MP 7.01.109
Magnetic Resonance–Guided Focused Ultrasound

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POLICY
Magnetic resonance–guided high-intensity ultrasound ablation may be considered medically necessary for pain palliation in adults with metastatic bone cancer who have failed or are not candidates for radiotherapy.

Magnetic resonance–guided high-intensity ultrasound ablation is considered investigational in all other situations including but not limited to:

- Treatment of uterine fibroids; and
- Treatment of other tumors (e.g., brain cancer, prostate cancer, breast cancer, desmoids).

POLICY GUIDELINES
Magnetic resonance–guided high-intensity ultrasound ablation of uterine fibroids is specifically identified by the following category III CPT codes:

0071T: Focused ultrasound ablation of uterine leiomyomata, including MR guidance; total leiomyomata volume of less than 200 cc of tissue
0072T: As above, but with total leiomyomata volume greater or equal to 200 cc of tissue.

These CPT codes should not be used with 51702 (insertion of temporary indwelling bladder catheter, simple) or 77022 (magnetic resonance imaging guidance for, and monitoring of, visceral tissue ablation). Before the introduction of the specific category III CPT codes, the procedure may have been coded using several codes describing the individual components of the procedure. CPT codes 0071T-0072T describe the comprehensive service.

The procedure may be performed in a magnetic resonance imaging suite with an open magnetic resonance imaging scanner, which might not be available at many institutions. The procedure is performed in an outpatient setting, with the patient under conscious sedation.

There are no specific CPT codes for the use of magnetic resonance–guided high-intensity ultrasound ablation in metastatic bone cancer. An unlisted code would be used based on the anatomic location of the metastasis being treated (e.g., 23929 for the clavicle) or perhaps an unlisted radiation oncology code.
(e.g., 77299 or 77499).

**BENEFIT APPLICATION**

**BLUECARD/NATIONAL ACCOUNT ISSUES**
State or federal mandates (e.g., a Federal Employee Program) may dictate that certain U.S. Food and Drug Administration–approved devices, drugs, or biologics may not be considered investigational, and thus these devices may be assessed only by their medical necessity.

Magnetic resonance–guided high-intensity ultrasound ablation of uterine fibroids is currently performed at a limited number of institutions; therefore, an out-of-network referral may be requested.

**BACKGROUND**

**UTERINE FIBROIDS**
Uterine fibroids are one of the most common conditions affecting women in the reproductive years. Symptoms of uterine fibroids include menorrhagia, pelvic pressure, or pain. Several approaches currently available to treat symptomatic uterine fibroids include: hysterectomy, abdominal myomectomy, laparoscopic and hysteroscopic myomectomy, hormone therapy, uterine artery embolization, and watchful waiting. Hysterectomy and various myomectomy procedures are considered the criterion standard treatment.

**METASTATIC BONE DISEASE**
Metastatic bone disease is one of the most common causes of cancer pain. Existing treatments include conservative measures (e.g., massage, exercise) and pharmacologic agents (e.g., analgesics, bisphosphonates, and corticosteroids). For patients who fail the above treatments, the standard care is to use external-beam radiotherapy. However, a substantial proportion of patients have residual pain after radiotherapy, and there is a need for alternative treatments for these patients. (One option, radiofrequency ablation, is addressed in related evidence review 7.01.95).

**MAGNETIC RESONANCE–GUIDED FOCUSED ULTRASOUND**
Magnetic resonance–guided focused ultrasound (MRgFUS) is a noninvasive treatment that combines 2 technologies: focused ultrasound and magnetic resonance imaging (MRI). The ultrasound beam penetrates through the soft tissues and, using MRI for guidance and monitoring, the beam can be focused on targeted sites. Ultrasound causes a local increase in temperature in the target tissue, resulting in coagulation necrosis while sparing the surrounding normal structures. Ultrasound waves from each sonication are directed at a focal point that has a maximum focal volume of 20 nm in diameter and 15 nm in height/length. This causes a rapid rise in temperature (i.e., to 65°C-85°C), which is sufficient to ablate tissue at the focal point. In addition to providing guidance, the associated MRI can provide online thermometric imaging that provides a temperature “map” to confirm the therapeutic effect of the ablation treatment and allow for real-time adjustment of the treatment parameters.

