Emerging Indications for a Novel Absorbable Hydrogel Spacer

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Speaker
Astellas, Augmenix, Bayer, Janssen, Pfizer

PI Clinical Trials
Allergan, Amgen, Astellas, Augmenix, Astra Zeneca, Cepheid, Dendreon, FKD Therapies, Ferring, Genome DX Biosciences, Genomic Health, Janssen, Merck, MDx Health, Myovent, Nucleix, OPKO, Pfizer, Precision Biopsy, Roche-Genetech, Spectrum, Veru
Prostate Cancer

• Incidence 164,690
• Mortality: 29,430

• Radiation is common treatment
  – 3D conformal radiation therapy (3D CRT)
  – Intensity-modulated radiation therapy (IMRT)
  – Stereotactic body radiotherapy (SBRT)
  – Brachytherapy (LDR & HDR)
  – Proton

• Complications
  – Urinary
  – GI
  – Sexual

1. American Cancer Society, Surveillance Research, 2018
• Rectum has been the dose-limiting factor
• Rectal Toxicity / Rectal complications
  – Bleeding, frequency, urgency, pain, fistulas
• Loss of QOL - Rectal injury can lead to bowel, urinary and sexual symptoms that can affect patient health and quality of life during RT and for years afterward
Radiation Exposure to Rectum is Inevitable without Prevention

- Rectal radiation is currently unavoidable
- Close proximity to prostate
- Prostate movement between treatments
- Prostate movement during treatments
GI toxicity Rates in Recent, Large, Multicenter, Hypo-fractionation Trials – 14% to 25%

Grade 2+ GI Toxicity

- **RTOG 0415 (5yr, n=1,092)**: 14.0%
  - 3D or IMRT w/IG
  - CRT = 73.8 Gy. in 41

- **CHHIP (5yr, n=3,216)**: 13.7%
  - IMRT +/- IG
  - CRT = 74.0 Gy. in 37

- **HYPRO (3yr, n=820)**: 17.7%
  - IMRT (97%) IG (95%)
  - CRT = 74.0 Gy. in 37

- **HYPRO (5yr, n=242)**: 24.9%
  - IMRT (97%) IG (95%)
  - CRT = 74.0 Gy. in 37

Perirectal spacing is being recognized as an important method to protect the rectum, as evidenced in a growing number of peer reviewed publications since 2007.
SpaceOAR Hydrogel

• Indication: SpaceOAR System is intended to temporarily position the anterior rectal wall away from the prostate during radiotherapy for prostate cancer and in creating this space it is the intent of SpaceOAR System to reduce the radiation dose delivered to the anterior rectum.

• FDA cleared April 2015

• SpaceOAR hydrogel temporarily positions the anterior rectal wall away from the prostate creating a space of ~1.3 cm

• The created space reduces radiation dose delivered to the anterior rectum, significantly reducing the risk of rectal adverse events

Prostate-rectum Spacing

Liquid Hydrogel precursors injected through 18G needle
Polymers in 10 sec

Solid Hydrogel maintains prostate – rectum separation during radiotherapy

Liquid Hydrolysis liquefies gel which is absorbed within 6 months

Transperineal Implantation

Pre implant
Axial T2 MRI images

3 month persistence

6 month absorption

Breaks down by Hydrolysis
**SpaceOAR System**

**Application**
- **Injected:** 18G, liquid hydrogel precursors
- **Solidifies:** within 10 seconds
- **Persistence:** lasts about 3 months
- **Absorbs:** in about 6 months
- **In office Procedure**
  - Local, regional or general anesthesia
  - One transperineal injection

**PEG hydrogel chemistry**
- **Gel polymerization**
  - Water based and polyethylene glycol polymer (PEG)
  - Does not heat up during polymerization
  - Breaks down via hydrolysis
  - Flows through perirectal fat, locking it in place

**Application**
- **Enables Dose Escalation & Hypofractionation**
  - ~1 cm (1/2”) space for 3 months
  - 73.5% reduction of rectal V70
  - 0% late GI toxicity greater than Grade 1
How I Do It: Hydrogel spacer placement in men scheduled to undergo prostate radiotherapy

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Hydrogel spacer placement between the prostate and rectum in men scheduled to undergo prostate radiotherapy is an emerging technique well suited for urologists. The hydrogel spacer reduces rectal injury during radiotherapy by displacing the rectum away from the high dose region. Following radiotherapy the hydrogel spacer then liquefies, is absorbed, and then clears via normal elimination in approximately 6 months. Hence we describe the appropriate patients eligible for this procedure, and the application technique we use in our clinic.

Key Words: prostate cancer, radiotherapy, hydrogel spacer, application, quality of life

Introduction
Prostate radiotherapy is an accepted modality for the treatment of prostate cancer. Despite significant advances in technology, patients continue to frequently experience long-term complications following prostate radiotherapy. For example, three recent prospective clinical trials found late Grade 2+ GI toxicity rates ranging from 14% to 25% in the 3.5 years following conventional prostate radiotherapy. Due to radiation sensitivity and proximity to the prostate, the rectum is referred to as the primary organ at risk (OAR) in prostate radiotherapy. This anatomical proximity can result in rectal toxicity and a decline in bowel-related quality of life. This proximity can also limit radiotherapy utilization in patients who experience a recurrence following prior radiotherapy, and in patients with inflammatory bowel diseases such as Crohn’s disease or ulcerative colitis.

