Optum

Transperineal Placement of Biodegradable Material

Clinical guidelines

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Indications

The transperineal placement of biodegradable material, periprostatic, (via needle) is considered medically necessary for use with radiotherapy for treating prostate cancer.

The transperineal placement of biodegradable material, periprostatic, (via needle) is considered not medically necessary for all other indications due to insufficient evidence of safety and/or efficacy.

General information

Prostate cancer is the most common cancer diagnosed in male patients in the United States (Siegel et al., 2022). Most patients present with localized or regional disease, and a majority of these may be eligible for curative treatment with radiotherapy. Acute and chronic toxicity are well-known side effects of radiotherapy. Acute toxicities are generally mild and self-limiting; however chronic toxicities, including urinary dysfunction, bowel dysfunction, sexual dysfunction, tissue necrosis, rectal bleeding, and fistula formation may be debilitating and morbid (Do et al., 2011). While advanced radiation techniques such as intensity-modulated radiotherapy (IMRT) and proton beam therapy (PBT) have been implemented to alleviate rectal toxicities, they do not completely eliminate the toxicity.

The prostate is located in the pelvis and bordered posterosuperiorly by the seminal vesicles and posteriorly by the rectum with only 2-3 mm of tissue separating the prostate and rectum (Mariados et al., 2015). This meager distance makes radiotherapy significantly challenging, as most cancers develop in the peripheral zone located posteriorly in the prostate gland (Laczko et al., 2005). The rectum is a dose-limiting critical structure in radiation treatment and is referred to as the primary Organ at Risk (OAR) in prostate radiotherapy (Baxter et al., 2005).

Biodegradable hydrogel is intended to temporarily position the anterior rectal wall away from the prostate during radiotherapy, thus reducing the dose delivered to the anterior rectum. The absorbable material creates and maintains a space for the entire course of radiotherapy treatment and is completely absorbed by the patient's body over time.

Documentation requirements

Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The documentation requirements outlined below are used to assess whether the member meets the clinical criteria for coverage but do not guarantee coverage of the service requested.

Medical notes documenting the following, when applicable:

- Diagnosis, including:
  - Cancer risk group, including staging of disease
  - Life expectancy
  - Results of diagnostic prostate biopsy
- Reports of all recent imaging studies and applicable diagnostics, including:
  - Results of prostate volume via transrectal ultrasound (TRUS)
- Physician treatment plan for radiotherapy

Clinical evidence

In a comprehensive narrative review, Harvey et al. (2023) examined the published data on the impact of hydrogel spacers on rectal dosimetry and toxicity. Analyzing a number of phase II and III clinical trials and subsequent meta-analyses, the administration of hydrogel spacers is safe and associated with limited perioperative morbidity. The impact on rectal dosimetry has been clearly established and use of hydrogel spacers is associated with reduced rectal toxicity, however data on the impact of spacer insertion on rectal toxicity in the setting of moderately hypofractionated or stereotactic body radiation therapy (SBRT) is limited. Only a few studies outlined patient-reported bowel bother outcomes, but all reported bowel quality-of life scores favoring patients who had spacer insertion compared to those who did not. Several areas for future research were identified including the role of hydrogel spacers in prostate stereotactic beam radiotherapy and post-radiotherapy local recurrence.

A Hayes health technology assessment (2021) summarized the evidence from 11 controlled or comparative studies published between 2015 and 2021. The assessment suggested a likely benefit of an absorbable perirectal spacer during radiation therapy for prostate cancer. There was uncertainty regarding the safety and efficacy of such spacers, and further studies were recommended to assess clinical usefulness and cost effectiveness.