The U.S. Food and Drug Administration (FDA) approved the ExAblate MRgFUS system (InSightec) for 2 indications: treatment of uterine fibroids (leiomyomata) and palliation of pain associated with tumors metastatic to bone. The ultrasound equipment is specifically designed to be compatible with magnetic resonance magnets, and it is integrated into standard clinical MRI units; it also includes a patient table, which has a cradle that houses the focused ultrasound transducer in water or a light oil bath. Some models have a detachable cradle; only certain cradle types can be used for palliation of pain associated with metastatic bone cancer. For treating pain associated with bone metastases, the aim of MRgFUS is to destroy nerves in the bone surface surrounding the tumor.
MRgFUS is also being investigated for the treatment of other tumors, including breast, prostate, brain, and desmoid tumors as well as non-spinal osteoid osteoma.

**REGULATORY STATUS**

In October 2004, the ExAblate® 2000 System (InSightec, Haifa, Israel) was approved by FDA through the premarket approval process for “ablation of uterine fibroid tissue in pre- or peri-menopausal women with symptomatic uterine fibroids who desire a uterine sparing procedure.” Treatment is indicated for women with a uterine gestational size of less than 24 weeks who have completed childbearing.

In October 2012, the ExAblate® System, Model 2000/2100/2100 VI, was approved by FDA through the premarket approval process for pain palliation in adult patients with metastatic bone cancer who have failed or are not candidates for radiotherapy. The device was evaluated through an expedited review process. FDA required a post-approval study with 70 patients to evaluate the effectiveness of the system under actual clinical conditions.

FDA product code: NRZ.

**RATIONALE**

This evidence review was created in July 2004 and has been updated regularly with searches of the MEDLINE database. This review was informed by a 2005 TEC Assessment on magnetic resonance–guided focused ultrasound (MRgFUS) for symptomatic uterine leiomyomata, which found the evidence of efficacy insufficient compared with conventional therapies.¹ The most recent literature update was performed through June 2, 2017.

Assessment of efficacy for therapeutic interventions such as MRgFUS involves the determination of whether the intervention improves health outcomes. The optimal study design for a therapeutic intervention is a randomized controlled trial (RCT) that includes clinically relevant measures of health outcomes. The technology should be compared with the best alternative treatment when available, as is the case of MRgFUS for treating uterine fibroids. In the case of subjective outcomes, such as pain or quality of life (QOL), a sham comparison is also appropriate. Nonrandomized comparative studies and uncontrolled studies can sometimes provide useful information on health outcomes but are prone to biases such as selection bias (e.g., non-comparability of treatment groups) and observational bias (e.g., the placebo effect). The following is a summary of the literature to date.

**UTERINE FIBROIDS**

Evidence for the use of MRgFUS for the treatment of uterine fibroids consists of 2 small RCTs and many observational studies.

**Randomized Controlled Trials**

In 2017, Barnard et al published preliminary results from Fibroid Interventions: Reducing Symptoms Today and Tomorrow (FIRSTT) study, a parallel RCT and cohort study comparing MRgFUS with fibroid embolization for the treatment of uterine fibroids.² For the RCT, patients were randomized to uterine artery embolization (UAE; n=22) or to MRgFUS (n=27). Patients and investigators were not blinded. Women who did not want to be randomized were enrolled in the cohort study; 16 underwent UAE and 16 underwent MRgFUS. Patients were instructed to keep diaries with the following information: medication use, return to normal activities, and symptoms. After 6 weeks of follow-up for the RCT patients, there were no differences between groups in symptoms such as fatigue, hot flashes, discomfort urinating, vaginal discharge, or constipation. Recovery was significantly faster in the MRgFUS group, as measured by the first day back to work and first day back to normal. Medication use (i.e., opioids, nonsteroidal anti-inflammatory drugs, acetaminophen or aspirin, nausea medication, bowel...
medication) was also significantly lower in the MRgFUS group. Analyses combining the RCT and cohort patients showed similar results. The MRgFUS procedure took significantly longer than the UAE procedure. A limitation of the trial was the inability to recruit more patients. Long-term follow-up results will be forthcoming.

