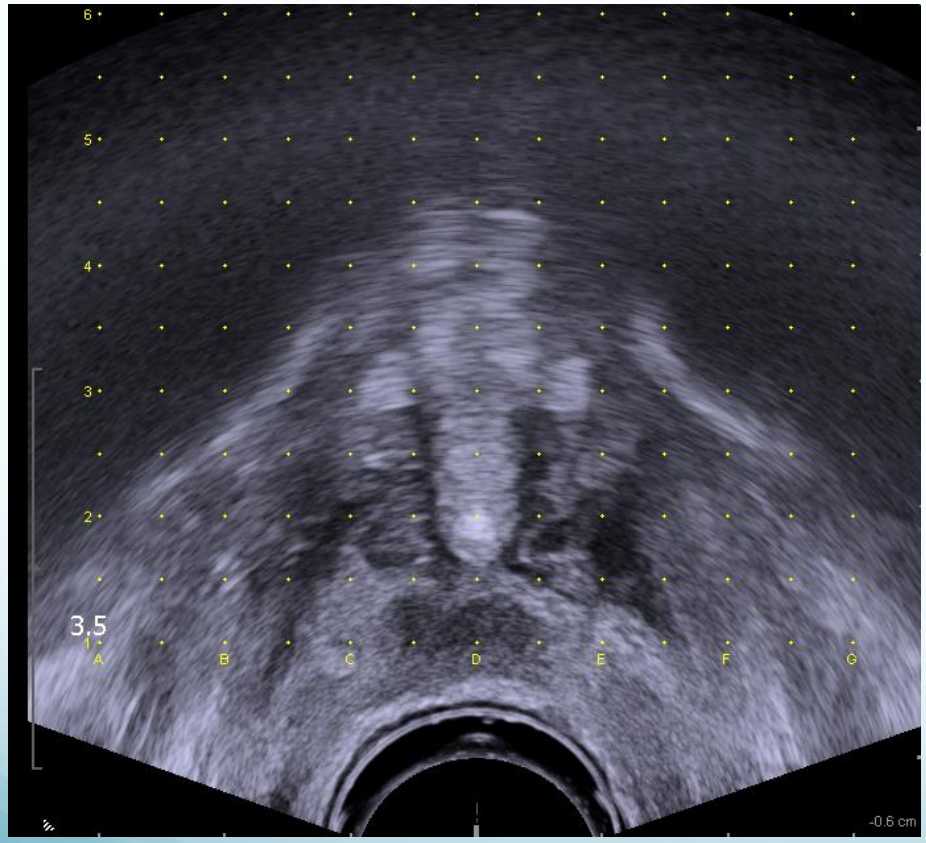
- Usual contraindications for radiotherapy
- Inflammatory bowel disease - but often referred, avoid active disease
- Short Urethro-rectal distance --- ??? distance
- Previous ano-rectal surgery

