Clinical Policy Title: High-intensity focused ultrasound

Clinical Policy Number: CCP.1364

Effective Date: April 1, 2018
Initial Review Date: February 6, 2018
Most Recent Review Date: March 5, 2019
Next Review Date: March 2020

Policy contains:
- High-intensity focused ultrasound.
- Prostate cancer.

Related policies:
- CCP.1047 Proton beam therapy.
- CCP.1117 Brachytherapy for localized prostate cancer.
- CCP.1142 Intensity modulated radiation therapy.
- CCP.1141 Immunotherapies for prostate cancer and acute lymphoblastic leukemia.
- CCP.1121 Genetic tests for prostate cancer diagnosis.
- CCP.1277 Fluorescence spectroscopy for prostate cancer diagnosis.
- CCP.1340 Laparoscopic prostatectomy.

ABOUT THIS POLICY: AmeriHealth Caritas has developed clinical policies to assist with making coverage determinations. AmeriHealth Caritas’ clinical policies are based on guidelines from established industry sources, such as the Centers for Medicare & Medicaid Services (CMS), state regulatory agencies, the American Medical Association (AMA), medical specialty professional societies, and peer-reviewed professional literature. These clinical policies along with other sources, such as plan benefits and state and federal laws and regulatory requirements, including any state- or plan-specific definition of “medically necessary,” and the specific facts of the particular situation are considered by AmeriHealth Caritas when making coverage determinations. In the event of conflict between this clinical policy and plan benefits and/or state or federal laws and/or regulatory requirements, the plan benefits and/or state and federal laws and/or regulatory requirements shall control. AmeriHealth Caritas’ clinical policies are for informational purposes only and not intended as medical advice or to direct treatment. Physicians and other health care providers are solely responsible for the treatment decisions for their patients. AmeriHealth Caritas’ clinical policies are reflective of evidence-based medicine at the time of review. As medical science evolves, AmeriHealth Caritas will update its clinical policies as necessary. AmeriHealth Caritas’ clinical policies are not guarantees of payment.

Coverage policy

AmeriHealth Caritas considers the use of high-intensity focused ultrasound for prostate cancer to be investigational, and therefore, not medically necessary.

Limitations:

All other uses of high-intensity focused ultrasound are considered investigational, and therefore, not medically necessary.
Alternative covered services:

- Brachytherapy.
- Chemotherapy.
- Cryotherapy (cryosurgery).
- External beam therapy.
- Hormone therapy.
- Intensity modulated radiation therapy.
- Prostatectomy.
- Proton beam therapy.
- Stereotactic body radiation therapy.

Background

In the U.S., prostate cancer is the most commonly diagnosed cancer in males, and has the third highest incidence of any cancer, other than breast and bronchus/lung. Although prostate cancer rates have declined by more than half since the early 1990s due to a reduction in screening among asymptomatic elderly men, an estimated total of 161,360 cases were diagnosed in 2017, with 26,730 dying from the disease. Almost all cases are diagnosed after age 50, and African Americans have a 60 percent greater incidence rate than whites. A total of 79 percent of cases are localized (Howlader, 2017).

The disorder can be treated using multiple types of therapies, including surgeries, radiation therapies, and hormones. In recent years, surveillance has become a more commonly employed technique for localized prostate cancer, since studies show that surgery and interventions did not result in reduced mortality from the disease, while resulting in long-term adverse effects in many patients.

High-intensity focused ultrasound is one non-invasive technique to treat prostate (and other) cancers and diseases. The technique transports energy using ultrasound waves to specific target points in the body, increasing temperature and bringing about other biological interactions. The first report of high-intensity focused ultrasound to treat prostate cancer occurred in 1994 (Kim, 2008).

High-intensity focused ultrasound raises the temperature of tissue rapidly to 60 degrees Celsius, which causes coagulation necrosis in seconds. Focusing on small areas minimizes damage to tissues. The treatment can also induce cell apoptosis, in which the nucleus of the cell self-destructs and the DNA rapidly degrades (Dubinsky, 2008).

On October 9, 2015, the U.S. Food and Drug Administration granted approval to use the transrectal high-intensity focused ultrasound device known as Sonablate™ 450 for prostate tissue ablation. The device thermally ablates tissue under imaging guidance (U.S. Food and Drug Administration, 2015). Other high-intensity focused ultrasound devices that are approved for prostate cancer include Ablatherm™ and the FocalOne™ (Kuru, 2015).
Most cases of high-intensity focused ultrasound employ the transrectal focal approach, while a minority uses the in-bore transurethral technique. Most cases are primary treatments of prostate cancer, with some used as salvage treatment for recurrence after radiation therapy.

