Microwave Thermotherapy

Policy

*Please see amendment for Pennsylvania Medicaid at the end of this CPB.*

Aetna considers microwave thermotherapy (also known as focused microwave thermotherapy and focused microwave phase array thermotherapy) experimental and investigational for the treatment of the following indications (not an all-inclusive list) because of insufficient evidence of its effectiveness for these indications.

- Bladder cancer
- Bone cancer/limb salvage
- Breast cancer
- Breast cancer metastasis
- Cervical ectopy
- Chronic low back pain
- Chronic neck pain
- Chronic pelvic pain syndrome (including cancer pelvic pain)
- Chronic prostatitis
- Dysmenorrhea
- Keratoconus
- Kidney cancer
- Lung cancer

Policy History

- Last Review: 01/10/2020
- Effective: 02/17/2004
- Next Review: 07/24/2020

Definitions

Additional Information

Clinical Policy Bulletin

Notes
- Nasopharyngeal cancer
- Osteosarcoma
- Pancreatic cancer

For microwave thermotherapy for benign prostatic hypertrophy, see:

CPB 0079 - Benign Prostatic Hypertrophy (BPH) Treatments
(../1_99/0079.html)

See:

CPB 0274 - Ablation of Hepatic Lesions
also (../200_299/0274.html)

Background

Microwave is an electromagnetic wave with a wavelength between that of infrared and short waves.

Breast Cancer

Recent clinical investigations have examined the feasibility of thermotherapy that uses focused microwaves for the treatment of primary breast cancer, based on the theory that heat could destroy microscopic carcinoma cells in the breast and reduce cancer recurrence. Heating the tumor and killing a large percentage or all of the tumor cells before surgery may improve the margins and reduce the possibility of inadvertently seeding viable cancer cells during the surgical procedure, thus reducing local recurrences in the breast. In addition, if a sufficient thermal dose is applied, thermotherapy treatment of early-stage breast cancer may destroy the tumor and completely eliminate the need for any further breast surgery or radiation therapy.
Gardner et al (2002) reported on the results of a pilot study of focused microwave phased array thermotherapy in the treatment of 10 patients with primary breast carcinomas beneath the skin ranging from 1 to 8 cm in maximum clinical size. After focused microwave phased array treatment, all patients underwent mastectomy. Eight of 10 patients had a significant tumor response (on the basis of tumor shrinkage measured by ultrasound) or tumor cell kill (on the basis of necrosis and aptosis measurements).

Singletary (2002) commented on the study by Gardner et al (2002) in an accompanying editorial: "These interesting preliminary results should provide needed background information for the implementation of a well-designed clinical trial to definitively test the usefulness of this new approach .... Nonetheless, as surgical excision with negative margins now offers excellent results, surgeons should be cautious about adopting these technologies outside the arena of clinical trials".

U.S. Food and Drug Administration-approved multi-center phase II studies of focused microwave phased array thermotherapy in larger groups of patients are currently ongoing (Gardner et al, 2002). In a phase II non-randomized clinical trial on dose-escalation study of microwave treatment for the treatment of early stage breast cancer (n = 25), Vargas et al (2004) concluded that thermotherapy causes tumor necrosis and can be performed safely with minimal morbidity. The degree of tumor necrosis is a function of the thermal dose. Future studies will evaluate the impact of high doses of thermotherapy on margin status and complete tumor ablation. In an editorial that accompanied the paper by Vargas and colleagues, Copeland and Bland (2004) stated that "current enthusiasm for minimally invasive techniques must be measured against the gold standard results available from segmental mastectomy ...... These techniques should not replace the tried and proven effective treatment of small
cancers of the breast with segmental mastectomy, sentinel lymph node biopsy, and intact breast radiotherapy until these newer approaches have been thoroughly studied.

