



**Kaiser Foundation Health Plan  
of Washington**

**Clinical Review Criteria**

**High Intensity Focused Ultrasound (HIFU) for the Treatment of Localized Prostate Cancer**

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**Criteria**

**For Medicare Members**

Source	Policy
CMS Coverage Manuals	None
National Coverage Determinations (NCD)	None
Local Coverage Determinations (LCD)	None
Local Coverage Article	None
KPWA Medical Policy	Due to the absence of an active NCD, LCD, or other coverage guidance, KPWA has elected to use <b>MCG* High Intensity Focused Ultrasound (HIFU), Prostate (A-0271)</b> for medical necessity determinations. This service is not covered per MCG guidelines. For access to the MCG Clinical Guidelines criteria, please see the MCG Guideline Index through the provider portal under Quick Access.

**For Non-Medicare Members**

Kaiser Permanente has elected to use the MCG\* High Intensity Focused Ultrasound (HIFU), Prostate (A-0271) for medical necessity determinations. This service is not covered per MCG guidelines. For access to the MCG Clinical Guidelines criteria, please see the MCG Guideline Index through the provider portal under Quick Access.

**\*MCG are proprietary and cannot be published and/or distributed.** However, on an individual member basis, Kaiser Permanente can share a copy of the specific criteria document used to make a utilization management decision. If one of your patients is being reviewed using these criteria, you may request a copy of the criteria by calling the Kaiser Permanente Clinical Review staff at 1-800-289-1363 or access the MCG Guideline Index using the link provided above.

**If requesting this service, please send the following documentation to support medical necessity:**

- Last 6 months of clinical notes from requesting provider &/or specialist (oncologist, radiologist, primary care provider)
- Most recent imaging

The following information was used in the development of this document and is provided as background only. It is provided for historical purposes and does not necessarily reflect the most current published literature. When significant new articles are published that impact treatment option, Kaiser Permanente will review as needed. This information is not to be used as coverage criteria. Please only refer to the criteria listed above for coverage determinations.

**Background**

Prostate cancer is the second most frequently diagnosed cancer across the globe (Wolff et al., 2015). A 2008-2010 data estimated that 15% of men in the United States will be diagnosed with prostate cancer at some point in their lives (Wolff et al., 2015). However, the mortality rate is low because it is a slow growing cancer.

Treatment is based on a number of factors including tumor stage, prostate specific antigen (PSA) value, Gleason score (GS), patient's age, concomitant diseases, life expectancy and patient's preference (Warmuth, Johansson, & Mad, 2010). A wide range of options are available for prostate cancer and these include active surveillance, watchful waiting, radical prostatectomy, hormone therapy, radiotherapy, external beam radiotherapy (EBRT), brachytherapy and chemotherapy (Wolff et al., 2015). High Intensity Focused Ultrasound (HIFU) and cryotherapy are being considered as treatment options.

HIFU is a procedure in which beams target localized tissue without destroying the surrounding tissue and the high energy produced by HIFU leads to coagulative necrosis (Dogra, Zhang, & Bhatt, 2009). Two mechanisms including hyperthermia and acoustic cavitation cause the destruction of the tissue (Kennedy, Ter Haar, & Cranston, 2014). First, high energy is produced and converted to heat as the ultrasound wave disseminates through the tissue. This high energy leads to extreme temperatures surpassing the threshold level of protein denaturation (>43-degree C) resulting in coagulative necrosis. In the surrounding areas of the target zone, temperatures decrease suddenly keeping the outside tissues unaffected. Second, the interaction between ultrasound and micro-bubbles of water in the sonicated tissue result in cavitation. Cavitation may lead to diffusion of energy reinforcing tissue destruction (Stride & Coussios, 2010).

For this procedure, a transducer, covered by a condom through which cooled water is circulated to cool the rectal wall, is inserted into the rectum and several images are taken. The transducers generate very precise small lesions destroying the prostate partially or completely (Cordeiro et al., 2012).

HIFU is non-invasive and non-ionizing technique that is believed to have some advantages over other thermal therapy such as cryotherapy, laser ablation, and photothermal therapy and radiofrequency interstitial tumor ablation (Cordeiro et al., 2012). Two types of systems have been approved by the Food and Drug Administration (FDA). These include the Sonablate 450 (developed by SonaCare Medical) and the Ablatherm HIFU (EDAP TMS SA) both of which received FDA approval in October and November 2015 respectively. HIFU is indicated for primary treatment and salvage treatment for localized prostate cancer.