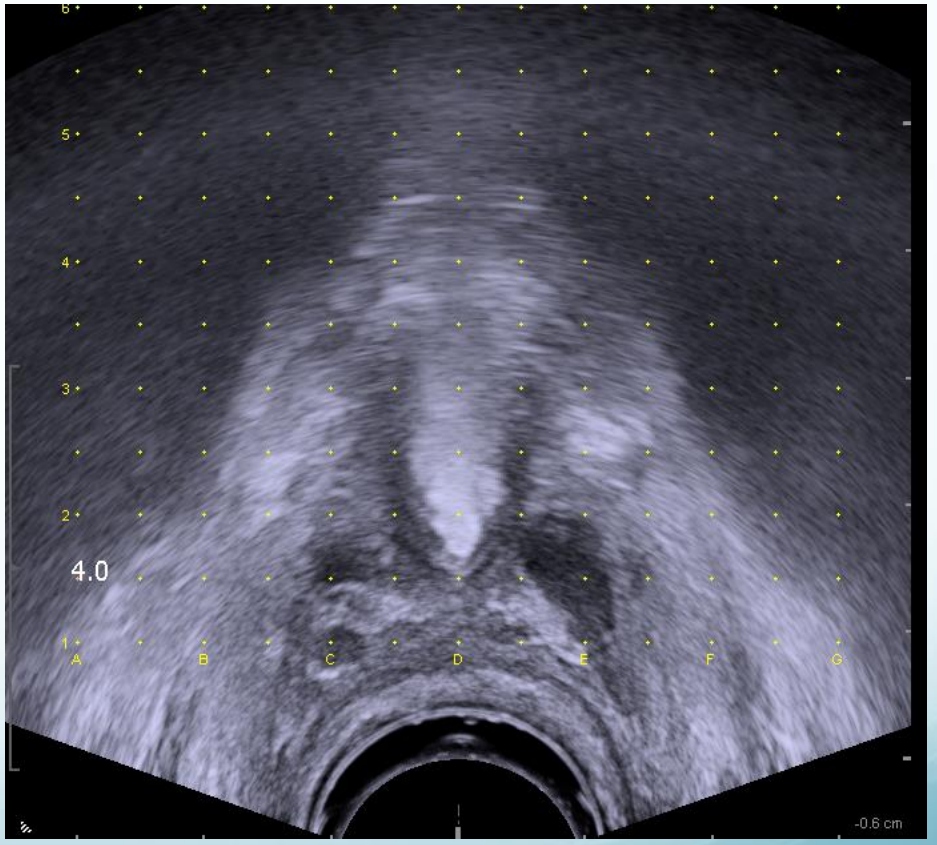
Rectal Toxicity - Patient selection



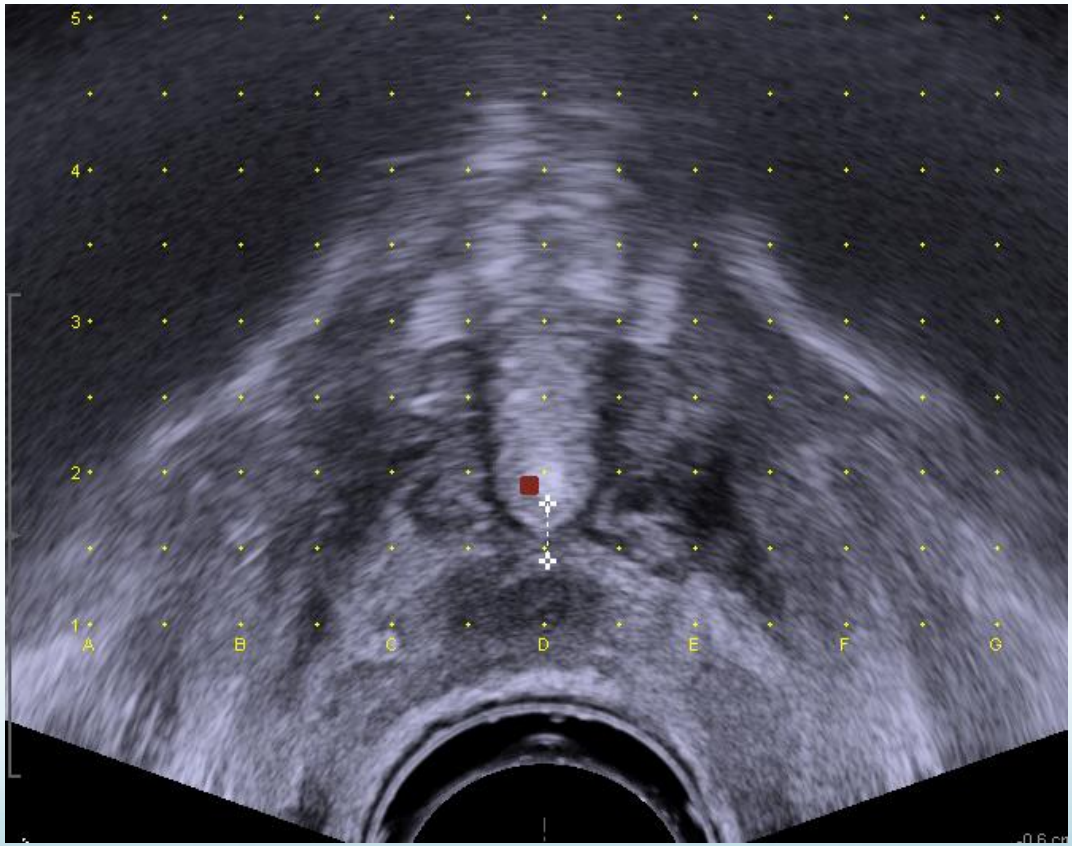


Rectal Toxicity - Patient selection

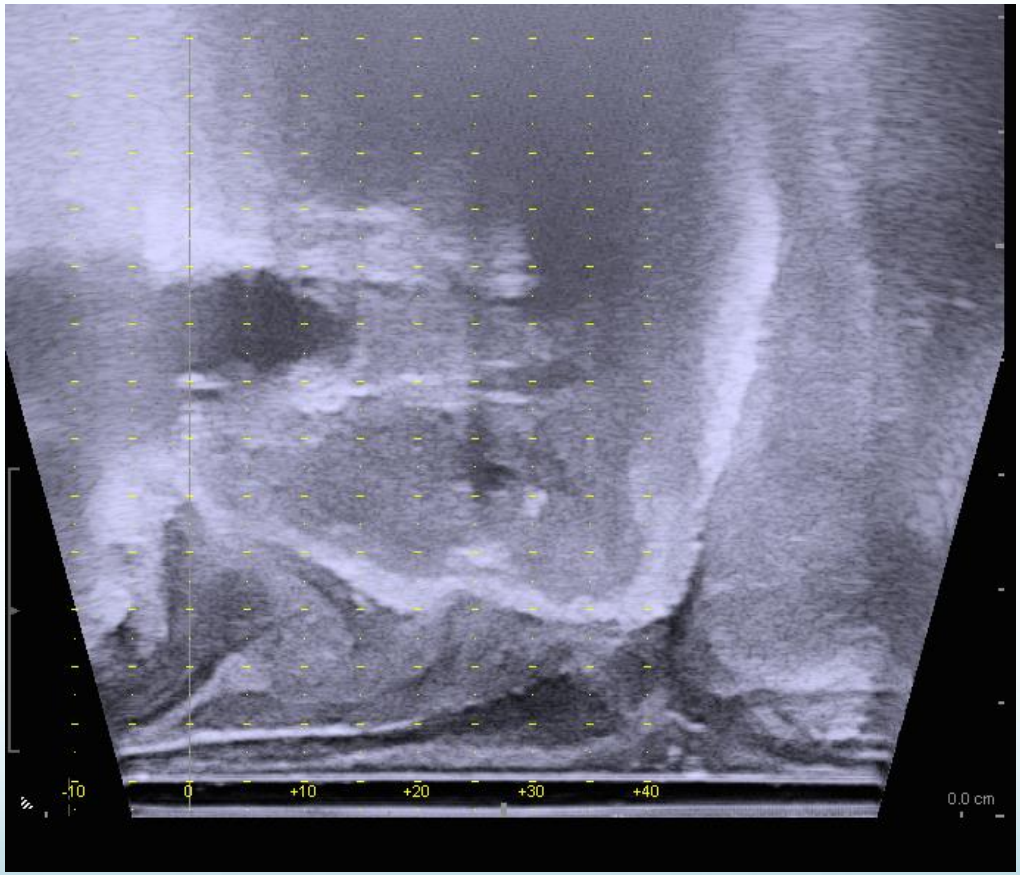




Rectal Toxicity - Patient selection



Rectal Toxicity - Patient selection



Rectal Sparing in Prostate Brachytherapy

- Problem
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- Treatment
- New and Novel developments

Prostate Brachytherapy -Planning

- Snyder et al Proctitis Grade >2 at 5ys
  - V100 ≤1.3 cc 5%
  - V100 >1.3 cc 18%

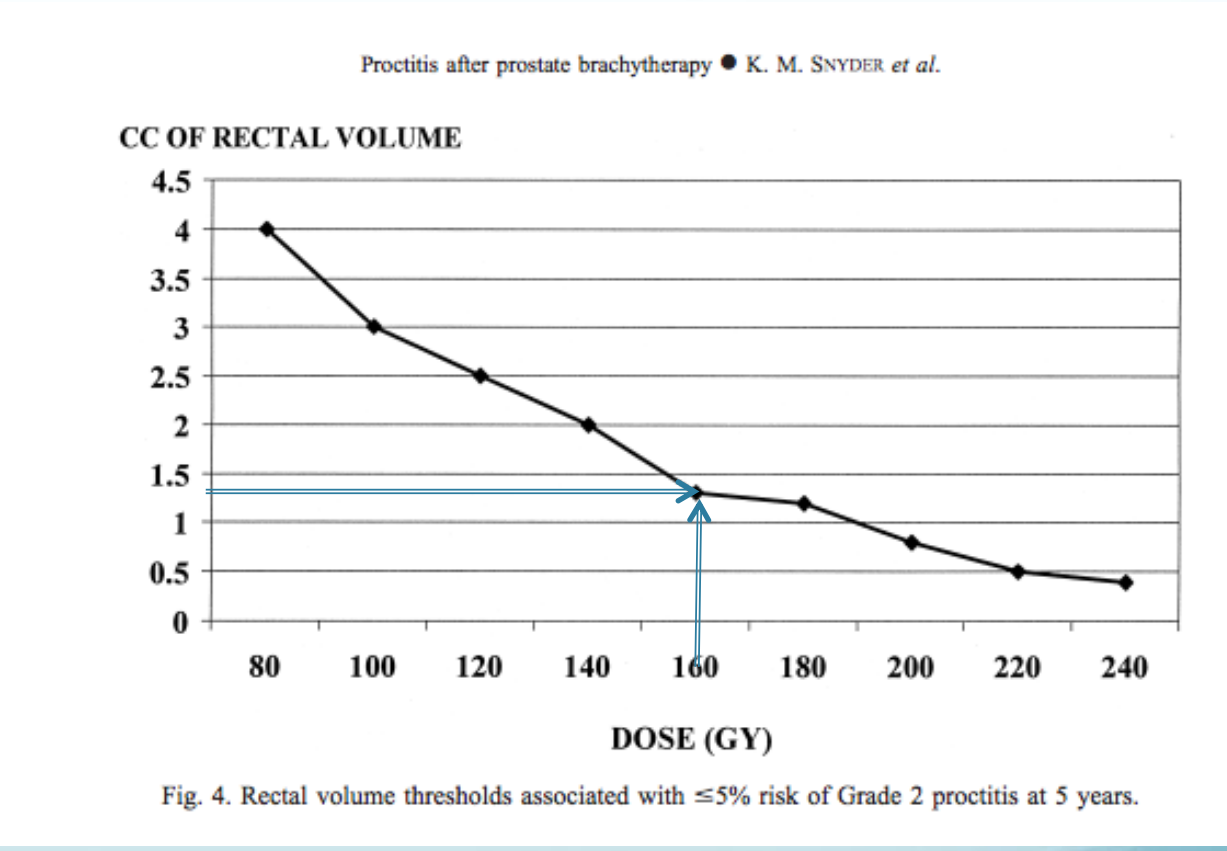

Fig. 4. Rectal volume thresholds associated with ≤5% risk of Grade 2 proctitis at 5 years.