Miller et al. (2020) conducted a systematic review and meta-analysis to evaluate the association between perirectal hydrogel spacer placement and clinical outcomes in men receiving radiotherapy for prostate cancer. The review included 7 studies (1 randomized clinical trial and 6 cohort studies) involving 1011 men (486 who received a hydrogel spacer and 525 controls) with a median duration of patient follow-up of 26 months (range, 3-63 months). The main outcomes of interest included procedural results, the percentage volume of rectum receiving at least 70 Gy radiation (v70), early (≤ 3 months) and late (>3 months) rectal toxic effects, and early and late changes in bowel-related quality of life (QOL). The success rate of hydrogel spacer placement was 97.0% (95% CI, 94.4%-98.8% [5 studies]), and the weighted mean perirectal separation distance was 11.2mm (95% CI, 10.1-12.3 mm [5 studies]). Procedural complications were mild and transient, occurring in 0% to 10% of patients within the studies. The hydrogel spacer group received 66% less v70 rectal irradiation compared with controls (3.5% vs 10.4%; mean difference, -6.5%; 95% CI, -10.5% to -2.5%; p = .001 [6 studies]). The risk of grade 2 or higher rectal toxic effects was comparable between groups in early follow-up (4.5% in hydrogel spacer group vs 4.1% in control group; risk ratio, 0.82; 95% CI, 0.52-1.28; p = .38 [6 studies]) but was 77% lower in the hydrogel spacer group in late follow-up (1.5% vs 5.7%; risk ratio, 0.23; 95% CI, 0.06-0.99; p = .05 [4 studies]). Changes in bowel-related (QOL) were comparable between groups in early follow-up (mean difference, 0.2; 95% CI, -3.1 to 3.4; p = .92 [2 studies]) but were greater in the hydrogel spacer group in late follow-up (mean difference, 5.4; 95% CI, 2.8-8.0; p < .001 [2 studies]). This review found that perirectal hydrogel spacer placement was associated with less rectal irradiation, fewer rectal toxic effects, and higher bowel-related QOL in long-term follow up.

Vaggers et al. (2020) conducted a systematic review of nine studies (671 patients and 537 controls) examining the role of polyethylene glycol (PEG) hydrogel spacers in patients undergoing radiation therapy for prostate cancer. Four studies used the DuraSeal Spinal Sealant and five studies used SpaceOar. Primary outcomes included procedure complications, failures, prostate-rectum separation, rectal dosimetry, acute and late gastrointestinal toxicity, procedure-related complications, and the technique used for hydrogel insertion. Little variation in technique was noted throughout the studies reviewed. The rectal spacing achieved varied between 7.7-16 mm. Failure of hydrogel insertion was seen only in 12 patients, mostly related to failure of hydrodissection in patients undergoing salvage prostate brachytherapy. Acute GI complications were mostly limited to grade 1 or 2 toxicity (*n* = 153, 33.7%) with low levels of grade 3 or 4 toxicity (*n* = 1; 0.22%*).* A significant reduction in rectal dosimetry was demonstrated.

Paetkau et al. (2019) retrospectively evaluated 13 patients with the SpaceOAR implant to determine future planning needs for patients with prostate cancer undergoing radiation therapy. Computerized tomography (CT) scans were obtained pre- and post-implant. A prescription of 60 Gy in 20 fractions was planned on both scans. Six treatment plans were produced per anonymized dataset using either a structure of rectum plus the hydrogel, termed composite rectum wall (CRW), or rectal wall (RW) as an

inverse optimization structure and IMRT or volumetric modulated arc (VMAT) as a treatment technique. Dose-volume histogram metrics were compared between plans to determine which optimization structure and treatment technique offered the maximum rectal dose sparing. RW structures offered a statistically significant decrease in rectal dose over CRW structures, whereas the treatment technique (IMRT vs VMAT) did not significantly affect the rectal dose. There was improvement seen in bladder and penile bulb dose when VMAT was used as a treatment technique. Overall, treatment plans using the RW optimization structure offered the lowest rectal dose while VMAT treatment technique offered the lowest bladder and penile bulb dose.

Wu et al. (2018) evaluated 18 consecutive patients who underwent transperineal ultrasound-guided placement of 10 mL of SpaceOAR hydrogel prior to high-dose-rate (HDR) brachytherapy for the treatment of prostate cancer. Treatment plans were generated using an inverse planning simulated annealing algorithm. Rectal dosimetry for these 18 patients was compared with 36 preceding patients treated with HDR brachytherapy without SpaceOAR. There was no difference in age, pretreatment prostate-specific antigen (PSA), Gleason score, clinical stage, prostate volume, or contoured rectal volume between those who received SpaceOAR and those who did not. Patients who received SpaceOAR hydrogel had significantly lower dose to the rectum as measured by percent of contoured organ at risk (median, V80 < 0.005% vs. 0.010%, p = 0.003; V75 < 0.005% vs. 0.14%, p < 0.0005; V70 0.09% vs. 0.88%, p < 0.0005; V60 = 1.16% vs. 3.08%. p < 0.0005); similar results were seen for rectal volume in cubic centimeters. One patient who received SpaceOAR developed a perineal abscess 1 month after treatment. The study demonstrated transperineal insertion of SpaceOAR hydrogel at the time of HDR brachytherapy is feasible and decreases rectal radiation dose. Additional investigation is needed with well-designed clinical trials and larger patient populations to further assess clinical impact.