**Searches**

AmeriHealth Caritas searched PubMed and the databases of:

- UK National Health Services Centre for Reviews and Dissemination.
- Agency for Healthcare Research and Quality.
- The Centers for Medicare & Medicaid Services.
- Cochrane reviews.

We conducted searches on January 11, 2019. Search term was: “high-intensity focused ultrasound.”

We included:

- **Systematic reviews**, which pool results from multiple studies to achieve larger sample sizes and greater precision of effect estimation than in smaller primary studies. Systematic reviews use predetermined transparent methods to minimize bias, effectively treating the review as a scientific endeavor, and are thus rated highest in evidence-grading hierarchies.
- **Guidelines based on systematic reviews**.
- **Economic analyses**, such as cost-effectiveness, and benefit or utility studies (but not simple cost studies), reporting both costs and outcomes — sometimes referred to as efficiency studies — which also rank near the top of evidence hierarchies.

**Findings**

Several U.S. professional medical societies have addressed high-intensity focused ultrasound in guidelines. The 2016 prostate cancer guideline from the National Comprehensive Cancer Network does not recommend the treatment, except in clinical trials (National Comprehensive Cancer Network, 2016). The American Urological Association recommends that clinicians inform patients that high-intensity focused ultrasound is not standard care for localized prostate cancer due to lack of sufficient evidence (American Urological Association, 2017). The American College of Radiology expert panel considers high-intensity focused ultrasound to be experimental (McLaughlin, 2016).

The European Association of Urology guideline on prostate cancer considers minimally invasive therapies such as high-intensity focused ultrasound to be experimental (Heidenreich, 2014). The National Institute for Health and Care Excellence, based in the United Kingdom, also recommends that patients be informed of uncertainty of efficacy and risks of the procedure, and that more research is needed on efficacy and risks (National Institute for Health and Care Excellence, 2012).
An early systematic review conducted by the French Association of Urology included 37 studies on high-intensity focused ultrasound as primary therapy for prostate cancer in men age 70 and over. It found the five-year disease-free survival rate ranged from 60 to 70 percent, and negative biopsy rates were observed in 64 to 93 percent of cases (Rebillard, 2008). The most common complications were stress urinary incontinence, urinary tract infection, urethral/bladder neck stenosis or strictures, and erectile dysfunction. Results were described as “promising” but required long-term follow-up studies before recommendations could be made (Rebillard, 2008).

A systematic review of 20 uncontrolled prospective case series (n = 3018) analyzed outcomes for prostate cancer patients treated with high-intensity frequency ultrasound. Biochemical disease-free survival at one, five, and seven years were 78 – 84, 45 – 84, and 69 percent, respectively. The negative biopsy rate was 86 and 80 percent at three and 15 months, respectively. Studies were judged to be low quality (Warmuth, 2010).

A review of 13,262 malignant and benign prostate cancer lesions treated with high-intensity focused ultrasound showed that cases using extracorporeal-guided devices did not have lower incidence of adverse effects than magnetic imaging devices. Fewer adverse events occurred in benign lesions than in malignant lesions (11.81 versus 21.65 percent, \(P < .0001\)) (Yu, 2011).

A systematic review of 31 studies, none randomized, assessed efficacy of high-intensity focused ultrasound on (mostly) localized prostate cancer. Follow-up periods ranged from 6.4 to 76.8 months. Seven- and eight-year disease free survival rates ranged from 69 to 84 percent. Complications most commonly identified were urinary retention, urinary tract infection, stress/urinary incontinence, and erectile dysfunction, which was highest at 20 to 81.6 percent (Cordeiro, 2012).

A systematic review of 34 clinical studies of high-intensity focused ultrasound, none randomized, included 29 studies of primary treatment and five as salvage treatment for recurrence after radiation therapy. The negative biopsy rates ranged from 35 to 95 percent in the primary treatment studies, and 73 to 84 percent in the salvage treatment studies. Authors concluded that widespread use of high-intensity focused ultrasound for prostate cancer treatment is not supported without confirmation of results in case studies (Lukka, 2011).