Agnese and Burak (2005) stated that a number of minimally invasive techniques for the treatment of early stage breast cancers are being investigated. Ablative therapies such as laser ablation, focused ultrasound, microwave ablation, radiofrequency ablation, and cryoablation have been described. All of these techniques have shown promise in the treatment of small cancers of the breast; however, additional research is needed to determine the efficacy of these techniques when they are used as the sole therapy and to determine the long-term local recurrence rates and survival associated with these treatment strategies. This is in agreement with the observations of Houston and Simmons (2005) who noted that “it is cautiously optimistic that these therapies can be used as a routine adjunct in the treatment of selected breast cancers. The challenge will lie in the ability to identify multifocal disease and in situ carcinoma as well as to ensure complete and effective eradication of the breast cancer”.

In a review on minimally invasive ablative therapies for invasive breast carcinomas, van Esser and colleagues (2007) concluded that all studies on minimally invasive ablative modalities published so far show that these techniques are feasible and safe. However, at this stage only T1 tumors should be ablated in a clinical trial setting; it is unclear which of the modalities is most suitable.

Dooley et al (2010) stated that pre-operative focused microwave thermotherapy (FMT) is a promising method for targeted treatment of breast cancer. These researchers reviewed results of 4 multi-institutional clinical studies of pre-operative FMT for treating invasive carcinomas in the intact breast. Externally applied wide-field adaptive phased-array FMT were investigated both as a pre-operative heat-alone
ablation treatment and as a combination treatment with pre-operative anthracycline-based chemotherapy for breast tumors ranging in ultrasound-measured size from 0.8 to 7.8 cm. In phase I, 8 of 10 (80%) patients receiving a single low-dose FMT prior to receiving mastectomy had a partial tumor response quantified by either ultrasound measurements of tumor volume reduction or by pathologic cell kill. In phase II, the FMT thermal dose was increased to establish a threshold dose to induce 100% pathologic tumor cell kill for invasive carcinomas prior to breast-conserving surgery (BCS). In a randomized study for patients with early-stage invasive breast cancer, of those patients receiving pre-operative FMT at ablative temperatures, 0 of 34 (0%) patients had positive tumor margins, whereas positive margins occurred in 4 of 41 (9.8%) of patients receiving BCS alone (p = 0.13). In a randomized study for patients with large tumors, based on ultrasound measurements the median tumor volume reduction was 88.4% (n = 14) for patients receiving FMT and neoadjuvant chemotherapy, compared with 58.8% (n = 10) reduction in the neoadjuvant chemotherapy-alone arm (p = 0.048). The authors concluded that wide-field adaptive phased-array FMT can be safely administered in a pre-operative setting, and data from randomized studies suggest both a reduction in positive tumor margins as a heat-alone treatment for early-stage breast cancer and a reduction in tumor volume when used in combination with anthracycline-based chemotherapy for patients with large breast cancer tumors. They stated that larger randomized studies are needed to verify these conclusions.

Zhao and Wu (2010) performed a systematic review on minimally-invasive thermal ablation of early-stage breast cancer. A broad search was conducted in Pubmed, Embase and the Cochrane databases between January 1990 and December 2009. Clinical results of the relevant articles were collected and analyzed. The analyzed studies were almost all feasibility or pilot studies using different energy sources, patients, tumor characteristics and ablation settings. They
were conducted in research settings for the assessment of technical safety and feasibility, and none of those was used alone in clinical practice. Despite many methodological differences, complete tumor ablation could be achieved in 76 to 100% of breast cancer patients treated with radiofrequency ablation, 13 to 76% in laser ablation, 0 to 8% in microwave ablation, 36 to 83% in cryoablation, and 20 to 100% in high-intensity focused ultrasound ablation. The authors concluded that minimally-invasive thermal ablation is a promising new tool for local destruction of small carcinomas of the breast. Moreover, they stated that large randomized control studies are needed to evaluate the long-term advantages of minimally-invasive thermal ablation techniques compared to the current breast conserving therapies.

