Subject: Cryotherapy for Prostate Cancer

Background: Cryotherapy is a minimally invasive treatment modality for prostate cancer in which freezing is used to destroy tumor cells. Cryotherapy is thought to be associated with minimal blood loss and pain and can be performed under spinal rather than general anesthesia. Techniques can be applied to the entire prostate gland or partially to localized areas where cancer is present.

Authorization: Prior authorization is required for all cryotherapy procedures requested for members enrolled in commercial (HMO, POS, and PPO) products.

Policy and Coverage Criteria:

Initial Treatment
Harvard Pilgrim Health Care (HPHC) considers cryotherapy as reasonable and medically necessary when documentation confirms member has not undergone previous local therapy for prostate cancer (e.g. radical prostatectomy or radiation) and has localized prostate cancer, stages T1-T3.

Recurrent Treatment
Harvard Pilgrim Health Care (HPHC) considers salvage cryosurgery of the prostate for recurrent cancer as reasonable and medically necessary for individuals with localized disease when documentation confirms ALL the following:

- Member has failed a trial of radiation therapy as their primary treatment; AND
- Member meets one of the following conditions:
  - Stage T2B or below, OR
  - Gleason score <9, OR
  - Prostate-specific antigen (PSA) <8 ng/mL

Exclusions: Harvard Pilgrim Health Care (HPHC) considers cryotherapy for prostate cancer as experimental/investigational for all other indications. In addition, HPHC does not cover:
- Focal cryoablation of the prostate

Supporting Information:
Cryoablation, also referred to as cryosurgery, cryotherapy, or cryosurgical ablation of the prostate (CSAP), is a minimally invasive surgical technique that involves in situ freezing by applying extremely cold temperature to destroy prostate tissue and reduce the size of the prostate gland. Cryotherapy is performed under local or general anesthesia. Multiple cryoprobes are placed through the perineum directly into the prostate. The cryoprobes are specially designed to conduct a continuous flow of liquid nitrogen or high-pressure argon gas to the tip, which produces very cold temperatures rapidly, freezing the prostatic tissue in an expanding or spherical fashion around each probe.
Cryoablation, or cryotherapy, of the prostate has been investigated as primary treatment alternative to surgery or radiotherapy for localized prostate cancer. It has also been evaluated as a second line or salvage treatment for patients with residual or recurrent cancer following radical prostatectomy or irradiation.

Li et al (2015) reported contemporary outcomes of salvage focal cryoablation for locally recurrent PCa after radiotherapy within the Cryo On-Line Data Registry. The outcomes indicated that salvage focal cryoablation can be an effective treatment with encouraging potency preservation for patients with locally recurrent PCa after radiotherapy. The authors noted that further studies are needed.

A prospective study by Rodriguez et al. (2014) including 108 patients with localized prostate cancer at clinical stage T1c-T2c were treated by primary cryoablation. The biochemical progression-free survival (BPFS) for low-, medium-, and high-risk patients was 96.4%, 91.2%, and 62.2%, respectively. Cancer-specific survival was 98.1%. Overall survival reached 94.4%. The authors concluded that cryotherapy is an effective and minimally invasive treatment for primary PC in well-selected cases, with low surgical risk and good results in terms of BPFS, cancer-specific survival, and overall survival.

A 2013 systematic review by Valerio et al. noted current, radical, whole-gland treatments for organ-confined prostate cancer are being questioned with respect to their side effects, cancer control, and cost. The review investigated focal cryotherapy as an alternative treatment and focused on baseline characteristics of the target population; preoperative evaluation to localize disease; and perioperative, functional, and disease control outcomes following focal therapy. The authors found focal therapy was mainly delivered to men with low and intermediate disease. Studies follow-up time varied between 0 and 11.1 years. For men who underwent focal cryotherapy as an initial treatment, pad-free continence ranged from 95-100%, erectile function ranged from 55-100%, and absence of clinically significant cancer ranged from 83-100%. Valerio et al. noted when the therapy is used with intention to treat, the perioperative, functional, and disease control outcomes are encouraging. However, follow times are short to medium-term. The authors called for robust comparative effectiveness studies to further validate the treatment.

An additional review by Kasivisvanathan et al. (2013) discussed the current status of focal therapy, highlighting controversies and emerging strategies that can influence treatment outcomes for the future. The group notes current trials do not present medium- and long-term oncological outcome data or comparisons with existing standards of care and there is no consensus on whether oncological control should be deemed the absence of any cancer or the absence of clinically significant cancer and whether this should be limited to the treated area or include the untreated prostate. Patient selection criteria are also inconsistent. The review notes there are several prospective trials in progress and further RCTs are needed comparing active surveillance or radical therapy with focal therapy.

Nguyen et al. (2013) reviewed clinical literature on focal cryotherapy for clinically localized prostate cancer. Outcomes on cancer control, complications and quality of life were reviewed and assessed. The authors found the biochemical disease-free survival at 5 years is comparable to whole gland treatment modalities. They concluded the treatment is safe and effective, and may improve failure rates in men who initially pursue active surveillance methods.

