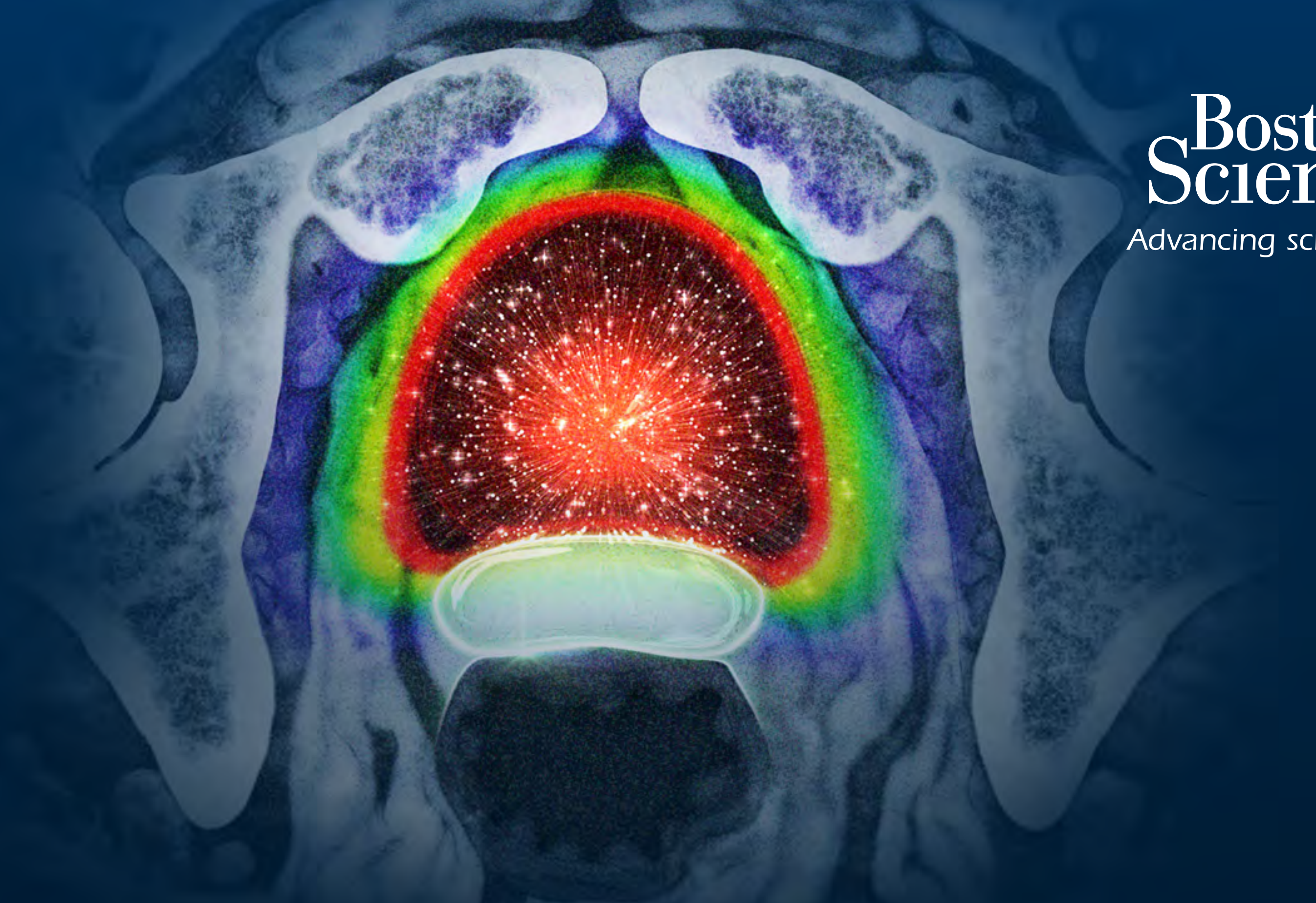

SpaceOAR™ Hydrogel Systems

Competitive Rheology Bench Study

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Executive summary

- SpaceOAR Vue™ Hydrogel, a polyethylene glycol (PEG)-based perirectal hydrogel spacer, is designed to temporarily position the anterior rectal wall away from the prostate in patients who are undergoing radiation therapy for prostate cancer.
- Perirectal hydrogel spacers are designed to maintain space between the rectum and the prostate for the duration of radiation treatment (up to 3 months).
- Rheology is the study of how materials deform and flow under stress. Certain rheological behaviors of the hydrogel spacers SpaceOAR Vue Hydrogel and Barrigel™ were tested in a lab setting.
- Forces ranging from 0.1 to 5.0 N (equivalent pressures ranging from 3 to 130 mmHg) were applied to hydrogel samples and the changes in hydrogel volume were tracked and compared.
- Average resting anorectal pressures reported in the literature range from 15 to 108 mmHg[1,2] while maximum "squeeze" pressures range from 69 to 350 mmHg.[3,4]
- At the maximum stress used in the rheological study (130 mmHg), there was a -7.0% change in volume of SpaceOAR Vue Hydrogel and a -42.2% change in volume of Barrigel.
- This bench study found that SpaceOAR Vue Hydrogel maintained its volume when exposed to pressures analogous to those seen in the anorectal space.
- Bench study results may not necessarily be indicative of clinical performance.

Introduction

Prostate cancer is the most common non-cutaneous cancer among men in the United States and is the second leading cause of cancer deaths, with about 313,780 new cases and 35,770 deaths estimated for 2025.[5] Radiotherapy is a standard, non-invasive treatment option with clinical outcomes comparable to surgery,[6,7] but it carries the risk of exposing healthy surrounding tissue to radiation. This inadvertent exposure can lead to toxic side effects, particularly affecting the rectum due to its proximity to the prostate and can significantly impact a patient's quality of life following treatment.

One method to mitigate radiation-related rectal toxicity prior to treatment is to temporarily increase the distance between the rectum and the prostate during prostate radiotherapy.[8] Typically, the anterior rectal wall is situated 2 to 3 mm from the posterior prostate border and is separated from the prostate and bladder by the multi-layered Denonvilliers' fascia. This tissue plane can be artificially expanded using materials like hydrogels. Hydrogels are intended to create space between organs at risk (OAR) during radiation therapy for the treatment of cancer. In the specific case of SpaceOAR Vue Hydrogel, the hydrogel is designed to create space between the prostate and the rectum to help reduce the radiation dose delivered to the anterior rectum in patients undergoing radiotherapy for prostate cancer.