Tian and colleagues (2017) noted that breast cancer is the leading cause of cancer related deaths in women and one of the most common cancers globally. The major obstacle in the management of breast cancer, especially at advanced stages, is metastasis. Metastasis in the advanced stages of breast cancer could decrease survival to approximately 5 years. The reasons could include lack of targeted receptors or chemotherapeutic agents for the management of advanced-stage breast cancer metastasis. The new emerging avenues for the management of this deadly pathological state include local manipulations like RFA, microwave thermotherapy, cryosurgery (cryotherapy), chemoembolization, radioembolization, breast surgery, or metastasectomy. Few single-institution reports showed improved survival in selected patients like those with oligometastatic stage IV breast cancer. The authors focused on these emerging new multi-modality therapeutic approaches for a possible efficient management.

Bladder Cancer

Lammers et al (2011) stated that due to the suboptimal clinical outcomes of current therapies for non-muscle-invasive bladder cancer (NMIBC), the search for better therapeutic options
continues. One option is chemo-hyperthermia (C-HT): microwave-induced hyperthermia (MwHT) with intravesical chemotherapy (ICT), typically mitomycin C (MMC). During the last 15 years, the combined regimen has been tested in different clinical settings. These investigators performed a systematic review to evaluate the efficacy of C-HT as a treatment for NMIBC. The review process followed the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines. An electronic search of the Medline, Embase, Cochrane Library, CancerLit, and ClinicalTrials.gov databases was undertaken. Relevant conference abstracts and urology journals were also searched manually. Two reviewers independently reviewed candidate studies for eligibility and abstracted data from studies that met inclusion criteria. The primary end-point was time to recurrence. Secondary end-points included time to progression, bladder preservation rate, and adverse event (AE) rate. A total of 22 studies met inclusion criteria and underwent data extraction. When possible, data were combined using random effects meta-analytic techniques. Recurrence was seen 59% less after C-HT than after MMC alone. Due to short follow-up, no conclusions can be drawn about time to recurrence and progression. The overall bladder preservation rate after C-HT was 87.6%. This rate appeared higher than after MMC alone, but valid comparison studies were lacking. Adverse events were higher with C-HT than with MMC alone, but this difference was not statistically significant. The authors concluded that published data suggested a 59% relative reduction in NMIBC recurrence when C-HT is compared with MMC alone; C-HT also appeared to improve bladder preservation rate. However, due to a limited number of randomized controlled trials (RCTs) and to heterogeneity in study design, definitive conclusions cannot be drawn. They stated that in the future, C-HT may become standard therapy for high-risk patients with recurrent tumors, for patients who are unsuitable for radical cystectomy, and in cases for which bacillus Calmette-Guerin (BCG) treatment is contraindicated.
Colombo and Moschini (2013) provided an updated review concerning the role of combined regimen (CT) based on MwHT (CT-MwHT) with ICT as a treatment for NMIBC. The review process followed the PRISMA guidelines. An electronic search of the Medline, Embase, Cochrane Library, CancerLit, and ClinicalTrials.gov databases was undertaken. Relevant conference abstracts and urology journals were also included. The primary end-point was the time to recurrence. Secondary end-points included time to progression, bladder preservation rate, and AE rate. A total of 24 studies met inclusion criteria and underwent data extraction. When feasible, data were combined using random-effects meta-analytic techniques. Recurrence was seen 59% less after CT-MwHT than after MMC alone, however, due to the short follow-up, no definitive conclusions can be drawn about the impact on the time to recurrence and progression. The overall bladder preservation rate after CT-MwHT was 87.6%. This rate appeared higher than after MMC alone, but valid comparison studies could not be drawn due to the absence of RCTs in neo-adjuvant settings. Adverse events were higher with CT-MwHT than with MMC alone, but this difference was not statistically significant. The authors concluded that published data suggested that recurrence rates for chemo-hyperthermia are substantially reduced compared with chemotherapy alone in adjuvant settings. Patients with refractory disease fared worse than those being treated with chemo-hyperthermia for their first tumor. Progression rates to muscle-invasive disease were markedly lower after combination treatment than after chemotherapy alone, with very high rates of bladder preservation. Tolerability was good, with few drop-outs in the clinical trials. The authors concluded that these findings support CT-MwHT in the future as a standard procedure for high-risk recurrent patients, for subjects in whom the treatment with BCG is contraindicated, and those unsuitable for radical cystectomy.
The 2013 update of the European Association of Urology’s guidelines on “Non-muscle-invasive urothelial carcinoma of the bladder” (Babjuk et al, 2013) did not mention microwave thermotherapy as a therapeutic option.