In 2016, a pilot sham-controlled randomized trial evaluating MRgFUS for the treatment of uterine fibroids was published by Jacoby et al.3 The trial included 20 premenopausal women with symptomatic uterine fibroids (women who were pregnant or had a desire for future children were excluded). Patients were randomized to MRgFUS with the ExAblate 2000 System (n=13) or to a sham treatment not using thermal energy (n=7). The investigators did not specify primary outcomes. The sample size was calculated to assess the feasibility of a larger trial, not to provide sufficient statistical power. All patients were assigned to the MRgFUS group and 6 of 7 in the placebo group received their allocated treatment; all patients who were treated completed 3 months of follow-up. Patients were unblinded at 3 months, and those in the sham group were given the option of active treatment.

QOL outcomes included the Uterine Fibroid Symptom and Quality of Life Questionnaire, which has subscales including the symptom severity score (SSS) and health related quality of life score. The 36-Item Short-Form Health Survey (SF-36), which includes the Mental Component Summary and Physical Component Summary, was also used. At 4- and 12-week follow-ups, there were no statistically significant differences (at the p<0.05 level) between the MRgFUS and the sham groups in the SSS, the health related quality of life score, and SF-36 Physical Component Summary or Mental Component Summary scores. Change in uterine and fibroid volume, however, differed significantly between groups at 12 weeks. Uterine volume decreased by 17% in the MRgFUS group and by 3% in the sham group (p=0.04). Total fibroid volume decreased by 18% in the MRgFUS group and did not change in the sham group (p=0.03). The authors concluded that women would be willing to participate in a sham-controlled randomized trial of MRgFUS and that larger trials were feasible.

**Systematic Reviews**

The remaining published studies are nonrandomized. A systematic review, published by Gizzo et al in 2014, identified 38 uncontrolled studies with a total of 2500 patients who underwent MRgFUS for the treatment of uterine fibroids.4 All published studies included women 18 years or older with symptomatic uterine fibroids, and most excluded patients who desired future pregnancies. Reviewers did not pool study findings but concluded that; overall, MRgFUS appeared to be a safe, noninvasive option for treating uterine fibroids. Future research was recommended to compare MRgFUS with other noninvasive procedures and to explore the fertility-sparing potential further.

**Nonrandomized Studies**

A nonrandomized pivotal study included in the Gizzo systematic review, designed for U.S. Food and Drug Administration (FDA) approval of the ExAblate 2000 device, evaluated 109 women treated with MRgFUS and 83 women treated with abdominal hysterectomy.5,6 The primary outcome was changed in SSS, part of the validated Uterine Fibroid Symptom and Quality of Life Questionnaire. Symptom severity was measured using 8 questions relevant to bulk and bleeding symptoms on a 0-to-100 scale, with the higher number representing greater symptom severity. Outcome data were initially reported for the MRgFUS group only. At 6-month follow-up, 71% of the MRgFUS group achieved a 10-point or greater reduction in SSS, but this decreased to 51% at 12 months. It is unclear what represents a clinically meaningful change in SSS. A threshold of more than 10 points was selected for the analysis, but this threshold is arbitrary and not substantiated by other research. Twenty-one percent of those treated by MRgFUS needed additional surgical treatment, and 4% underwent a repeat MRgFUS by 12 months.

**Original Policy Date:** July 2004
Fennessy et al (2007) compared 2 variations on the MRgFUS procedure. They treated patients with the original protocol (33% of fibroid volume with a 120-minute maximum treatment time, n=96) or modified protocol (50% treatment volume, 180-minute maximum treatment time, and a second treatment if within a 14-day period, n=64). In the original group, the non-perfused (effectively treated) area was calculated at 17% of fibroid volume compared with 26% of fibroid volume with the modified protocol. Overall, SSS decreased from 62 at baseline to 33 at 12 months, with fewer patients in the modified group choosing alternative treatment (28% vs 37%, respectively). Interpretation of these results was limited by the large loss to follow-up; 55 (57%) patients from the original treatment protocol completed follow-up. Only 21 (33%) patients from the modified protocol group were evaluable at 12-month follow-up.

In 2009, Taran et al reported on outcomes between MRgFUS and hysterectomy in women with uterine fibroids. The main outcome measure was SF-36 scores. Safety data were also presented. A significantly higher proportion of women in the hysterectomy group (82/83 [99%]) reported at least 1 adverse event compared with women in the MRgFUS group (88/109 [81%]). Pain or discomfort as well as adverse events associated with the gastrointestinal tract, dermatologic system, nervous system, and cardiovascular system were significantly more common in the hysterectomy group. However, a similar proportion reported a serious adverse event, 9 (8%) of 109 in the MRgFUS group and 8 (10%) of 83 in the hysterectomy group. At 6 months, there were significantly higher scores in the hysterectomy group on 2 of 8 SF-36 subscales; scores on the remaining subscales did not differ significantly between groups. SF-36 subscale scores were subject to a multiple comparison bias; a large number of statistical comparisons were done for secondary outcomes, and p values were not adjusted.

