FAQ About Prostate Cancer Treatment and SpaceOAR System

SpaceOAR® Frequently Asked Questions (FAQ)

Prostate Cancer Background

1. **What is prostate cancer?**
   The vast majority of prostate cancers develop in the prostate gland of the male reproductive system. Most prostate cancers occur in men over the age of 50,[1] and more than 80 percent are found in the early stages when cancer cells are confined to the prostate.[2] Prostate tumors most often occur in the lower part of the prostate, known as the peripheral zone,[3] or the area closest to the rectal wall. Prostate cancer is detected by the prostate-specific antigen (PSA) test of the patient's blood, by a digital rectal exam and a prostate biopsy.

2. **What is the prevalence of prostate cancer?**
   According to the American Cancer Society (ACS), prostate cancer is the second-most-common cancer in American men and the second-leading cause of cancer-related death in the U.S. ACS estimates that more than 220,000 new cases of prostate cancer will be diagnosed in 2015 and more than 27,500 men will die from the disease this year.[4] Worldwide prostate cancer incidence and mortality are expected to grow to 1.7 million new cases per year and 499,000 new deaths by the year 2030.[5]

3. **What are the treatment options for prostate cancer patients?**
   There are several treatment options for early-stage prostate cancer patients, including surgery, radiation therapy, watchful waiting and active surveillance.[6] Surgery (or prostatectomy) involves removing the prostate gland and surrounding tissue and can be performed as open, robotic or laparoscopic surgery. Watchful waiting involves frequent monitoring of symptoms and active surveillance relies on periodic testing, including prostate biopsies, to determine if the cancer is growing or becoming more aggressive.

Radiation Treatment for Prostate Cancer

4. **What is radiation therapy?**
   Radiation therapy is a non-invasive treatment technique that uses high-energy rays or particles to kill cancer cells. It is a common and highly effective treatment for prostate cancer.

5. **What are the different types of radiation therapy options?**

   External Beam Radiation Therapy (EBRT): EBRT is a form of radiation therapy in which radiation beams are focused on the cancer from a machine located outside the body. There are two types of EBRT: intensity modulated radiation therapy (IMRT) and stereotactic body radiation therapy (SBRT). IMRT is the most common form EBRT used today. During IMRT treatment, a computer-driven machine moves around the patient as it delivers radiation, shaping the radiation beams and adjusting the beam's intensity as it moves. This allows doctors to limit the dose to normal tissues and deliver higher doses of radiation to the tumor. SBRT uses advanced image guidance systems to target and deliver large doses of radiation to a precise area. Treatment with IMRT takes place over several weeks while treatment with SBRT generally lasts only several days.

   Proton Beam Radiation Therapy: Unlike other forms of radiation therapy that use x-ray beams, proton beam radiation therapy focuses beams of protons on the cancer. While this treatment option utilizes a different form of energy to treat prostate cancer, the proton beams are aimed using techniques similar to EBRT.

   Brachytherapy: Also known as internal radiotherapy, brachytherapy is a form of radiotherapy where a radiation source is placed directly into the prostate.

6. **What are the side effects from prostate cancer radiation treatment?**
   The most common side effect of prostate cancer radiation treatment is damage to the rectum, which is located just below the prostate. In up to 85 percent of cases, prostate tumors form in

the lower part of the prostate in the area closest to the rectal wall.[7] This close proximity means that radiation delivered to the prostate tumor often impacts the rectum. Potential damage caused by radiation exposure to the rectum can result in bowel complications, such as diarrhea, bleeding and pain.[8] These side effects can be temporary or last for years.

There is a strong desire among patients and physicians alike to effectively treat prostate tumors while minimizing side effects.

SpaceOAR® System, a New Tool for Prostate Cancer Radiation Treatment

7. **What is SpaceOAR System? How does it work?**
   SpaceOAR (OAR stands for "organ at risk") System is a temporary injectable gel that protects the rectum in men undergoing radiation therapy for prostate cancer. **It is the first and only prostate cancer spacing device to receive Food and Drug Administration (FDA) clearance.** No other rectum-sparing hydrogels are available in the U.S or abroad. SpaceOAR hydrogel can be used with all radiation therapy modalities.