Rectal Sparing in Prostate Brachytherapy

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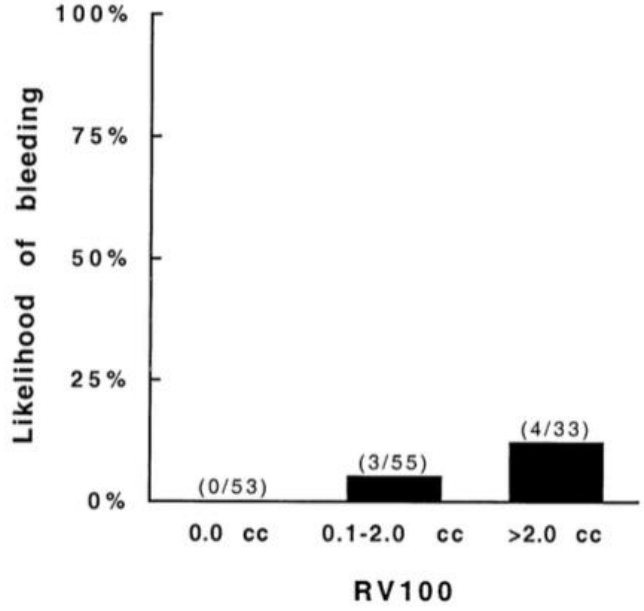
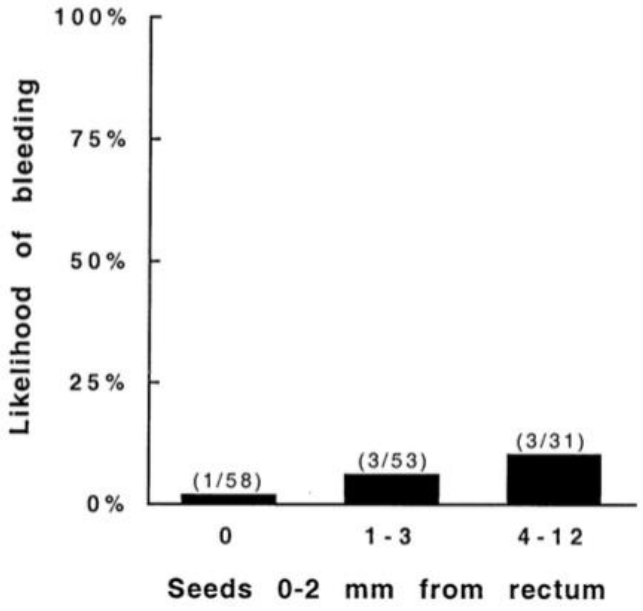
Brachytherapy Rectal Toxicity - Technique

CLINICAL INVESTIGATION **Prostate**

PERIRECTAL SEEDS AS A RISK FACTOR FOR PROSTATE BRACHYTHERAPY-RELATED RECTAL BLEEDING

AMY MUELLER, M.D.,* KENT WALLNER, M.D.,*†‡ GREGORY MERRICK, M.D.,§ ERIC FORD, PH.D.,*† STEVEN SUTLIEF, PH.D.,*† WILLIAM CAVANAGH, M.S.,* AND WAYNE BUTLER, PH.D.§





Brachytherapy Rectal Toxicity - Technique

- Use Sagittal imaging particularly on the 1 and 1.5 rows
- Allow 3-5 mm from seed to rectal wall
- Ensure distal seed train not implanted into rectum
- Posterior row - Implant 5mm anteriorly - steer needle posteriorly if necessary
- Deflate rectal balloon

Brachytherapy Rectal Toxicity - Technique

Brachytherapy Rectal Toxicity - Technique

Rectal toxicity and rectal dosimetry in low-dose-rate ^{125}I permanent prostate implants: A long-term study in 1006 patients

Mira Keyes[1,*], Ingrid Spadinger[1], Mitchell Liu[1], Tom Pickles[1], Howard Pai[2], Amy Hayden[1], Veronika Moravan[1], Ross Halperin[3], Michael McKenzie[1], Winkle Kwan[4], Alexander Agranovic[4], Vince Lapointe[1], W. James Morris[1]

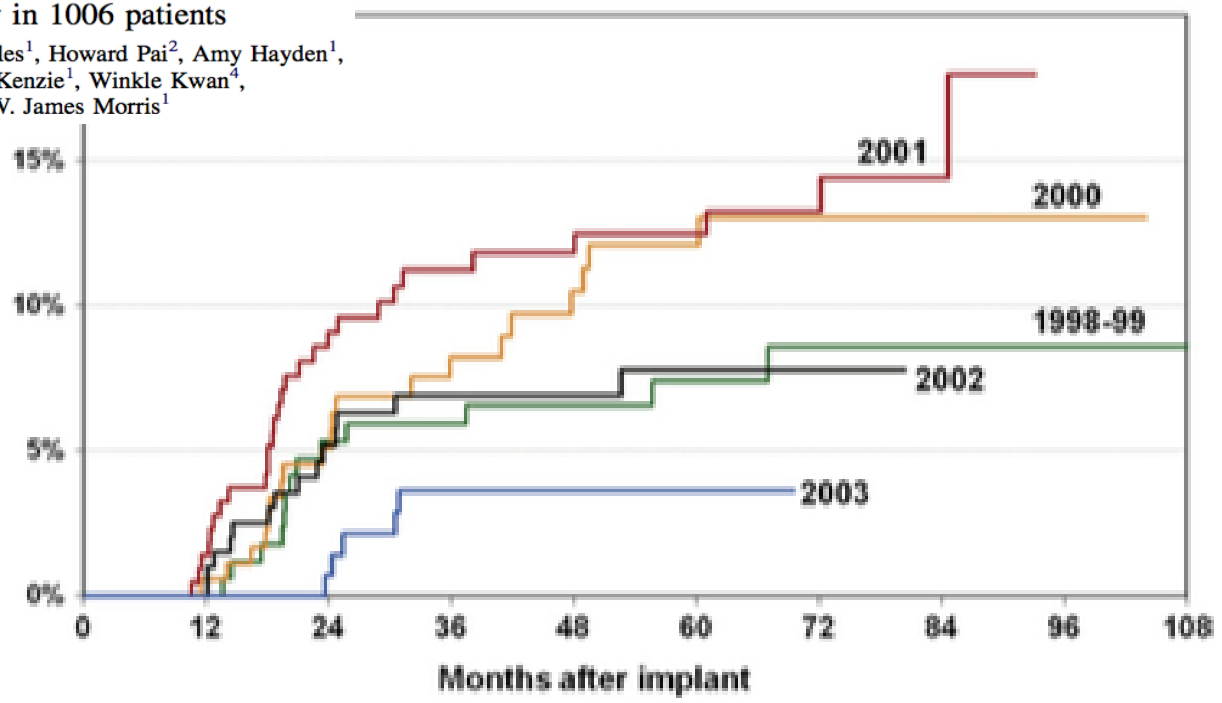


Fig. 2. Kaplan–Meier curves for late rectal Radiation Therapy Oncology Group ≥2, illustrating the institutional learning curve.