A review of 130 studies (n = 34,124) compared localized prostate cancer treatment outcomes between high-intensity focused ultrasound (21 of the studies, n = 4,000), cryotherapy, and external beam radiation therapy, all relatively non-invasive therapies. Four-year survival rates were highest for high-intensity focused ultrasound (99 percent), but not significantly greater than cryotherapy (93 percent) and beam therapy (91 percent). Similar outcomes were found for other cancer-specific outcomes, but quality of life outcomes were very limited (Ramsay, 2015).

In a 2015 article with one systematic review and 18 trials, documenting an overall five-year survival from 80 to 89 percent and the five-year prostate cancer survival was 97 to 99 percent. The effect of high-intensity focused ultrasound on quality of life remains undetermined (Veereman, 2015).
A review of 13 studies (n = 543) of partial prostate gland ablation using high-intensity focused ultrasound followed patients from 0.5 to 10.6 years, with complications reported in nearly half (254) of the patients, and 76 (14 percent) receiving further oncologic treatment. Post-operative erectile dysfunction and urinary incontinence ranged from 0 to 50 percent. Authors concluded that this technique may be a safe option for localized prostate cancer, pending further studies (Golan, 2017).

A systematic review of 37 studies (n=3,230) of focal therapy for prostate cancer treatment included 13 studies (n = 346) using high-intensity focused ultrasound, and followed patients a median of 12 months. Eleven studies used the trans-rectal focal approach, while the other two used the in-bore transurethral technique. All patients survived, all had pad-free continence, and 88.6 percent had potency preservation. The significant adverse effect rate was 1.5 percent, while 7.8 percent transitioned to a second therapy. Authors deemed focal therapies to be relatively safe, although oncological outcomes had not been evaluated against the standard of care (Valerio, 2017).

A systematic review of 14 non-randomized studies compared first-line treatment for patients with low-to moderate-risk prostate cancer for cryotherapy (n = 350) and high intensity focused ultrasound (n = 1107). For these two procedures (cryotherapy outcomes listed first), similar results were documented for ranges of disease recurrence (13 – 26 percent versus 7.3 – 67.9 percent); continence at 12 months (97.6 – 100 percent versus 96 – 100 percent); sexual potency rates (86 – 100 percent versus 76.9 – 100 percent for hemiablation, and 39 percent for total ablation); with focal cryotherapy and slightly lower rates for hemiablation (76.9 to 100 percent) and total therapy (39 percent). Potency rates varied among types of high-intensity focused ultrasound, i.e., 89, 52 – 80, and 33 – 78 percent for focal therapy, hemiablation and total therapy, respectively (Donis Canet, 2017).

A study of salvage procedures for prostate cancer addressed in 63 articles compared outcomes for salvage radical prostatectomy (25 articles) with three non-invasive salvage procedures, including high-intensity focused ultrasound (eight articles). No differences were found between surgical and non-surgical patients in functional, toxicity, and oncological outcomes, and better continence outcomes were identified for non-surgical procedures (Philippou, 2017).

Numerous other studies have been published on the efficacy of high-intensity focused ultrasound for hepatocellular, pancreatic, and breast cancer, plus osteoid osteoma, Parkinson’s disease/tremors, uterine fibroids, acute fractures, thyroid nodules, and musculoskeletal diseases.

Policy updates:

Systematic reviews added in January 2019 included a study of patient-reported outcomes for various types of localized prostate cancer treatment; those undergoing high-intensity focused ultrasound reported no significant changes after one year (Avila, 2018). Another review of five studies showed that
erectile function declined one month after surgery, but returned to baseline after six months (Faure Walker, 2018).
A total of two peer-reviewed references were added to, and two peer-reviewed references removed from this policy in January, 2019.

The policy number was changed from CP#13.02.04 to CCP.1364 in January 2019.

References

Professional society guidelines/other:


InterQual®: CP: High intensity focused ultrasound.


Peer-reviewed references:


**Centers for Medicare & Medicaid National Coverage Determinations:**

No National Coverage Determinations identified as of the writing of this policy.

**Local Coverage Determinations:**

No Local Coverage Determinations identified as of the writing of this policy.

**Commonly submitted codes**

Below are the most commonly submitted codes for the service(s)/item(s) subject to this policy. This is not an exhaustive list of codes. Providers are expected to consult the appropriate coding manuals and bill accordingly.

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<td>Focused ultrasound ablation/therapeutic intervention, other than uterine leiomyomata, with magnetic resonance (MR) guidance</td>
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<td>C9747</td>
<td>Ablation of prostate, transrectal, high intensity focused ultrasound (hifu), including imaging guidance</td>
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