The ability to temporarily displace the rectum out of the high-dose radiation field surrounding the prostate could improve conventional radiotherapy. It could also enable radiation dose escalation, hypofractionation and salvage radiotherapy. This may result in safer delivery of radiation for patients with bowel issues who may otherwise be precluded for therapy. Figure 1. SpaceOAR System (Aurora Inc, Bedford, MA, USA) is the only product approved as a prostate-rectum spacer in the United States, Canada, Europe, Australia and Japan. The spacer is placed via a transperineal injection of liquid hydrogel...
TUCC Procedure Preparation

• Performed in office under local anesthetic with sedation
• Patient prep
  – Fleets enema 2hrs in advance
  – Levaquin 500mg orally prior to procedure
  – Vicodin 5/325 and Valium 5mg 1 hr prior
  – Prilocaine cream applied at least 30 mins prior
• Treatment room
  – Bed with either table or floor mounted stepper
  – Lithotomy position
  – Transrectal ultrasound probe
  – Dedicated ultrasound tech is helpful
• Ioban drape useful for scrotum
Procedure Overview

• Kit preparation

• 2% lidocaine local anesthetic used subcutaneously via 22G spinal needle
System Application

Animation Application Video
Procedural Ultrasound
Patients
• T1 or T2, Gleason Score ≤ 7, PSA ≤ 20ng/mL, ≤ 50% positive cores

Design
• Prospective, randomized parallel arm, single-blind, multicenter, controlled

Size
• 222 patients, randomized 2:1 (Spacer: control)

Sites
• 20 US Sites

Procedure Design
• Anesthesia: General (37%), local (32%), MAC (25%)
• Prophylactic antibiotics: 95% of patients
• Fiducial/Spacer implant: Transperineal

**US Pivotal Study Overview - RESULTS**

**Perirectal Space**

<table>
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<tr>
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<th>Post implant</th>
<th>12 weeks</th>
<th>13 weeks</th>
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<tr>
<td></td>
<td>12.6 ± 3.9 mm</td>
<td>10.9 ± 5.8 mm</td>
<td>6.8 ± 5.4 mm</td>
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Technical success: 99% (gel present)

12 months: Absorbed

Difficulty: 99% of appliers rated the procedure easy or very easy

Safety Results:

- No device related adverse events
- No delays to onset of IMRT
- No implant infections
- No rectal wall ulcerations
- 10% with mild transient procedure events


In the pivotal trial, SpaceOAR patients did not experience any Grade 2 or greater rectal toxicity (e.g. proctitis, rectal bleeding, or fecal incontinence).\textsuperscript{1,2}

US Pivotal Study Late Rectal Toxicity vs Control

- **75%** relative reduction in late grade 1+ rectal toxicity
- **100%** relative reduction in late grade 2+ rectal toxicity
- **Zero** late grade 2+ rectal toxicity
- **73%** relative reduction in cumulative grade 1+ urinary incontinence

Sexual Function

- SpaceOAR reduced average and maximum radiation to penile bulb (10/30 GY)
- 59% had low baseline sexual function (EPIC) score < 60

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<th>SpaceOAR</th>
<th>vs.</th>
<th>Controls</th>
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<tr>
<td>Adequate baseline sexual QOL/maintained at 3 years</td>
<td>57.7%*</td>
<td></td>
<td>44.6%*</td>
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<tr>
<td>Baseline potent men/retained sufficient erections for intercourse</td>
<td>66.7%*</td>
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<td>37.5%*</td>
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*At Phase III - 3 year follow up

Contraindications

- Not recommended for locally advanced prostate cancer
  - ? tumor seeding
- Prior HIFU, cryotherapy, radiotherapy
- Clinically significant coagulopathies or active bleeding
- Prostatitis
- Anorectal inflammatory disease (UC/Crohn’s)
Toxicities

- No reports of rectal perforation, rectal infection, serious rectal bleeding

- 1 report of necrotic rectal ulceration two months post SpaceOAR placement/I-125 brachytherapy
SpaceOAR Experience at TUCC

• Medicare coverage since March 8, 2018
• Medicare reimbursement is $3,863.96
• Commercial coverage varies and often requires appeal
• Commercial reimbursement $3950 to $6,604
• TUCC collects $3,865 from commercial patients
  – Patients refunded when we collect from insurance
• Fiducial reimbursement reduced by 50% - $70
Summary

- SpaceOAR is currently the only FDA approved prostate cancer spacing device available in the US
- Easily implemented into an existing urologist practice
- In-office procedure/local anesthesia awake patents
- Technically feasible and readily mastered
- Well tolerated by patients
- Significant toxicity reduction – enhancing optimal patient care
- Favorable reimbursement
THANK YOU