## Medical Technology Assessment Committee (MTAC)

### *High Intensity Focused Ultrasound (HIFU) for the treatment of localized Prostate Cancer*

**MTAC REVIEW: 06/21/2016**

**Evidence Conclusion:** INTC reviewed the technology in 2008 and concludes that there is insufficient evidence to determine whether the technology is medically appropriate for any patient and that the existing evidence regarding how HIFU treats prostate cancer is of insufficient quantity and quality. In April 2016, INTC conducted another review of the technology and concludes that: "the body of evidence that is available from which to assess the efficacy and safety of HIFU for localized prostate cancer (as primary and salvage therapy) is very low quality. The risk of bias in existing studies is high. Across studies, there is variation and/or lack of information regarding patient selection criteria, how HIFU was delivered, how outcomes were measured, and how long patients were followed"

INTC review can be adopted.

#### **HIFU for Primary and Salvage therapy**

**Systematic Review of the Efficacy and Safety of High-Intensity Focused Ultrasound for the Primary and Salvage Treatment (Warmuth, Johansson, & Mad, 2010)** (evidence table 1) The aim of this study was to assess the efficacy and safety of HIFU in the primary and salvage treatment for prostate cancer. The primary outcomes were the biochemical disease-free survival rate, the negative biopsy rate, overall survival rates, prostate cancer-specific survival rates, adverse events, and QOL. The literature search was performed from 200 to 2010 and included 20 case series (with more than 50 participants) in which 93% of patients were treated with primary therapy and 7% for salvage HIFU. For all HIFU procedures, the biochemical disease-free survival rate was between 78% and 84%, 45%- 84%, and 69% at 1, 5, and 7 years, respectively. The negative biopsy rate was 86% at 3 months and 80% at 15 months. Overall survival rate and prostate-cancer specific survival rate were reported in 1 study and were 90% and 100% at 5 years and 83% and 98% at 8 years, respectively. Adverse events were mainly related to the urinary tract (1-58%), potency (1-77%) and rectum (0-15%).

The study has several limitations including the study design lacking control group, long term follow-up was not available and the quality of evidence of included studies was low, surrogate outcomes were used and the central question is whether surrogate outcomes corroborate with overall survival, QOL, and prostate cancer specific survival, and the possibility for publication bias. The evidence is of low quality; therefore, results should be interpreted with caution.

**Ablative therapy for people with localized prostate cancer: a systematic review and economic evaluation (Ramsay et al., 2015)** (evidence table 2) This systematic review indicates that the biochemical failure rate of HIFU was higher (statistically significant) than that of EBRT at 1 year but no statistically significant difference was observed at 5 years. The results also indicate statistically significant lower rate of disease free survival for HIFU compared to EBRT at 1 year. At 4 years, overall survival was better for HIFU compared to EBRT. Compared to RP, there was an increased risk of biochemical failure for HIFU at 1 and 5 years. But this difference was not significant. Also, in term of disease free survival, no statistical significant difference was noted when HIFU was compared to RP at 1 year. At 3 years, the difference was not statistically significant. For urinary incontinence, erectile dysfunction, or bowel problems (not in the table), data were insufficient to reach a conclusion. Results were not statistically significant for dysuria or urinary retention. Nonetheless, high proportion of urethral stricture was observed for HIFU. When comparing HIFU to active surveillance (AS) (not on the table), there was no difference in overall survival or erectile dysfunction. The results are mixed and due to the poor quality of case series included in the review, with the lack of long term findings, the result should be interpreted with caution.

### **HIFU for Salvage therapy**

#### **High intensity focused ultrasound (HIFU) for definitive treatment of prostate cancer (Cordeiro et al., 2012)**

The purpose of this review was to update the available literature on HFU as definitive treatment of prostate cancer and to describe the techniques extensively and give an overview of historical background. Searched was conducted from 200 to December 2011. The search included case series with more than 50 participants assessing efficacy and safety of HIFU. No RCTs were identified and only 33 uncontrolled studies were identified. HIFU as salvage therapy after EBRT was assessed in two case series. The mean age was 68 years with mean preoperative PSA ranged from 6.89 to 7.73 ng/mL and Gleason score (GS) was  $\geq 8$ . Prostate volume preoperatively ranged from 18-21.4 mL; 34-56% received neoadjuvant androgen-deprivation therapy (NADT). Patients were followed for 15-18 months. The negative biopsy rate ranged from 73-80%; patients achieving  $PSA \leq 5$  ng/ml was 61% in one study; the mean PSA Nadir ranged from 1.97-2.38 ng/ml and disease-free survival ranged from 38-53% (30 mos-36mos). In terms of complications, urinary retention represented 7.8%, urinary tract infections (1.4- 3.5%), urinary incontinence (7-31.5%), bladder stenosis (17%), rectal urethral fistula 3 weeks after HIFU (3-6%) and erectile dysfunction was not assessed. The authors concluded that HIFU seems to control cancer on the short to medium term with less adverse events compared to established therapies. There was heterogeneity among the studies; individual studies are case series resulting in low quality evidence. In addition, long term data was not available. Therefore, results should be interpreted with caution.