SpaceOAR Vue Hydrogel (Boston Scientific, Inc.) is a polyethylene glycol (PEG)-based hydrogel and contains approximately 1% iodine by volume covalently bound to PEG, which is constituted in situ when injected into the patient. The iodine component of SpaceOAR Vue Hydrogel allows it to be easily viewed on CT and daily cone-beam CT scans for image-guided radiation therapy. Barrigel (Teleflex), another hydrogel spacer, is a non-animal stabilized hyaluronic acid (NASHA) hydrogel that is provided to the implanter as a pre-polymerized hydrogel.

The purpose of this report is to compare certain rheological behaviors of SpaceOAR Vue Hydrogel and Barrigel when exposed to different loads. Rheology is the study of how materials flow under stress and examines their resistance to flow. To accompany this analysis, a literature search was done to determine average resting anorectal pressures in healthy volunteers to provide context to the rheological behavior of these two hydrogels and how they maintain space for the duration of radiation therapy following placement. This study was conducted internally by Boston Scientific.

Methods

Rheological testing

The experiment involved preparing the hydrogels as detailed in each product's IFU and injecting 3 mL of the solution into a cylinder. Cylinder dimensions and the amount of hydrogel were consistent across samples. A sample was placed under a universal testing machine (Instron®) where a compression plate was initially set close to the plunger, which had been previously placed on top of the hydrogel sample (Figure 1). Force was applied and stopped once the target force was reached, and the plate was then returned to its original position. Starting with an initial force of 0.1 N, the force was incrementally increased by 0.1 N up to 5.0 N (equivalent to 3 to 130 mmHg in testing conditions). Each time, the final plunger height was measured to record any corresponding change in hydrogel thickness (deformation), and hydrogel sample height was converted to change in volume based on the constant cylinder dimensions. Figure 2 illustrates how hydrogel samples responded to stress with elastic or plastic behaviors.