Brachytherapy Rectal Toxicity - Technique

Late rectal toxicity	*p*-Values	HR
RTOG late ≥1		
Baseline IPSS	0.0379	1.02 (1.001–1.04)
Acute RTOG ≥1	0.0001	1.793 (1.386–2.319)
VR_{100}	0.0001	1.263 (1.146–1.391)
RTOG late ≥ 2		
Implant order (learning curve)	0.0273	0.999 (0.998–1.0)
Acute RTOG ≥1	0.0074	2.181 (1.217–3.562)
Acute RTOG ≥2	0.0288	2.181 (1.084–4.387)
VR_{100}	0.0304	1.223 (1.019–1.467)

RTOG = Radiation Therapy Oncology Group; VR = rectal volume in cc; IPSS = International Prostate Symptom Score; OR = odds ratio; HR = hazard ratio.

Rectal Sparing in Prostate Brachytherapy

- Problem
- Patient selection
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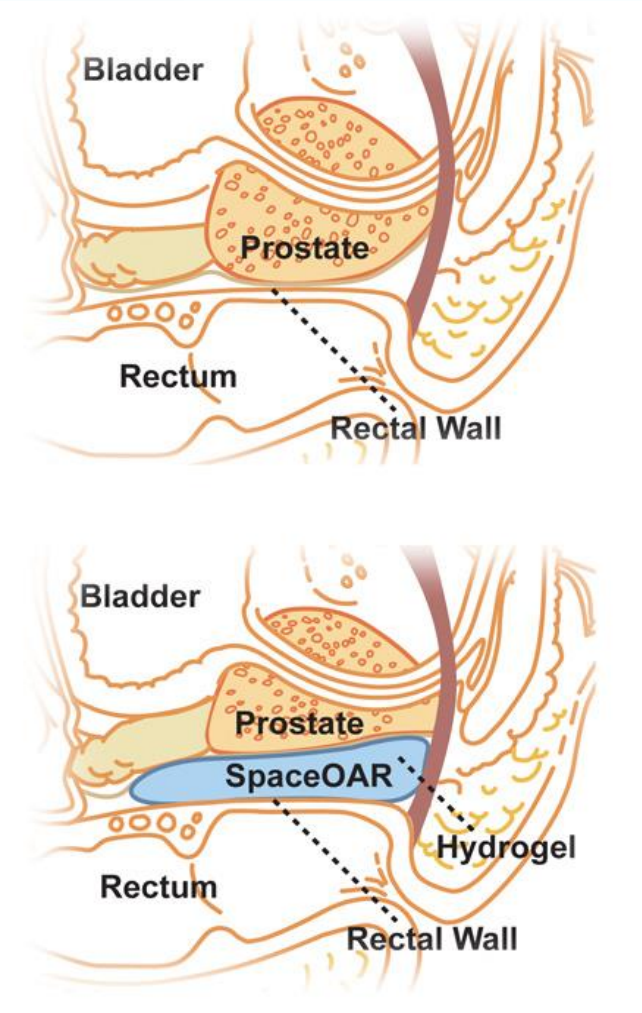
- New and Novel developments



Spacer Substances

- **Hyaluronic acid**

  -Wilder 8-18mm AP in prostate IMRT patients. Rectal V70 reduced from 25% to 4%

  -Prada (n=57), *randomised,* 27 received HA injection into anterior perirectal fat. Mean separation15mm achieved, rectal Dmax reduced from 7Gy to 5Gy. Spacer still present when patients scanned 9 months later.

  -Cheaper, biocompatible, but long residence times in body

- **Collagen**

  -Noyes; difficult to procure, human collagen very expensive and difficult to obtain, immunological reactions with bovine collagen

- **Polyethylene glycol**

  -Susil 20ml PEG hydrogel in cadavers; mean separation 12.5mm, rectal V70 decreased from 20% to <5%. **10mm of separation sufficient to achieve mean rectal V70 reduction of ~80%**

  -Pinkawa (n=18); 10ml hydrogel injected prior to prostate IMRT/3DCRT; mean separation 10mm, rectal V50, V60, V70, V76 decreased by 22%, 35%, 56%, 89%