Furthermore, National Comprehensive Cancer Network (NCCN)’s clinical practice guideline on “Bladder cancer” (Version 2.2015) does not mention microwave thermotherapy as a therapeutic option.

**Lung Cancer**

Wasser and Dupuy (2008) noted that recent years have witnessed the refinement and significant growth of several new, minimally invasive approaches for the non-surgical treatment of primary lung malignancies. For select patients, these technologies offer an attractive treatment option given their availability in the outpatient setting and low associated morbidity and mortality. Microwave ablation (MWA) represents the most recent addition to the growing armamentarium of available ablative technologies. Administered in a manner similar to radiofrequency ablation, the lung tumor is localized under imaging guidance, and a microwave antenna is placed directly into the tumor bed. In contrast to existing thermos-ablative technologies, however, microwave treatment offers several key theoretical advantages. These include consistently higher intra-tumoral temperatures, larger ablation volumes, reduced treatment times, and improved convection profile. The authors concluded that as a nascent technology, efficacy and outcomes data for MWA of pulmonary malignancies remained relatively lacking compared with other thermos-ablative techniques; however, early trials have demonstrated promising results. It is hoped that further refinements in the clinical application of this technology will continue to improve the care of patients with lung cancer.
In a retrospective study, Carrafiello et al (2010) evaluated the feasibility, safety and effectiveness of MWA in 9 patients with unresectable lung tumor. Ten lesions were treated in 10 ablation sessions in 9 patients. The treatments were performed with a microwave generator with 45 W and 915 MHz connected to a 14.5-gauge antenna for 10 mins. Antenna placement was performed with computed tomography (CT) fluoroscopy guidance or XperGuide. All patients underwent CT follow-up at 1, 3 and 6 months from the procedure. Technical success was obtained in all cases; mortality at 30 days was 0 %. The authors concluded that the findings of this study showed that in selected patients, MWA is a valid alternative to other ablative techniques. Moreover, they stated that further studies are needed to demonstrate the short- and long-term effects of this technique and to make a comparison with other available ablation systems, especially with radiofrequency.

An UpToDate review on “Image-guided ablation of lung tumors” (Dupuy, 2015) states that “Multiple, image-guided ablative techniques are being developed for use in patients with primary non-small cell lung cancer or oligometastatic pulmonary lesions in whom surgery is not an option. Radiofrequency ablation is the most studied technique, but other approaches under development include microwave ablation, laser ablation, cryoablation, and irreversible electroporation”.

Furthermore, NCCN’s clinical practice guideline on “Non-small cell lung cancers” (Version 7.2015) does not mention microwave thermotherapy as a therapeutic option.

Nasopharyngeal Cancer

In a retrospective study, Wen and colleagues (2014) evaluated the contribution of intra-cavitary hyperthermia in patients with nasopharyngeal carcinoma who received radiation therapy. Patients with nasopharyngeal carcinoma were treated with
radiotherapy alone or with radiotherapy plus hyperthermia of the primary tumor. All patients were treated in a uniform fashion by definitive-intent radiotherapy in both groups. In the radiotherapy plus hyperthermia group, patients were treated with microwave heating hyperthermia delivered twice-weekly in combination with radiation. Between November 1992 and September 1994, a total of 225 patients were recruited; with 98 patients matched to the criteria of either treatment group (49 in the radiotherapy and 49 in the radiotherapy plus hyperthermia group). Ninety-eight patients were included in the treatment response and 87 patients in the survival analysis according to the intent-to-treat principle (11 patients were lost to follow-up). Overall survival (OS) did not show a significant difference between the 2 groups (81 versus 86 months of median survival time, respectively, p = 0.068). However, there were significant differences not only in progression-free survival (PFS; median months of 60 versus 100, respectively, p = 0.036), but also in local PFS (median months of 54 versus 111, respectively, p = 0.029) between the radiotherapy and radiotherapy plus hyperthermia groups. No statistical difference was noted in the cumulative incidence of grade 3 adverse events or late radiation morbidity during follow-up between the 2 study groups. The authors concluded that the findings of this retrospective study showed that hyperthermia combined with radiation therapy can improve PFS as well as local PFS; however no increase in OS was observed. Thus, the inclusion of hyperthermia in the treatment of nasopharyngeal carcinoma using radiation offers no survival benefit but may help to improve the current standard of care consisting of radiation and chemotherapy.