A 2007 publication reported 24-month follow-up from 3 phase 3 trials and 1 post-marketing study (total N=416 patients). The study found a relation between the non-perfused fibroid volume ratio and the probability of undergoing additional leiomyoma treatment. For non-perfused volume ratios of 20% to 50%, there was a 25% probability of additional treatment. Patients with a non-perfused volume ratio of less than 20% had a 40% probability of additional treatment. No shrinkage (and a trend toward growth) was seen with non-perfused volume ratios of 10% or less. Most women had limited treatments, with 57% of the patients having a non-perfused volume of 20% or less and 34% of the patients having a non-perfused volume between 30% and 70%. Fewer than 3% of women had a non-perfused volume ratio of 70% or greater. These results raise questions about the amount of non-perfusion achieved with the treatment protocols.

A 2011 case series included 40 women treated with MRgFUS for symptomatic uterine fibroids at 1 center in the United States. The primary study end points were change from baseline in QOL and symptom severity scores. (Higher scores on the QOL measure and lower scores on the symptom severity measure indicated improvement.) Mean SSS in the 29 (73%) patients who completed the 3-year follow-up was 64.8 at baseline and 17.0 at 3 years, representing a mean reduction of 47.8 points. Mean QOL score at baseline was 44.1 and at the 3-year follow-up was 83.9, a mean improvement of 39.8 points. Both improvements were statistically significant. Another representative case series (2011) reported 12-month outcomes data on 130 women treated with MRgFUS. Eight women had additional procedures to relieve symptoms within 1 year of MRgFUS treatment; seven underwent a hysterectomy, and one underwent endometrial ablation. Data on symptom relief at 12 months were available for 70 (54%) of 130 patients. Fifty-one (73%) of the 70 reported excellent symptom relief.

The following studies were published after the Gizzo systematic review. In 2016, Chen et al evaluated 107 women undergoing MRgFUS for the treatment of uterine fibroids. Efficacy was defined as the
proportion of patients with at least 10% fibroid shrinkage from baseline, as measured by MRI. At the 6-month follow-up, 93% efficacy was reported.

In 2013, Froeling et al reported on 121 women with symptomatic uterine fibroids who were eligible for treatment with MRgFUS and UAE.\(^{13}\) Forty-four (36%) women were lost to follow-up. Follow-up data at 60 months were available for 77 women, 41 in the UAE group, and 36 in the MRgFUS group. The primary outcome was rate of reintervention (eg, repeat MRgFUS, myomectomy, hysterectomy, endometrial ablation). During follow-up, 5 (12%) women in the UAE group and 24 (67%) women in the MRgFUS group experienced a reintervention (statistical comparison not reported). Health-related QOL scores (secondary outcomes) were significantly better in the UAE group than in the MRgFUS group at follow-up.

**Fertility Following MRgFUS for Treatment of Uterine Fibroids**
A prospective registry of pregnancies after MRgFUS had been maintained by the manufacturer of the ExAblate device. A 2010 article reported that there were 54 known pregnancies a mean of 8 months after treatment.\(^{14}\) They included 8 pregnancies from clinical trials designed for women who did not desire pregnancy, 26 pregnancies after commercial treatment, and 20 pregnancies in 17 patients from an ongoing study of MRgFUS in women trying to conceive. Twenty-two (42%) of the 54 pregnancies resulted in deliveries and 11 were ongoing beyond 20 weeks at the time the article was written. There were 14 (26%) miscarriages and 7 (13%) elective terminations. Among the 22 live births, mean live birth weight was 3.3 kg, and the vaginal delivery rate was 64%. The article provided initial information on the impact of MRgFUS on uterine fibroids in pregnancy; findings suggested that fertility may be maintained but that the number of cases was too small to draw definitive conclusions. The study also did not address the possible impact of MRgFUS treatment on the future ability to become pregnant.