  ->90% water by weight, Biocompatible, hydrolyses after 3-4 months, TGA approved

Rectal Sparing in Prostate Brachytherapy - Spacers

ELSEVIER

Brachytherapy 12 (2013) 368–374

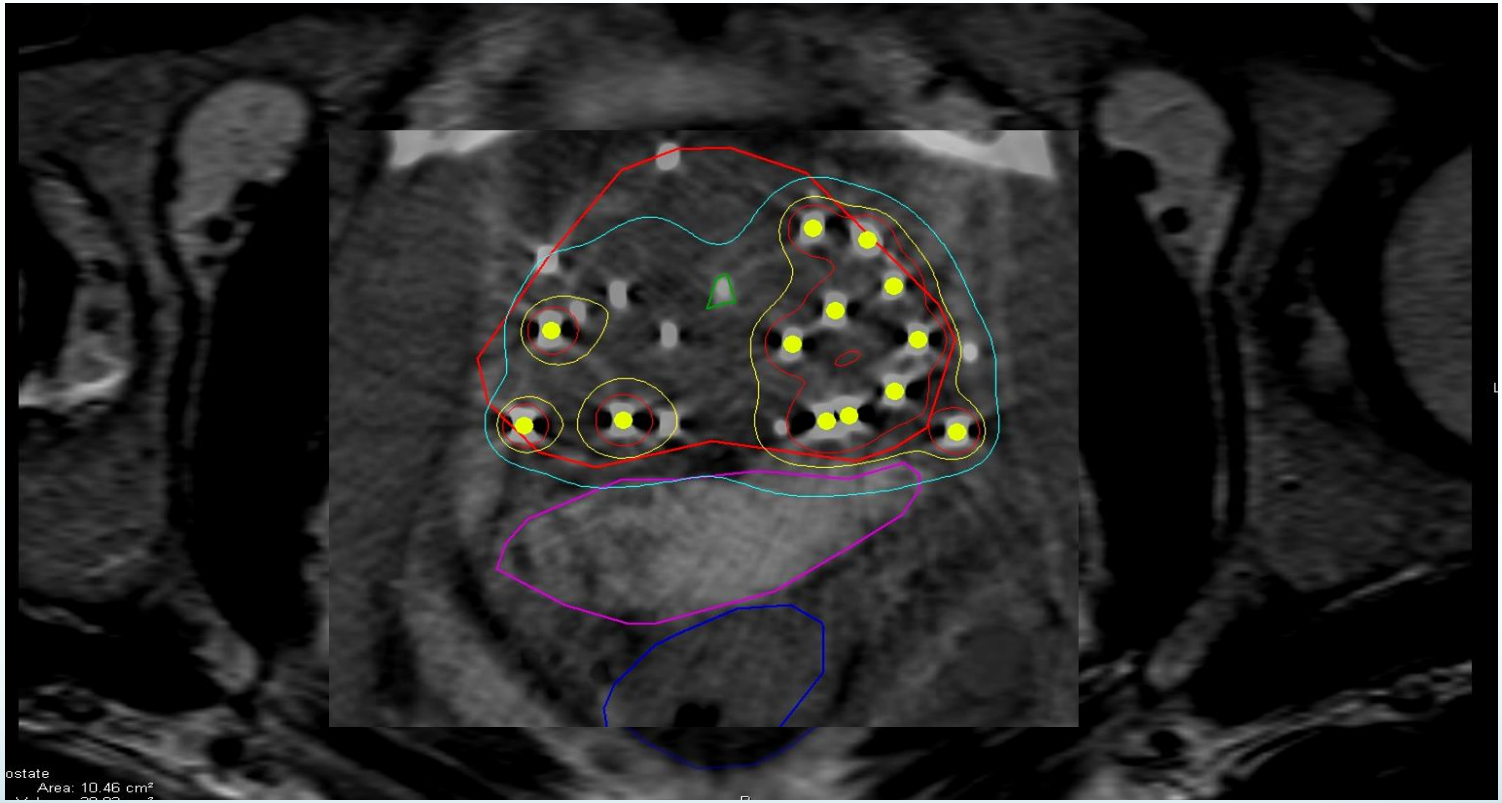
BRACHYTHERAPY

First report of transperineal polyethylene glycol hydrogel spacer use to curtail rectal radiation dose after permanent iodine-125 prostate brachytherapy

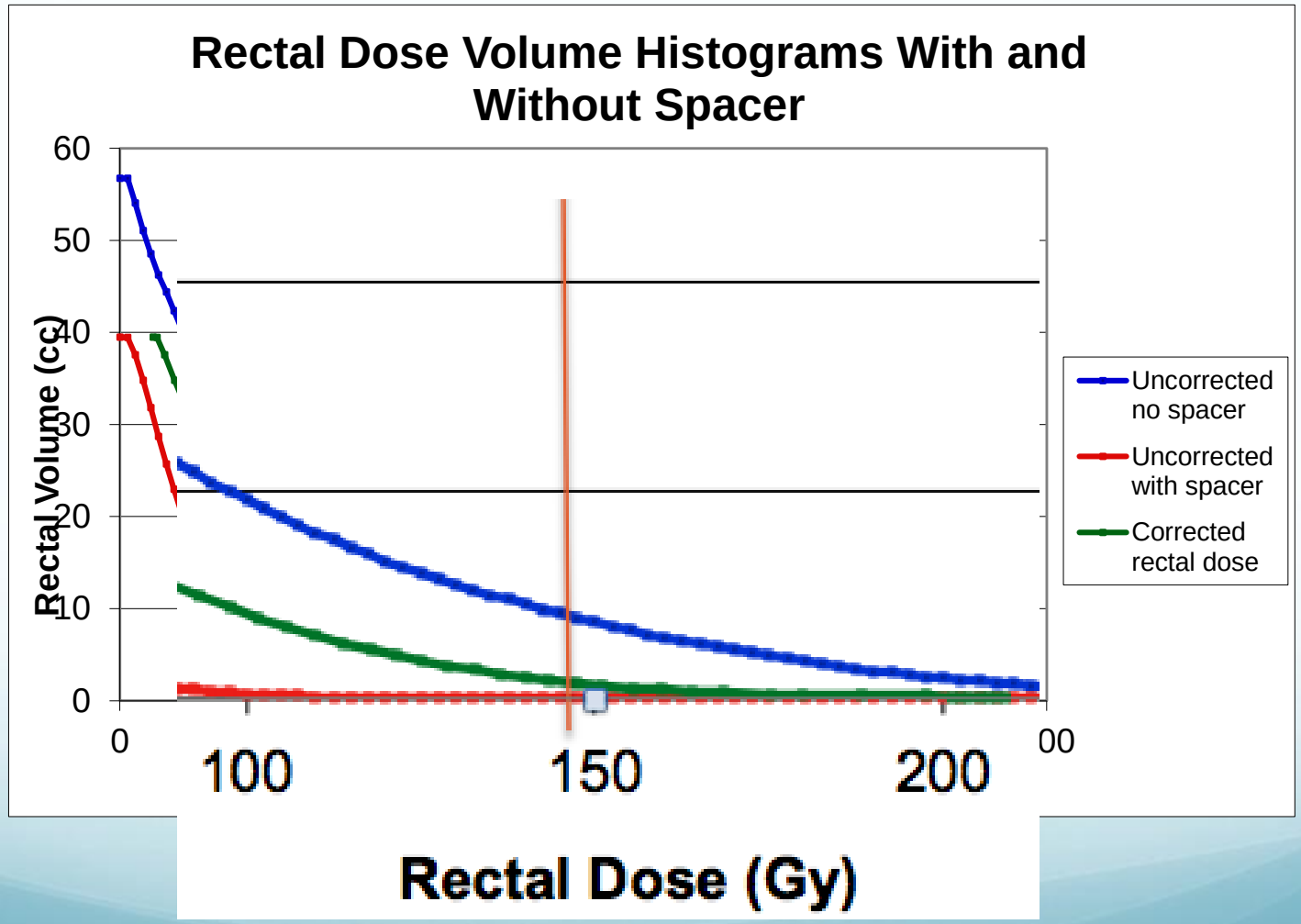
Nadine Beydoun[1,*], Joseph A. Bucci[1], Yaw S. Chin[1], David Malouf[2], Ese Enari[1], Samuel D. Painter[1]

[1]*Department of Radiation Oncology, St George Hospital, Kogarah, New South Wales, Australia*
[2]*Department of Urology, St George Hospital, Kogarah, New South Wales, Australia*

Rectal Sparing in Brachytherapy - Spacers



Rectal DVH


Rectal Dose Volume Histograms With and Without Spacer
Rectal Volume (cc)
60
50
40
30
20
10
0
0
100
150
200
00
Rectal Dose (Gy)
Uncorrected no spacer
Uncorrected with spacer
Corrected rectal dose

Rectal Sparing in Brachytherapy - Spacers

Group	Rectal Toxicity Early		Rectal Toxicity ≥ 6 months	
HDR	**G1-2**	**G≥3**	**G1-2**	**G≥3**
	0	1 rectal pain /infection	0	1 fistula 12 months post-HDR
Seed	**G1-2**	**G≥3**	**G1-2**	**G≥3**
	1 rectal pain	1 rectal ulcer	0	0
Post-seed	**G1-2**	**G≥3**	**G1-2**	**G≥3**
	1 rectal pain	0	0	0
EBRT	**G1-2**	**G≥3**	**G1-2**	**G≥3**
	2 diarrhoea, 2 rectal pain	0	0	0