Figure 1. Sample set up under the universal testing machine. The compression plate on the machine moved down, applying a force onto the plunger. This transferred that force onto the hydrogel sample placed at the bottom of the cylinder. Changes in plunger height were recorded and later used to calculate change in sample volume.

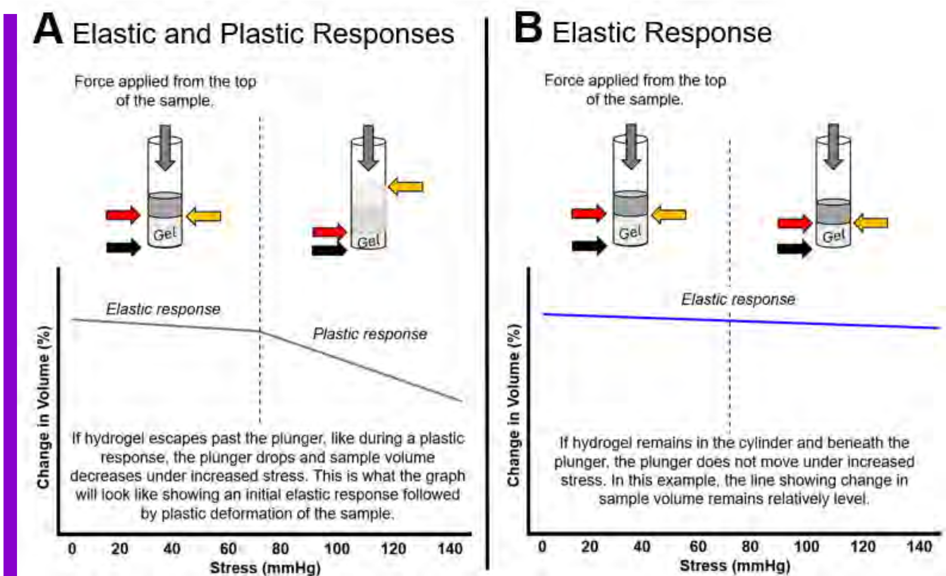

Figure 2. Illustrations of the same rheological testing with two different behaviors observed from different types of samples. The bottom of the plunger (red arrow) was tracked relative to the bottom of the testing cylinder (black arrow), which equaled plunger height. **A** depicts an example of elastic behavior followed by a plastic response with increased stress. Under increased stress, the sample escaped past the plunger and up the sides of the cylinder (yellow arrow), which demonstrated a plastic response. Below the illustration is what graphing that behavior looks like. **B** shows a different example of when the hydrogel sample remained below the plunger (red arrow) even in the presence of increased stress, demonstrating a consistent elastic response. The resulting graph shows a more level horizontal line, which indicates very little change in sample volume.

Literature search

An Embase search was done to identify average resting anorectal pressures and maximum "squeeze" pressures reported in healthy volunteers using these terms: "anorectal pressure," "rectum pressure," and "anal resting pressure." A total of 167 articles were identified in the search. These articles were screened for those containing data on anorectal pressures in healthy adults, and men in particular if reported separately from women. The majority of these articles reported anorectal pressure in mmHg where mean resting pressures ranged from 15 to 108 mmHg in healthy volunteers.[1,2] A few studies defined a normal resting pressure as below 80 mmHg.[9-11] In certain testing scenarios, when the patient was asked to "squeeze," maximum pressures collected from healthy volunteers ranged from 69 to 350 mmHg.[3,4]

Types of deformation

Elastic: the material withstands stress and maintains its shape

Plastic: the material permanently changes its shape in response to stress

Range of anorectal pressures found in the literature

Resting: 15 – 108 mmHg

Max squeeze: 69 – 350 mmHg

Results

Figure 3A shows the percent change in hydrogel sample volume with increasing amounts of stress. Plastic deformation was observed in the Barrigel samples at the applied forces of approximately 40 to 130 mmHg by the material being extruded upwards within the test fixture and not returning to the original shape after the force was removed. During this plastic response, Barrigel was unable to retain its shape or return to its original shape. The maximum volume change of SpaceOAR Vue Hydrogel was -7.0% and -42.2% for Barrigel at 130 mmHg.