**Section Summary: Uterine Fibroids**
For the treatment of uterine fibroids, there are 2 small RCTs, one with 49 women that compared MRgFUS with UAE and one with 20 women that had a sham control. Several nonrandomized studies have also compared MRgFUS with a different treatment. The sham-controlled randomized trial concluded that a larger trial would be feasible. The trial reported significantly lower fibroid volumes in the active treatment group; however, there were no statistically significant differences in QOL between the groups. The other RCT reported no significant differences in medication use or symptoms between the MRgFUS and UAE groups. Recovery was significantly faster in the MRgFUS group than in the UAE group. The pivotal FDA trial had several limitations: no randomization, data on the comparison group were not published until 5 years after data on the treatment group, unclear clinical significance of primary outcome, and no follow-up data beyond 1 year. In the 2013 comparative study, outcomes appeared to be better with UAE than with MRgFUS. There is insufficient evidence on the long-term treatment effects, recurrence rates, and impact on future fertility and pregnancy of this therapy.

**PALLIATIVE TREATMENT OF BONE METASTASES**
Evidence for the use of MRgFUS for the treatment of painful bone metastases consists of a large RCT and many observational studies.

An RCT evaluating the ExAblate System for the treatment of painful bone metastases was published by Hurwitz et al in 2014.\(^{15}\) Findings from this trial were available on the FDA website, because this trial was used as evidence for FDA approval. The trial included patients with at least 3 months of life expectancy who had bone metastases that were painful, despite radiotherapy, or who were unsuitable for or declined radiotherapy. Patients rated tumor pain on a numeric rating scale (NRS) at 4 or higher on a 10-point scale. While they could have up to 5 painful lesions, only 1 lesion was treated, and it had to cause
at least 2 points greater pain on the NRS than any other lesion. Also targeted tumors needed to be device-accessible.

Study participants were randomized 3:1 to active (n=122) or sham (n=39) MRgFUS treatment. Ten patients in the treatment group and four in the sham group did not receive the allocated treatment. An additional 26 patients in the treatment group and 23 in the sham group did not complete the 3-month follow-up. A larger proportion of the placebo group dropped out: 17 (49%) of 35 who were treated decided to have rescue MRgFUS treatment after a lack of response to placebo. A modified intention-to-treat analysis was used that included patients who had at least 1 MRgFUS or placebo sonication. Missing values were imputed using the last-observation carried forward method.

The primary efficacy end point, assessed at 3 months, was a composite outcome comprised of change in baseline in worst NRS score and morphine equivalent daily dose (MEDD) intake. Patients were considered responders if their worst NRS score decreased by at least 2 points and if their MEDD intake did not increase more than 25% from baseline to 3 months. NRS scores and MEDD intake were reported separately as secondary outcomes.

Seventy-two (64%) of 112 patients in the MRgFUS group and 7 (20%) of 35 patients in the control group were considered responders, as previously defined. The difference was statistically significant (p=0.01), favoring active treatment. When the 2 measures comprising the primary end point were analyzed separately, there was a statistically significant difference between groups in change in worst NRS score and a nonsignificant difference in change from baseline in pain medication. The NRS score decreased by a mean (SD) of 3.6 (3.1) points in the MRgFUS group and by a mean of 0.7 (2.4) in the placebo group (p<0.01). Change in MEDD from baseline was 3.7 in the MRgFUS group and 15.3 in the placebo group. Fifty-one (46%) patients in the MRgFUS group and 1 (3%) in the placebo group experienced at least 1 adverse event. Most adverse events were transient, with the most common being sonication pain, experienced by 36 (32%) patients in the MRgFUS group. In 17 (15%) patients, sonication pain was severe; 3 patients did not complete treatment due to pain. The most clinically significant adverse events that lasted more than a week were third-degree skin burns in 1 patient (associated with noncompliance with the treatment protocol) and fracture in 2 patients (one of which was outside the treatment location). Potential limitations of the trial included a nonconventional primary outcome measure and the small initial size of the sham group. Moreover, a large number of sham patients (66%) did not complete the 3-month follow-up; the authors indicated that this low completion rate was due to lack of response to placebo treatment.