   SpaceOAR System is placed in a patient prior to radiation therapy through a minimally invasive, outpatient procedure. The SpaceOAR hydrogel is injected through a small needle into the space between the prostate and rectum while the patient is under local or general anesthesia.

   Ultrasound imaging allows the physician to see and place the hydrogel in the proper location. On average, SpaceOAR hydrogel creates about a 0.5 inch (or 1.3 cm) space between the prostate and rectum, allowing physicians to treat the prostate with much less rectum radiation injury and fewer complications. The gel remains in place for about three months during radiation treatment, and then liquefies, is absorbed and cleared from the body in the patient's urine.

   The 30-minute procedure is minimally invasive and typically performed in a hospital, surgery center or doctor's office. Often, SpaceOAR System is inserted during the same procedure where small gold markers (called fiducials) are placed in the prostate to track its movement during radiation treatment.

8. **What is SpaceOAR hydrogel made of? Is it safe?**
   SpaceOAR hydrogel is made of polyethylene glycol (PEG). PEG is widely used in cosmetics and drugs because it is non-toxic and well tolerated by the body. In SpaceOAR hydrogel the PEG is injected as a liquid that, within seconds, solidifies into a soft, gel-like synthetic material that expands and creates space between the prostate and rectum. Because it contains mostly water, it is called a "hydrogel."

   Hydrogels have been used successfully in medical treatment around the world more than 2 million times in a variety of procedures. Multiple studies have demonstrated that the material is biocompatible and safe to use in the body. Similar hydrogels are approved in the U.S., Europe, Australia and other countries for use on some of the most sensitive tissues in the body. In the U.S., hydrogels are currently used in brain, spine, lung and eye procedures.

9. **Is placement of SpaceOAR System invasive? What do patients feel during and after SpaceOAR System is placed?**
   Placement of SpaceOAR System is minimally invasive. The gel is delivered via a small needle between the prostate and rectum. Patients can choose to be put to sleep with sedatives during the procedure (similar to patients undergoing a colonoscopy), receive local anesthesia to numb the injection area or undergo general anesthesia.

   Following the placement, some patients may experience tenderness or fullness at the injection site. These symptoms typically last for less than 24 hours.

10. **What are the benefits of SpaceOAR System?**
    The goal of radiation therapy is to maximize radiation to the tumor while avoiding or minimizing radiation to surrounding normal tissue. The prostate and rectum are located very close together, separated by only a small space. Due to the close proximity, the rectum can be at risk for radiation exposure during prostate cancer radiation treatment.

    By separating the prostate from the rectum, SpaceOAR hydrogel reduces radiation exposure to the rectum during treatment and may reduce, or possibly eliminate, damage to the rectum and associated side effects.

    In clinical trials, applying SpaceOAR System to patients reduced their rectal V70 (volume of rectum receiving 70 Gray) radiation by 73 percent. This reduction resulted in benefits to patients including less rectal pain and a 71 percent reduction in long-term rectal complications.

    In addition, 1 year following radiation treatment clinical trial patients who received SpaceOAR System were 46 percent less likely to experience long-term bowel quality of life issues—such as diarrhea, rectal urgency and incontinence, than patients who did not receive SpaceOAR System. As a result, SpaceOAR System helped men to maintain their normal activities and lifestyle.

11. **What happens to SpaceOAR hydrogel after radiation treatment is complete? Does it need to be removed?**
    After injection, SpaceOAR hydrogel remains as a soft gel separating the prostate from the rectum for about three months during which radiation therapy is administered. After those three months SpaceOAR hydrogel gradually begins to liquefy. Within six months, SpaceOAR hydrogel completely liquefies, is naturally absorbed by the body and cleared via the urine. Because of the SpaceOAR hydrogel's unique ability to liquefy, no procedure is needed to remove it and patients feel nothing as the gel gradually absorbs.