Rectal Sparing in Prostate Brachytherapy

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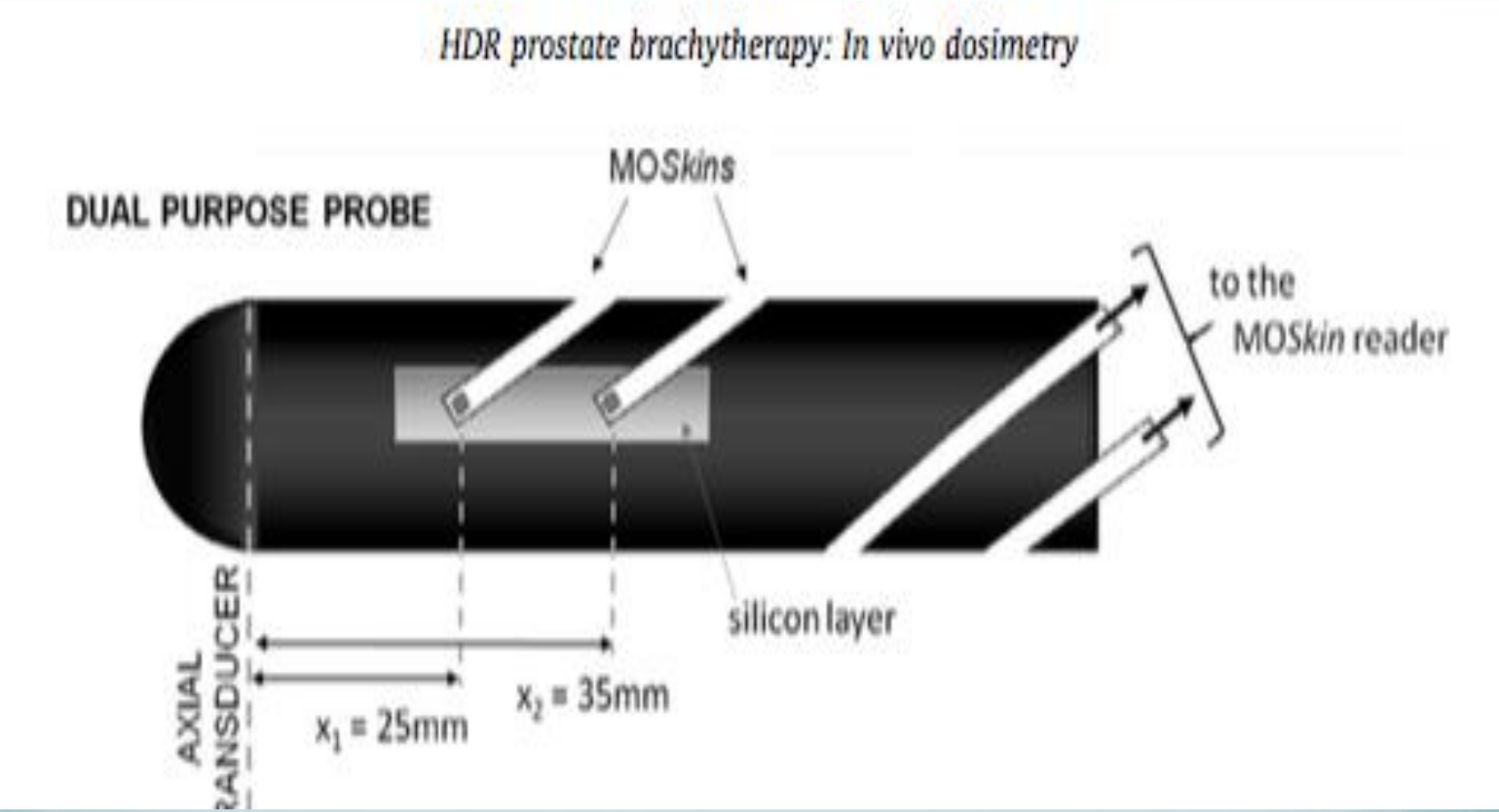
Rectal Sparing in Prostate Brachytherapy - Quality Assurance



Rectal Sparing in Prostate Brachytherapy

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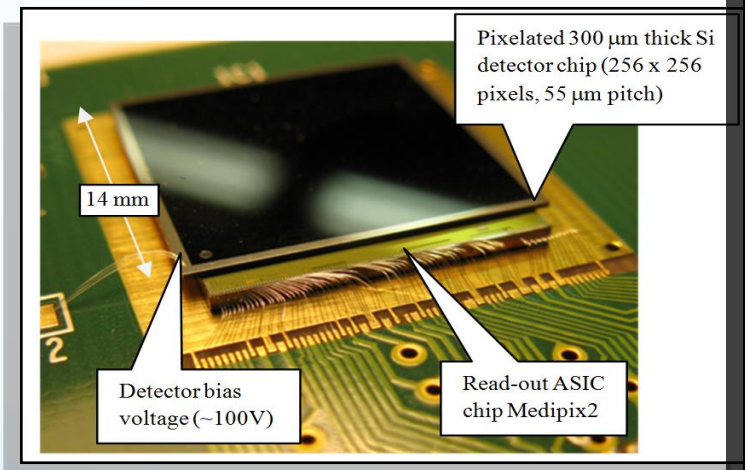
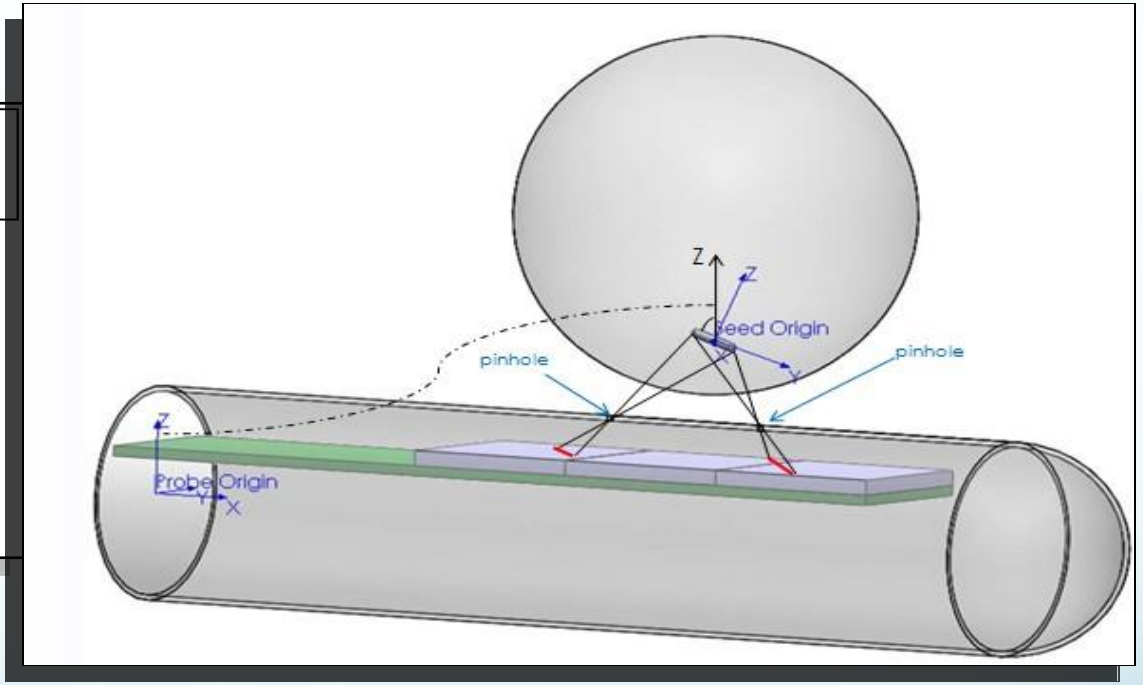
Dosimetric and Seed position Imaging