Taggar et al. (2018) conducted a prospective cohort study to evaluate placement of an absorbable rectal hydrogel spacer in 74 patients with prostate cancer undergoing low-dose-rate (LDR) brachytherapy with palladium-103. Rectal dosimetry was compared with a consecutive cohort of 136 patients treated with seed implantation without a spacer. On average, 11.2-mm (SD 3.3) separation was achieved between the prostate and the rectum. The resultant mean rectal volume receiving 100% of prescribed dose (V 100%), dose to 1 cc of rectum (D1cc), and dose to 2 cc of rectum (D2cc) were 0 (SD 0.05 cc), 25.3% (SD 12.7), and 20.5%(SD 9.9), respectively. All rectal dosimetric parameters improved significantly for the cohort with spacer placement as compared with the non-spacer cohort. Injections of rectal spacer is feasible in the post-LDR brachytherapy setting and reduces dose to the rectum with minimal toxicity. Prostate and urethral dosimetries do not appear to be affected by the placement of a spacer.

Hamstra et al. (2017) reported the results of their single-blind phase III trial of image guided IMRT in 222 men randomized 2:1 to the placement of a perirectal spacer or control group prior to receiving 79.2 Gy in 1.8 Gy fractions to the prostate for the treatment of low- or intermediate-risk prostate cancer. The 3-year incidence of grade ≥ 1 (9.2% vs 2.0%; p - .028) and grade ≥ 2 (5.7% vs 0%; p = .012) rectal toxicity favored the spacer group. Grade ≥ 1 urinary incontinence was also lower in the spacer group (15% vs 4%; p = .046), with no difference in grade ≥ 2 urinary toxicity (7% vs 7%; p = .7). From 6 months onward, bowel QOL consistently favored the spacer group (p = .002), with the difference at 3 years (5.8 points; p < .05) meeting the threshold for a minimally important difference (MID). The control group had a 3.9-point greater decline in urinary QOL compared with the spacer group at 3 years (p < .05), but the difference did not meet the prespecified MID threshold. At 3 years, more men in the control group than in the spacer group had experienced a MID decline in bowel QOL (41% vs 14%; p = .002) and urinary QOL (30% vs 17%; p = .04). This study demonstrated that the benefit of a hydrogel spacer in reducing the rectal dose, toxicity, and QOL declines following IMRT for prostate cancer was maintained or increased with a longer follow-up period.

Pinkawa et al. (2017) sought to evaluate quality of life (QOL) changes up to five years after prostate cancer radiation therapy (RT) with a hydrogel spacer. In the years 2010 to 2011, 114 patients received external beam radiation therapy to the prostate; 54 men were selected to undergo placement of a hydrogel spacer prior to the beginning of RT. Treatment was performed applying fractions of 2 Gy up to a total dose of 76 Gy (n = 96) or 78 Gy (n = 18, all with hydrogel). Patients were surveyed before RT; at the end of the final day of RT; and a median time of 2 months, 17 months, and 63 months after RT using a validated questionnaire (Expanded Prostate Cancer Index Composite). A mean score change of > 5

points was defined as clinically relevant. For patients treated with a hydrogel spacer, mean bowel function and bother score changes of > 5 points in comparison with baseline levels were found only at the end of RT (10-15 points; p < .01). No spacer patients reported moderate or big problems with his bowel habits overall. Mean bother score changes of 21 points at the end of RT, 8 points at 2 months, 7 points at 17 months, and 6 points at 63 months after RT were found for patients treated without a spacer. A bowel bother score change > 10 points was found in 6% vs 32% (p < .01) at 17 months and in 5% vs 14% (p = .2) at 63 months with vs without a spacer. These favorable findings support the use of hydrogel spacers to increase RT tolerability, particularly with respect to preventing long-term bowel problems.

Applicable Codes

CPT® Code	Description
55874	Transperineal placement of biodegradable material, periprostatic, single or multiple injection(s), including image guidance, when performed

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HCPCS Code	Description
C1889	Implantable/insertable device, not otherwise classified

ICD-10 CM Codes	Description
C61	Malignant neoplasm of prostate

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Review and Approval History	
Version	**Description of Activity**
1.0	April 12, 2023. New guideline approved by Optum Clinical Guideline Advisory Committee