In addition to the single RCT, several manufacturer-sponsored case series have evaluated MRgFUS for pain palliation in bone metastases. In 2009, Liberman et al published findings of a multicenter prospective study conducted in Canada, Israel, and Germany. The study included 31 patients with painful bone metastases who had failed or refused other treatment options; 25 (81%) patients were available for 3-month follow-up. Mean visual analog scale score decreased from 5.9 at baseline to 1.8 three months after treatment. Thirteen of 25 patients who used non-opioid analgesics and 6 of 10 who used opioids decreased medication use after treatment. Neither group reported treatment-related adverse events.

In a 2017 recent case series, Arrigoni et al evaluated use of MRgFUS in 14 patients with intra-articular benign bone lesions who were followed for 12 months. Pain was measured by visual analog scale and all patients underwent computed tomography and magnetic resonance imaging. Mean pain scores significantly decreased from 7.8 pretreatment to 2.0 at 6-month follow-up to 0.6 at 12-month follow-up (p<0.001). No patients reported worse symptoms and none reported the procedure unsuccessful.
Diagnostic imaging supported the clinical findings and showed calcification of the lesion, lack of contrast enhancement, and resolution of bone edema.

**Section Summary: Palliative Treatment of Bone Metastases**

The evidence base consists of a single industry-sponsored RCT that found significant improvement after MRgFUS in a composite outcome comprised of reduction in pain and morphine use, and in pain reduction as a stand-alone outcome. This trial was appropriately sham-controlled. A substantial proportion of patients in the treatment group experienced adverse events, but most adverse events were transient and not severe. Several case series has also reported improvements in pain and patient satisfaction with MRgFUS.

**TREATMENT OF OTHER TUMORS**

Only small case series have been published on the safety and/or efficacy of MRgFUS for treating tumors related to breast cancer, brain cancer, prostate cancer, and nonspinal osteoid osteoma.

The most recent case series on the use of MRgFUS for breast cancer ablation was published in 2016. Ten patients with early-stage invasive breast cancer underwent MRgFUS prior to surgical resection. Ablation was confirmed histopathologically in 6 of these patients. The investigators concluded that MRgFUS is safe and feasible. A noted limitation is the long procedure time (average, 145 minutes), due to waiting time after contrast injection and time to find a proper magnetic resonance navigator signal.

In addition, several case series have investigated the use of MRgFUS for desmoid tumors. One by Avedian et al (2016) used MRgFUS to treat 9 patients with desmoid tumors. Five patients were available for follow-up for at least 12 months. Mean decrease in tumor size was 36% (95% CI, 7% to 66%). Bucknor et al (2017) described the use of MRgFUS to treat 3 patients with large aggressive desmoid tumors within the posterior thigh. Each patient received multiple MRgFUS treatments. In this case series, the authors noted that the use of MRgFUS for desmoid tumors required different treatment parameters than those used for fibroids or bone lesions, due to differences in vascularity of the target tissue and the need for effective skin protection when using MRgFUS on extremities. Ghanouni et al (2017) used MRgFUS to treat 15 patients with extra-abdominal desmoid tumors. Treatment times ranged from 0.8 to 8 hours. Results were presented on 9 patients (3 were lost to follow-up before 6 months, 3 received additional treatments). Seven of 9 patients experienced durable clinical benefits, with a median reduction in tumor volume of 98%. Treatment-related adverse events included skin burns, nerve injury, and off-target heating.

**Section Summary: Treatment of Other Tumors**

Currently, evidence on the use of MRgFUS for the treatment of other tumors consists of small case series. There are several ongoing trials evaluating the safety and efficacy of MRgFUS for other tumors, with completion dates in later 2017 and in the coming years. Trials on several soft tissue tumors and breast cancer have been completed in the past year and have yet to be published (see Table 1).

**SUMMARY OF EVIDENCE**

For individuals who have uterine fibroids who receive magnetic resonance–guided focused ultrasound (MRgFUS), the evidence includes 2 small randomized controlled trials (RCTs), nonrandomized comparative studies, and case series. Relevant outcomes are symptoms, quality of life, resource utilization, and treatment-related morbidity. One RCT (N=20) has reported some health outcomes, but its primary purpose was to determine the feasibility of a larger trial. It did not find statistically significant differences in quality of life outcomes between active and sham treatment groups, but it did find lower fibroid volumes after active treatment. This pivotal Food and Drug Administration trial was not...
randomized, the clinical significance of the primary outcome was unclear, and there were no follow-up data beyond 1 year. The second RCT (N=49) is ongoing; it has provided preliminary results at 6 weeks posttreatment, comparing MRgFUS with uterine artery embolization (UAE). The 2 groups were comparable in medication use and symptom improvement following treatments. Patients in the MRgFUS group reported recovering significantly faster than patients in the UAE group, as measured by time to return to work and time to normal activities. In a separate 2013 comparative study, outcomes appeared to be better with UAE than with MRgFUS. We lack insufficient data on the long-term treatment effects, recurrence rates, and impact on future fertility and pregnancy. The evidence is insufficient to determine the effects of the technology on health outcomes.