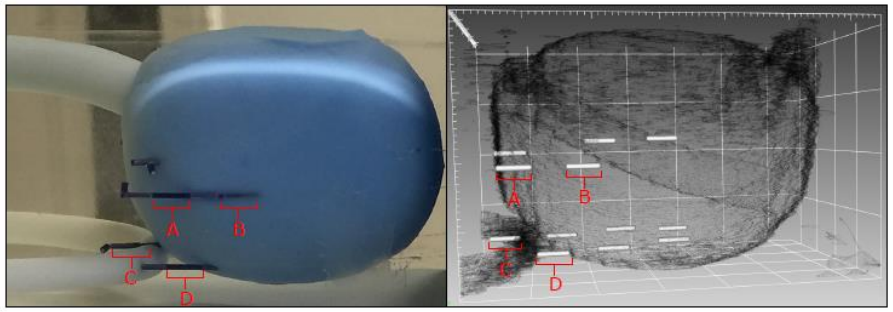
Medipix

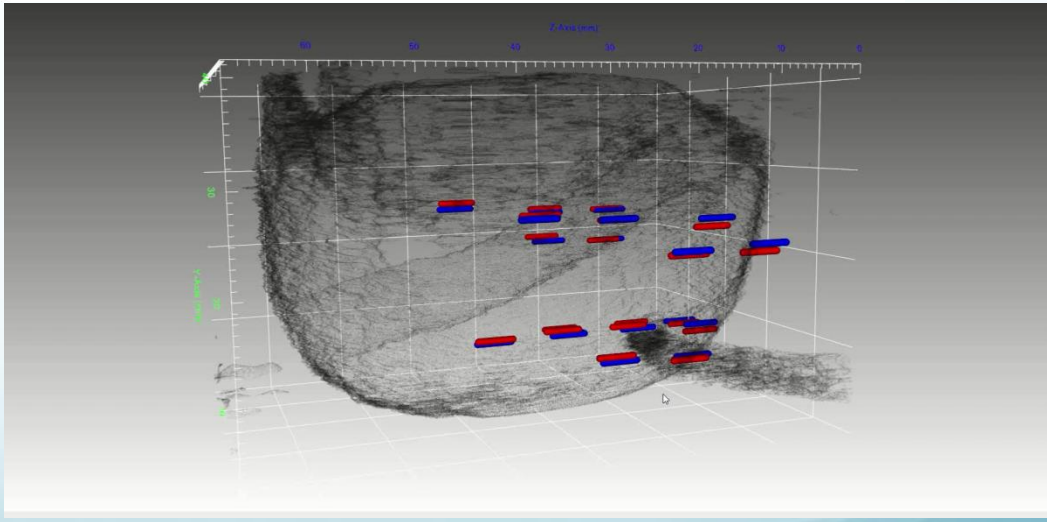




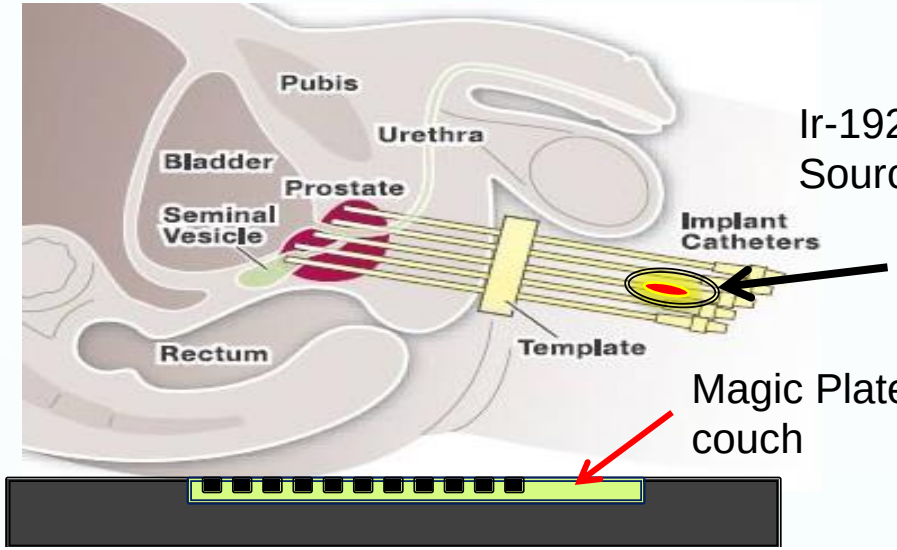
BrachyView ™

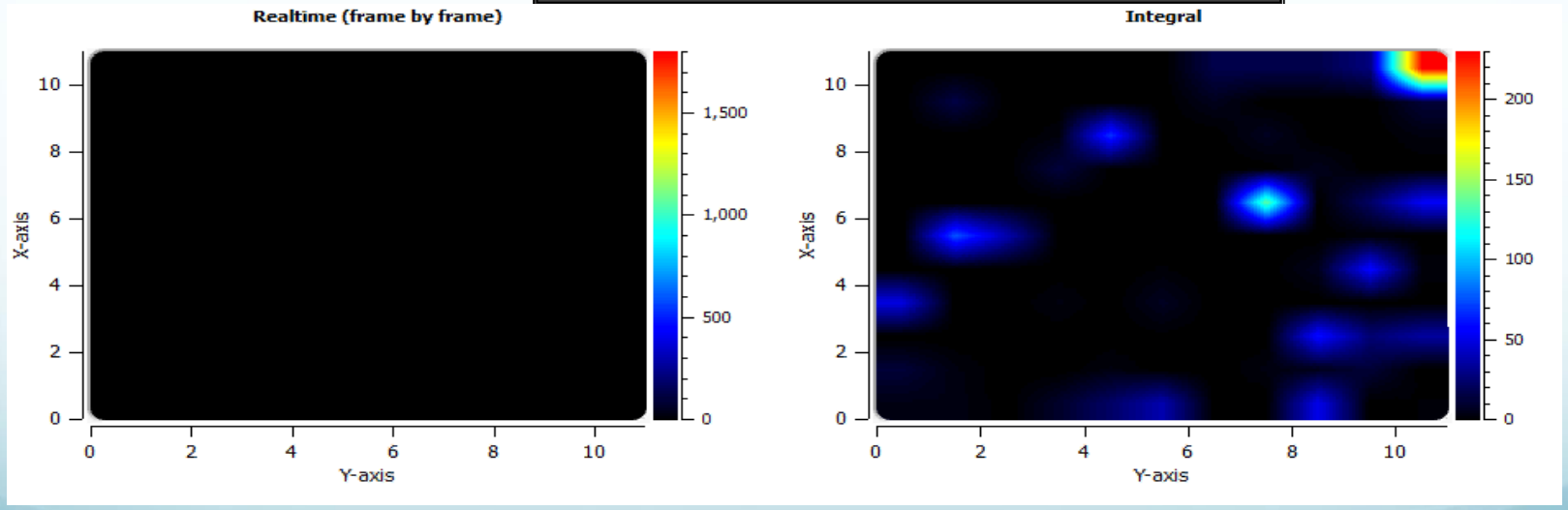
- In-phantom test of BrachyView
  - Ultrasound (anatomy)
  - CT seed locations (blue)
  - BrachyView seed locations (red)
- BrachyView - a solution for a device which meets the criteria for real-time monitoring and intervention