Furthermore, NCCN's clinical practice guideline on “Head and neck cancers” (Version 1.2015) does not mention microwave thermotherapy as a therapeutic option.

Pancreatic Cancer
Keane and colleagues (2014) stated that unresectable locally advanced pancreatic cancer (LAPC) with or without metastatic disease is associated with a very poor prognosis. Current standard therapy is limited to chemotherapy or chemoradiotherapy. Few regimens have been shown to have a substantial survival advantage and novel treatment strategies are urgently needed. Thermal and laser based ablative techniques are widely used in many solid organ malignancies. Initial studies in the pancreas were associated with significant morbidity and mortality, which limited widespread adoption. Modifications to the various applications, in particular combining the techniques with high quality imaging such as computed tomography and intra-operative or endoscopic ultrasound has enabled real time treatment monitoring and significant improvements in safety.

The authors conducted a systematic review of the literature up to October 2013; search terms included microwave ablation. They noted that initial studies suggested that ablative therapies may confer an additional survival benefit over best supportive care; however RCTs are needed to validate these findings.

Rombouts et al (2015) noted that LAPC is associated with a very poor prognosis. Current palliative chemoradiotherapy provides only a marginal survival benefit of 2 to 3 months. Several innovative local ablative therapies have been explored as new treatment options. These researchers provided an overview of the clinical outcomes of these ablative therapies. They performed a systematic search in PubMed, Embase and the Cochrane Library was performed to identify clinical studies, published before June 1, 2014, involving ablative therapies in LAPC. Outcomes of interest were safety, survival, quality of life and pain. After screening 1,037 articles, 38 clinical studies involving 1,164 patients with LAPC, treated with ablative therapies, were included. These studies concerned radiofrequency ablation (RFA) (7 studies), irreversible electroporation (IRE) (4), stereotactic body radiation therapy (SBRT) (16), high-intensity focused
ultrasound (HIFU) (5), iodine-125 (2), iodine-125-cryosurgery (2), photodynamic therapy (1) and microwave ablation (1). All strategies appeared to be feasible and safe. Outcomes for post-operative, procedure-related morbidity and mortality were reported only for RFA (4 to 22 and 0 to 11 %, respectively), IRE (9 to 15 and 0 to 4 %) and SBRT (0 to 25 and 0 %). Median survival of up to 25.6, 20.2, 24.0 and 12.6 months was reported for RFA, IRE, SBRT and HIFU, respectively. Pain relief was demonstrated for RFA, IRE, SBRT and HIFU. Quality-of-life outcomes were reported only for SBRT, and showed promising results.

Furthermore, NCCN's clinical practice guideline on “Pancreatic adenocarcinoma” (Version 2.2015) does not mention microwave thermotherapy as a therapeutic option.