For individuals with painful metastatic bone cancer who have failed or are not candidates for radiotherapy who receive MRgFUS, the evidence includes a sham-controlled randomized trial and several case series. Relevant outcomes are symptoms, functional outcomes, health status measures, quality of life, and treatment-related morbidity. The RCT found statistically significant improvements after MRgFUS in a composite outcome comprised of a reduction in pain and morphine use, and in pain reduction as a stand-alone outcome. A substantial proportion of patients in the treatment group experienced adverse events, but most was not severe and was transient. The case series also reported reductions in pain following MRgFUS treatment. The evidence is sufficient to determine that the technology results in a meaningful improvement in the net health outcome.

For individuals with other tumors (e.g., breast cancer, brain cancer, prostate cancer, or desmoid) or non-spinal osteoid osteoma who receives MRgFUS, the evidence includes small case series. Relevant outcomes are symptoms, health status measures, and treatment-related morbidity. The evidence is insufficient to determine the effects of the technology on health outcomes.

SUPPLEMENTAL INFORMATION

PRACTICE GUIDELINES AND POSITION STATEMENTS

Society of Obstetricians and Gynaecologists of Canada
In 2015, the Society of Obstetricians and Gynaecologists of Canada published practice guidelines on the management of uterine fibroids in women with otherwise unexplained infertility. The guidelines found no studies comparing magnetic resonance-guided focused ultrasound (MRgFUS) with myomectomy or in women with fibroids who have infertility as their primary complaint, and thus additional data would be needed before the treatment could be offered to this patient population.

American Society for Radiation Oncology
In 2011, the American Society for Radiation Oncology published guidelines on palliative radiotherapy for bone metastases, which stated that external-beam radiotherapy continues to be the primary therapy for treating painful uncomplicated bone metastases. The guidelines did not mention MRgFUS and did not offer specific recommendations for patients who fail or are not candidates for radiotherapy.

National Comprehensive Cancer Network
Guidelines from the National Comprehensive Cancer Network on breast cancer (v.2.2017), brain cancer (v.1.2016), and prostate cancer (v.2.2017) do not mention MRgFUS as a treatment option.

U.S. PREVENTIVE SERVICES TASK FORCE RECOMMENDATIONS
Not applicable.
**MEDICARE NATIONAL COVERAGE**
There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

**ONGOING AND UNPUBLISHED CLINICAL TRIALS**
Some currently ongoing and unpublished trials that might influence this review are listed in Table 1.

<table>
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<tr>
<th>NCT No.</th>
<th>Trial Name</th>
<th>Planned Enrollment</th>
<th>Completion Date</th>
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<td>NCT01965002</td>
<td>A Feasibility Study to Evaluate the Safety and Effectiveness of ExAblate Magnetic Resonance Imaging Guided High-Intensity Focused Ultrasound Treatment of Soft Tissue Tumors of the Extremities</td>
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<td>Feb 2017 (ongoing)</td>
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<td>NCT00981578a</td>
<td>A Feasibility Study to Evaluate the Safety and Initial Effectiveness of ExAblate MR Guided Focused Ultrasound Surgery in the Treatment of Pain Resulting from Metastatic Bone Tumors with the ExAblate 2100 Conformal Bone System</td>
<td>50</td>
<td>Jun 2017</td>
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<td>NCT01833806a</td>
<td>A Phase IV Post Approval Clinical Study of ExAblate Treatment of Metastatic Bone Tumors for the Palliation of Pain</td>
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<td>A Study to Evaluate the Safety and Feasibility of Transcranial MRI-Guided Focused Ultrasound Surgery in the Treatment of Brain Tumors</td>
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<td>NCT00147056a</td>
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<td>NCT00995878</td>
<td>The FIRSTT Study: Comparing Focused Ultrasound and Uterine Artery Embolization for Uterine Fibroids</td>
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<td>NCT01091883a</td>
<td>Phase IIIA Study Comparing the Safety and Effectiveness of MR Guided Focused Ultrasound and External Beam Radiation for Treatment of Metastatic Bone Tumors and Multiple Myeloma</td>
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<td>NCT02968784a</td>
<td>Focal ExAblate MR Guided Focused Ultrasound Treatment for Management of Organ-Confined Intermediate Risk Prostate Cancer: Evaluation of Safety and Effectiveness</td>
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<td>Jun 2019</td>
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<td>NCT02260752</td>
<td>Comparing Options for Management: Patient Centered Results for Uterine Fibroids</td>
<td>10,000</td>
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<td>NCT01657942a</td>
<td>Focal MR Guided Focused Ultrasound Treatment of Localized Low and Intermediate Risk Prostate Lesions</td>
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<td>NCT02794558a</td>
<td>A Clinical Study to Evaluate the Safety and Effectiveness of MR Guided Focused Ultrasound Surgery in the Treatment</td>
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### Unpublished