12. **Are there special preparations patients need to make before SpaceOAR System placement?**
    Patients should check with their doctor for required preparations prior to SpaceOAR System application.

13. **How soon can patients resume normal activities following placement of SpaceOAR System?**
    Patients should be able to immediately resume their activities, but should be sure to check with their doctor for any restrictions associated with the procedure and/or their radiation treatment.

14. **Can radiation treatment cause the SpaceOAR hydrogel to change form or breakdown?**
    Radiation does not breakdown the SpaceOAR hydrogel. Rigorous testing found that radiation exposure does not change the hydrogel's chemical properties, safety or effectiveness.

15. **What are the key findings from the SpaceOAR System clinical trial?**
    A prospective, randomized clinical trial involving 222 patients at 20 sites across the U.S. found that SpaceOAR System was safe and well tolerated in patients, with no device-related adverse events. Gel placement was highly successful (99 percent success rate) and created an average of 0.5 inches or 1.3 centimeters of space between the prostate and rectum, producing a 74 percent reduction in rectal V70 radiation exposure, resulting in:

    - 76 percent less rectal pain during radiation treatment,
    - 71 percent less rectal toxicity (complications) 15 months after treatment, and
    - 46 percent reduction in patients experiencing a negative impact on bowel quality of life 1 year following radiation treatment.

16. **Is SpaceOAR System available in the U.S.? What is it approved to treat?**
SpaceOAR System is commercially available in the U.S. and received FDA clearance on April 1, 2015. It is approved to treat men receiving radiation therapy for treatment of prostate cancer. SpaceOAR System received its CE Mark in July 2010 and is also commercially available in Europe and Australia.

17. **Are there any risks associated with SpaceOAR System?**
As with any medical device there are potential risks. In addition to the risks associated with any medical procedure, there are the potential complications that may be associated with the use of the SpaceOAR System that include, but are not limited to: pain associated with SpaceOAR hydrogel injection; pain or discomfort associated with SpaceOAR hydrogel; needle penetration of the bladder, prostate, rectal wall, rectum or urethra; injection of SpaceOAR hydrogel into the bladder, prostate, rectal wall, rectum or urethra; local inflammatory reactions; infection; injection of air, fluid or SpaceOAR hydrogel intravascularly; urinary retention; rectal mucosal damage, ulcers or necrosis; bleeding; constipation; and rectal urgency.

18. **How does payment for SpaceOAR System work?**
Augmenix, the maker of SpaceOAR System, is working with the Centers for Medicare & Medicaid Services (CMS), as well as private payers, to establish insurance coverage. Payment is currently handled by physicians and patients on a case-by-case basis.

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[1] American Cancer Society Prostate Cancer: http://www.cancer.org/acs/groups/cid/documents/webcontent/003134-pdf.pdf

[2] Surveillance, Epidemiology, and End Results Program: http://seer.cancer.gov/statfacts/html/prost.html 3 Radiology (2006) 239 (3): 784-792. doi: 10.1148/radiol.2392050949 First published online: June 2006 http://pubs.rsna.org/doi/pdf/10.1148/radiol.2392050949

[4] American Cancer Society Prostate Cancer: http://www.cancer.org/acs/groups/cid/documents/webcontent/003134-pdf.pdf

[5] European Urology (2012) 61 (6): 1093-1095: http://www.europeanurology.com/article/S0302- 2838%2812%2900339-9/pdf/prostate-cancer-epidemic-in-sight

[6] American Cancer Society Expert Voices: http://www.cancer.org/cancer/news/expertvoices/post/2013/06/13/choosing-the-best-prostate-cancer- treatment-for-you.aspx

[7] Radiology (2006) 239 (3): 784-792. doi: 10.1148/radiol.2392050949 First published online: June 2006 http://pubs.rsna.org/doi/pdf/10.1148/radiol.2392050949

[8] http://www.ncbi.nlm.nih.gov/books/NBK82315/pdf/TOC.pdf