Cervical Ectopy

Tang and colleagues (2015) evaluated the safety and effectiveness of focused ultrasound therapy (FU) and MW therapy for cervical ectopy (CE). These investigators searched PubMed, Embase, the Cochrane Library, Chinese Biomedical Literature Database (CBM), Chinese Scientific Journals Database (VIP), China Academic Journals Full-text Database (CNKI), and WanFang Data for RCTs comparing FU with MW therapy for women with symptomatic CE from inception to August 30, 2014. Two review authors independently screened for eligible studies according to the inclusion and exclusion criteria, extracted data and assessed risk of bias of included RCTs. Then, meta-analysis was performed using the RevMan 5.2 software. Funnel plots were used to evaluate publication bias. A total of 33 RCTs with 11,759 participants were included. All studies had high risk of bias. The results of meta-analysis indicated that compared to MW therapy, FU significantly reduced the risk of vaginal bleeding (relative risk [RR] = 0.09, 95 % confidence interval [CI]: 0.05 to 0.17, p < 0.00001) and vaginal discharge (RR = 0.10, 95 % CI: 0.04 to 0.24, p < 0.00001), increased the cure rate (RR = 1.10, 95 %
CI: 1.05 to 1.15, p < 0.0001) and the total effectiveness rate (RR = 1.04, 95% CI: 1.02 to 1.06, p = 0.0005), and decreased the recurrence rate (RR = 0.13, 95% CI: 0.02 to 1.00, p = 0.05); however, this last difference was not statistically significant. The authors concluded that the current available evidence suggested that FU is safer and more effective than MW therapy for treating CE. However, they noted that some limitations will reduce the reliability of their results; and further well-designed clinical trials are needed to provide further clarification.

Chronic Low Back / Neck Pain

Durmus et al (2014) examined the effect of therapeutic microwave diathermy (MD) on pain, disability, trunk muscle strength, walking performance, mobility, quality of life (QOL), and depression in the patients with chronic low back pain (CLBP). A total of 39 patients were included in this study. The patients were randomized into 2 groups: Group 1 (n = 19) received MD treatment and exercises; Group 2 (n = 20) was given only exercises. The pain (visual analog scale [VAS]), disability (Oswestry Disability Questionnaire and pain disability index), walking performance (6-minute walking test [6MWT]), depression and QOL (36-item short form health survey [SF-36]) of all participants were evaluated. Patients were assessed before treatment (BT), after treatment (AT), and at a 1-month follow-up (FU). The patients with CLBP in each group had significant improvements in pain, disability, muscle strength, endurance, 6MWT, mobility, QOL, and depression AT and FU when compared with their initial status. There was no statistically significant difference between the groups regarding the change scores between AT-BT test and FU-BT test. The authors concluded that since a 2,450-MHz MD showed no beneficial effects on clinical parameters, exercise program could be preferable for the treatment of patients with CLBP alone.
In a double-blind, RCT, Andrade Ortega et al (2014) determine the effectiveness of MD to treat non-specific chronic neck pain. The patient sample consisted of 149 patients with non-specific chronic neck pain. The study outcome measures are as follows: at baseline, pain intensity (using a VAS), disability (Neck Disability Index), and health-related QOL (SF-36); at 3 weeks, baseline measures and patients' perceived overall outcome and satisfaction with the treatment; and at 6 months, 3-week measures, therapeutic co-interventions, and adherence to exercises. Patients were allocated randomly to 3 groups: (i) the 1st group received continuous MD, (ii) the 2nd group was administered pulsed microwaves, and (iii) the 3rd group (the control group) received unplugged microwaves. All 3 groups received the same general treatment: range of motion, isometric exercises, and transcutaneous electrical nerve stimulation. The 3 groups had reduced pain and disability, and improvement was seen in some dimensions of the SF-36. However, there were no differences found in any of the parameters measured among the 3 therapeutic groups. The authors concluded that MD did not provide additional benefit to a treatment regimen of chronic neck pain that already involves other treatment approaches.

**Chronic Prostatitis / Chronic Pelvic Pain Syndrome**

Cascella and associates (2017) stated that pain is a common and debilitating symptom in pelvic cancer diseases. Failure in controlling this pain through pharmacological approaches calls for employing multi-modal management and invasive techniques. Various strategies are commonly used for this purpose, including palliative radiotherapy, epidural medications and intra-thecal administration of analgesic and local anesthetic drugs with pumps, and neural or plexus blockade. This review focused on the features of minimally invasive palliative procedures (MIPPs), such as cementoplasty, cryoablation, electrochemotherapy, irreversible electroporation, laser-induced thermotherapy, MWA, and RFA as well as their role in palliation of cancer pelvic pain. Despite
the evidence of safety and effectiveness of these interventions, there are still many barriers to accessing MIPPs, including the availability of trained staff, the lack of precise criteria of indication, and the high costs.