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<tr>
<th>NCT</th>
<th>Study Description</th>
<th>Patients</th>
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<tr>
<td>NCT01285960a</td>
<td>A Clinical Study to Evaluate Safety of the ExAblate Model 2100 Type 1.1 System in the Treatment of Symptomatic Uterine Fibroids</td>
<td>106</td>
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<td>(completed)</td>
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<td>NCT01620359a</td>
<td>Study of ExAblate Focused Ultrasound Ablation of Breast Cancer under MR Guidance and MRI Evaluation of Ablation</td>
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<td>Jul 2016</td>
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<td>NCT01834937a</td>
<td>A Post Approval Registry: ExAblate Treatment of Metastatic Bone Tumors for the Palliation of Pain</td>
<td>17</td>
<td>Apr 2017</td>
<td>(completed)</td>
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NCT: national clinical trial.

*a Denotes industry-sponsored or cosponsored trial.

## REFERENCES


CODES

<table>
<thead>
<tr>
<th>Codes</th>
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<td>CPT</td>
<td>0071T</td>
<td>Focused ultrasound ablation of uterine leiomyomata, including MR guidance; total leiomyomata volume of less than 200 cc of tissue</td>
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<td>CPT</td>
<td>0072T</td>
<td>; total leiomyomata volume greater or equal to 200 cc of tissue</td>
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<td>HCPCS</td>
<td>C9734</td>
<td>Focused ultrasound ablation/therapeutic intervention, other than uterine leiomyomata, with magnetic resonance (MR) guidance</td>
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<td>ICD-10-CM</td>
<td>C79.51</td>
<td>Secondary malignant neoplasm of bone</td>
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<td>ICD-10-CM</td>
<td>D25.0-D25.9</td>
<td>Leiomyoma of uterus code range</td>
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<td>ICD-10-PCS</td>
<td>BU36ZZZ</td>
<td>Imaging, female reproductive system, magnetic resonance imaging (MRI), uterus, no contrast</td>
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Type of Service
Place of Service

POLICY HISTORY

<table>
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<tr>
<td>02/13/14</td>
<td>Replace policy</td>
<td>Policy updated with literature review through January 6, 2014; references 2, 6, and 14 added; other references renumbered or removed</td>
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<td>02/12/15</td>
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<td>Policy updated with literature review through January 6, 2015. Statement added the MRgFUS may be considered medically necessary for pain palliation in adult patients with metastatic bone cancer who failed or are not candidates for radiotherapy. Bullet point on bone</td>
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Original Policy Date: July 2004
Magnetic Resonance–Guided Focused Ultrasound

<table>
<thead>
<tr>
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<td>02/11/16</td>
<td>Replace policy</td>
<td>Policy updated with literature review through December 15, 2015; references 2 and 23 added. Policy statements unchanged. Global change to policy to remove “imaging” (eg, title, policy statement) to standardize terminology to magnetic resonance–guided focused ultrasound (MRgFUS).</td>
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<tr>
<td>02/24/17</td>
<td>Replace policy</td>
<td>Blue Cross of Idaho annual review; no change to policy.</td>
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<tr>
<td>07/25/17</td>
<td>Replace policy</td>
<td>Policy updated with literature review through June 2, 2017; references 2, 12, 18, 23, and 27-29 added. Policy statements unchanged.</td>
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