### **Additional studies**

Subsequent studies (assessing HIFU as primary or salvage therapy) to the systematic reviews aforementioned were non-randomized controlled trial and did not compare HIFU to other treatment options. Accurate conclusions cannot be made from these studies. Summary of additional studies for HIFU as primary therapy: Nine non-RCTs (Aoun et al., 2015; Sebastien Crouzet et al., 2014; Dickinson et al., 2016; Feijoo et al., 2016; Ganzer et al., 2013; Liu & Chiang, 2016; Mearini et al., 2015; Uchida et al., 2015; van Velthoven et al., 2015) were examined and were for the most part observational studies. The sample size ranged from 50 to 1002; follow-up varied from 12 to 108 months. Of the nine studies, only two were comparative (Aoun et al., 2015; Liu & Chiang, 2016) and the findings from these two studies indicate: for Liu, 2016 (HIFU vs. cryoablation), no differences between biochemical recurrence rates were found; for Aoun, 2015 (HIFU vs. brachytherapy), similar survival outcomes were observed with greater biochemical recurrence free survival in the brachytherapy group. Summary of additional studies for HIFU as salvage therapy: Five observational studies (Baco et al., 2014; Sébastien Crouzet et al., 2012; Song et al., 2014; Uddin Ahmed et al., 2012; Yutkin et al., 2014) were examined; the sample size varied from 19 to 290; follow-up ranged from 19.8 months to 51.6 months and there was heterogeneity in the measures of outcomes. The survival rates varied as well.

### **Conclusion:**

- No RCTs comparing HIFU to other treatment options were identified.
- The available evidence is of low quality since it is represented by non-comparative, case series/observational studies.
- The overall concerns are the lack of control group and long-term follow-up, the use of surrogate outcomes raising the question of consistency with overall survival and QOL, and the variations in patient populations and biochemical progression-free survival.
- Conclusion on efficacy and safety of HIFU for the treatment of localized prostate cancer or recurrent localized prostate cancer cannot be drawn at this time.

**Articles:** No RCTs were identified. The following articles are selected for critical appraisal: Systematic Review of the Efficacy and Safety of High-Intensity Focused Ultrasound for the Primary and Salvage Treatment (Warmuth et al., 2010) (evidence table 1) Ablative therapy for people with localized prostate cancer: a systematic review and economic evaluation (Ramsay et al., 2015) (evidence table 2) High intensity focused ultrasound (HIFU) for definitive treatment of prostate cancer (Cordeiro et al., 2012)

The use of High Intensity Focused Ultrasound (HIFU) for the treatment of localized Prostate Cancer does not meet the *Kaiser Permanente Medical Technology Assessment Criteria*.

## Applicable Codes

### Considered Not Medically Necessary:

CPT® or HCPC Codes	Description
55880	Ablation of malignant prostate tissue, transrectal, with high intensity-focused ultrasound (HIFU), including ultrasound guidance
C9734	Focused ultrasound ablation/therapeutic intervention, other than uterine leiomyomata, with magnetic resonance (MR) guidance

**\*Note:** Codes may not be all-inclusive. Deleted codes and codes not in effect at the time of service may not be covered.

\*\*To verify authorization requirements for a specific code by plan type, please use the [Pre-authorization Code Check](#).

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07/05/2016	07/05/2016 <sup>MPC</sup> , 05/02/2017 <sup>MPC</sup> , 03/06/2018 <sup>MPC</sup> , 03/05/2019 <sup>MPC</sup> , 03/03/2020 <sup>MPC</sup> , 03/02/2021 <sup>MPC</sup> , 03/01/2022 <sup>MPC</sup> , 03/07/2023 <sup>MPC</sup>	01/07/2022

<sup>MPC</sup> Medical Policy Committee

Revision History	Description
05/02/2017	Adopted MCG A-0271
05/02/2017	Adopted Non-Medicare policy for Medicare members
03/16/2021	Added new CPT code 55880 effective 1/1/2021
01/07/2022	Removed diagnosis codes for HIFU