From the literature search, pressures obtained from anorectal manometry studies suggest that "normal" resting anorectal pressures are typically less than 80 mmHg.[9-11] Although maximum pressures exerted during squeeze were reported as high as 350 mmHg in healthy volunteers,[4] this experiment had a maximum stress of 130 mmHg. We used 80 mmHg to compare the percent volume change of SpaceOAR Vue Hydrogel and Barrigel at normal resting and elevated pressures (Figure 3B).

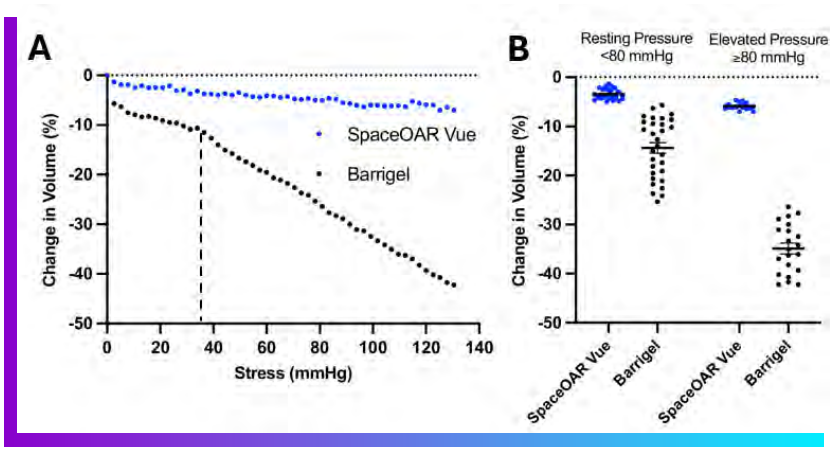

Figure 3. A shows changes in volume with increasing stress. The vertical dashed line represents the point where plastic deformation was observed in Barrigel samples (approximately 40 mmHg). **B** shows changes in volume grouped by hydrogel type and by resting and elevated pressures, as defined in the literature.[9-11]

	SpaceOAR Vue Hydrogel	Barrigel
Displays an *elastic response* up to applied forces that are equivalent to 40 mmHg of pressure	X	X
Maintains an *elastic response* from 40 to 130 mmHg of pressure	X	
Resists *plastic deformation* from 40 to 130 mmHg of pressure	X	
Maximum change in volume at 130 mmHg of pressure	-7.0%	-42.2%

Conclusion

When under stress of 3 to 130 mmHg, SpaceOAR Vue Hydrogel retained its original shape and material was not extruded upwards through the test cylinder, demonstrating a behavior consistent with elastic deformation.

When Barrigel was exposed to stress ranging from 3 to 130 mmHg, it exhibited an elastic response up to approximately 40 mmHg. When stress exceeded 40 mmHg, Barrigel was observed to respond with permanent deformation evident by the material being extruded past the plunger and up the walls of the test cylinder. This behavior demonstrates a plastic response.

Permanent plastic deformation was observed in Barrigel when under pressures >40 mmHg

A literature search determined that mean resting anorectal pressures range from 15 to 108 mmHg in healthy volunteers and maximum pressures range from 69 to 350 mmHg. Under experimental conditions, at the maximum testing pressure of 130 mmHg, SpaceOAR Vue Hydrogel presented a change in volume of -7.0% while Barrigel presented a change in volume of -42.2%.

Barrigel showed a greater variability in volume change compared to SpaceOAR Vue Hydrogel at lower pressures (below 80 mmHg) and at higher pressures (above 80 mmHg).

Overall, when under stress exceeding 40 mmHg in a bench study, Barrigel was unable to retain its shape or return to its original shape, resulting in a permanent deformation of the material. In this experiment, SpaceOAR Vue Hydrogel was able to retain its original shape after stress was applied.

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