- Simulated operation





Rectal Sparing in Prostate Brachytherapy - New and Novel Developments

- The histone H2AX is phosphorylated to γH2AX at the sites of radiation

Osman *et al. Radiation Oncology* (2017) 12:53
DOI 10.1186/s13014-017-0792-1

Radiation Oncology

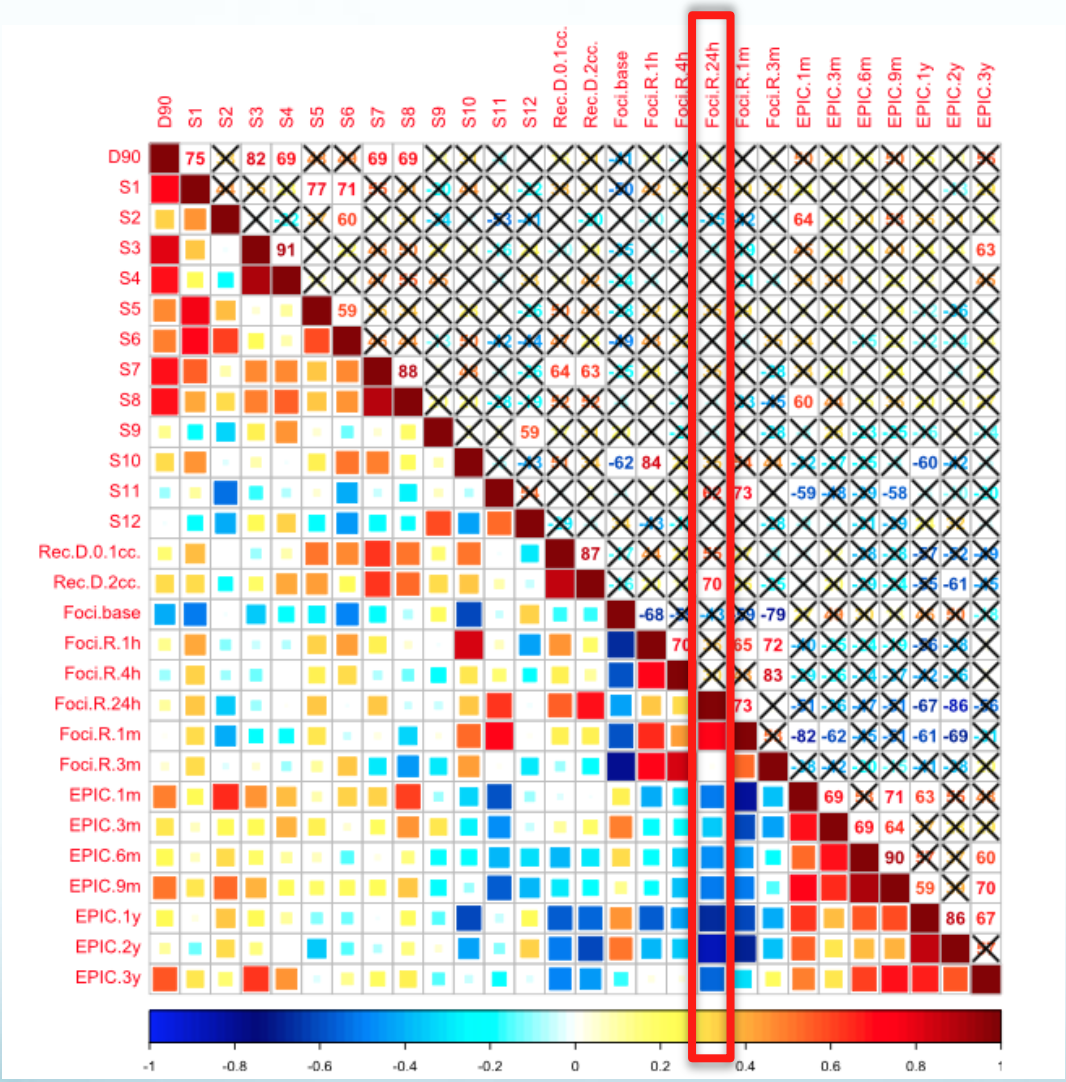
RESEARCH Open Access

Prostate cancer treated with brachytherapy; an exploratory study of dose-dependent biomarkers and quality of life

Sarah O. S. Osman[1*], Simon Horn[1], Darren Brady[1], Stephen J. McMahon[1], Ahamed B. Mohamed Yoosuf[2], Darren Mitchell[3], Karen Crowther[2], Ciara A. Lyons[1], Alan R. Hounsell[1,2], Kevin M. Prise[1], Conor K. McGarry[1,2], Suneil Jain[1,3] and Joe M. O'Sullivan[1,3]

Rectal Sparing in Prostate Brachytherapy - New and Novel Developments

- The histone H2AX is phosphorylated to γH2AX at the sites of radiation induced DNA double-strand breaks (dsb's), where it co-localises with the DNA repair protein 53BP1
- DNA dsb's were investigated by staining lymphocytes with immunofluorescence antibodies to γH2AX and 53BP1 proteins
- Assay could have clinical utility as method for intervention
  - to reduce rectal dose using perirectal hydrogel spacers for patients with high levels of circulating DSBs at early time-points after seed implant


D90
S1
S2
S3
S4
S5
S6
S7
S8
S9
S10
S11
S12
Rec.D.0.1cc.
Rec.D.2cc.
Foci.base
Foci.R.1h
Foci.R.4h
Foci.R.24h
Foci.R.1m
Foci.R.3m
EPIC.1m
EPIC.3m
EPIC.6m
EPIC.9m
EPIC.1y
EPIC.2y
EPIC.3y
-1
-0.8
-0.6
-0.4
-0.2
0
0.2
0.4
0.6
0.8
1

Rectal Sparing in Brachytherapy - Conclusions

- Devastating complication careful planning and technique essential
- PEG hydrogel effectively increases prostate rectum separation and reduces rectal radiation exposure
- Safe in EBRT and post-seed implantation
  - Use in brachytherapy patients concurrently with their implant should be avoided
- Real time quality assurance should be a goal
- Predictive tools for individualisation on the horizon














THANK YOU