A 2013 review by Sverrisson et al. assessed the oncologic and functional outcomes of cryosurgery for localized prostate cancer. The review found the outcomes of cryosurgery improved over time with intermediate biochemical disease-free survival rates now comparable to other treatments.
A 2011 review by Finley and Belldegrun looked at salvage cryotherapy for radiation-recurrent prostate cancer. Their analysis of the literature found technological inroads have led to salvage cryotherapy as a viable treatment option with curative intent for radio-recurrent prostate cancer. Durable biochemical relapse-free rates range from 34% to 68% depending on the definition. They also found complication rates have trended down with advances in technique and technology.

Simmons et al. (2011) published a practical guide to prostate cancer diagnosis and management. The review noted refinements in cryoablative therapy have improved the safety and efficacy of the procedure in the last decade. While it is recognized by the American Urological Association as a viable primary cancer monotherapy, it is most commonly used as a salvage therapy after failure of radiation therapy.

**Guidelines:**
The 2018 National Comprehensive Cancer Network (NCCN) Guideline for Prostate Cancer notes, "Cryosurgery, also known as cryotherapy or cryoablation, treats prostate tumors by freezing and is a treatment option when radiation therapy fails. Cryoablation is often done as an outpatient procedure where thin needles are inserted by imaging tests in order to place it through the perineum and into the prostate.

Based on a report from the National Institute for Health and Care Excellence (NICE) guidelines, current evidence on focal therapy using cryoablation for localized prostate cancer raises no major safety concerns. However, evidence on efficacy is limited in quantity and there is a concern that prostate cancer is commonly multifocal. Therefore, this procedure should only be used with special arrangements for clinical governance, consent and audit or research.

Cryosurgery of the prostate gland, also known as cryosurgical ablation of the prostate (CSAP), destroys prostate tissue by applying extremely cold temperatures in order to reduce the size of the prostate gland. It is safe and effective, as well as medically necessary and appropriate, as primary treatment for patients with clinically localized prostate cancer, Stages T1-T3.

The American Joint Committee on Cancer (AJCC) and the International Union for Cancer Control (UICC) maintain the TNM classification system as a tool to stage different types of cancer based on certain standards. There are 4 categories to describe the local extent of a prostate tumor, ranging from T1 to T4 with subcategories.

<table>
<thead>
<tr>
<th>Category</th>
<th>Description</th>
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<tbody>
<tr>
<td>T1</td>
<td>Digitally unrecognized tumor</td>
</tr>
<tr>
<td>T1A</td>
<td>Less than 5% of the transurethral resection of the prostate (TURP) specimen, or low-to-medium grade tumor</td>
</tr>
<tr>
<td>T1B</td>
<td>Greater than 5% of the TURP specimen, or high-grade tumor</td>
</tr>
<tr>
<td>T1C</td>
<td>Tumor detected by elevated prostate-specific antigen (PSA)</td>
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<tr>
<td>T2</td>
<td>Digitally palpable tumor confined to the prostate</td>
</tr>
<tr>
<td>T2A</td>
<td>Less than ½ of one lobe</td>
</tr>
<tr>
<td>T2B</td>
<td>Greater than ½ of one lobe</td>
</tr>
<tr>
<td>T2C</td>
<td>Tumors involve both lobes</td>
</tr>
<tr>
<td>T3</td>
<td>Cancer extending beyond the prostate capsule</td>
</tr>
<tr>
<td>T3A</td>
<td>Tumor extends outside of the prostate, but not the seminal vesicles</td>
</tr>
<tr>
<td>T3B</td>
<td>Tumor has spread to the seminal vesicles</td>
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A 2010 Best Practice Guideline from the American Urological Association (AUA, 2010) concluded that cryosurgery guided by ultrasound and temperature monitoring is an option for recurrent clinically organ-confined prostate cancer after radiation therapy. As with other salvage therapies for curative intent, cryosurgery should be considered early for patients defined as radiation failures. Refinements in the surgical technique and equipment have resulted in significantly less morbidity than previously reported as well as encouraging short-term PSA results.

**Coding:**

Codes are listed below for informational purposes only, and do not guarantee member coverage or provider reimbursement. The list may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible.

<table>
<thead>
<tr>
<th>CPT® Codes</th>
<th>Description</th>
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<tbody>
<tr>
<td>55873</td>
<td>Cryosurgical ablation of the prostate (including ultrasonic guidance for interstitial cryosurgical probe placement)</td>
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**References:**

Cryotherapy for Prostate Cancer


Summary of Changes:

<table>
<thead>
<tr>
<th>Date</th>
<th>Changes:</th>
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<tbody>
<tr>
<td>10/19</td>
<td>Annual review; references and supporting information updated</td>
</tr>
<tr>
<td>3/18</td>
<td>References and guidelines updated; policy coverage criteria refined</td>
</tr>
</tbody>
</table>

Approved by Medical Policy Committee: 10/9/19
Approved by Clinical Policy Operational Committee: 10/09; 10/11; 10/13; 10/15; 4/17; 3/18; 10/19
Policy Effective Date: 12/1/19
Initiated: 10/09