Furthermore, an UpToDate review on “Chronic prostatitis/chronic pelvic pain syndrome” (Pontari, 2016) does not mention microwave therapy as a therapeutic option.

**Keratoconus**

In a prospective clinical trial, Celik and associates (2015) evaluated the safety and effectiveness of a new microwave thermokeratoplasty procedure combined with accelerated corneal collagen crosslinking (CXL) to improve visual function in patients with keratoconus. Patients with keratoconus who had the combined procedure were evaluated over 12 months post-operatively. The main outcome measures were changes in logMAR uncorrected (UDVA) and corrected (CDVA) distance visual acuities and in keratometry (K) values. The study enrolled 24 eyes of 24 patients aged 18 to 45 years. The attempted corrections ranged from -1.60 to -6.50 diopters (D). The mean pre-operative UDVA of 0.66 logMAR ± 0.26 (SD) significantly improved to 0.39 ± 0.21 logMAR 1 month post-operatively. However, by 6 months, the mean UDVA had regressed to 0.58 ± 0.21 logMAR. At 12 months, the mean UDVA was 0.62 ± 0.17 logMAR. The mean K value was 49.11 ± 2.43 D pre-operatively, 43.50 ± 3.04 D 1 month post-operatively, 47.52 ± 2.99 D at 6 months, and 48.37 ± 3.00 D at 12 months. There were no cases of significant endothelial cell loss or loss of CDVA lines at 12 months. The authors concluded that the new thermokeratoplasty procedure followed by accelerated CXL produced the desired reduction in K values and improvement in post-operative UDVA without significant side effects. However, the early and complete regression of the thermokeratoplasty effect showed the need for further advancement of this technology.
Bone Cancer / Limb Salvage

Fan and associates (2016) stated that the current application of limb salvage process has some unsolved problems, such as prosthesis loosening, which severely limits the function of the preserved limbs. Innovative approaches are needed to further improve functional outcome. Instead of en-bloc resection of tumor-bearing bone, it is dissected from the surrounding normal tissues, followed by devitalizing the bone segment and the extra-cortical bulk by microwave-induced hyperthermia in-situ through the antenna array. From May 1999 to March 2012, a total of 544 patients with malignant bone tumors of the extremities were treated by the novel method. The 3-year survival rate was 59.1% for high-grade malignancy, 88.7% for low-grade malignancy. In the majority of patients, cosmetic and useful limbs were preserved. Local recurrence rate was 9.8% for the high-grade malignancy (mainly occurred at the early stage of the research). The overall fracture rate was 2.6%. Deep infection rate was 1.8%. The complication rate was lower than that reported in the literature. After heat necrosis, the dead bone maintains both the osteoconduction and osteoinduction properties. The authors concluded that the application of microwave-induced hyperthermia for treatment of malignant bone tumors, except in late diagnosed cases where tumor-bearing bone was destroyed to do biological reconstruction, is an effective, simple, and inexpensive method. They stated that the oncological and functional results were encouraging.

Han and colleagues (2017) noted that amputation has been the standard surgical treatment for distal tibia osteosarcoma owing to its unique anatomic features. Preliminary research suggested that microwave-induced hyperthermia may have a role in treating osteosarcoma in some locations of the body (such as the pelvis), but to the authors’ knowledge, no comparative study has evaluated its effectiveness in a difficult-to-treat location like the distal tibia. In a retrospective study, these researchers examined if microwave-induced
hyperthermia results in (i) improved survival, (ii) decreased local recurrence, (iii) improved Musculoskeletal Tumor Society (MSTS) scores, or (iv) fewer complications than amputation in patients with a distal tibial osteosarcoma. Between 2000 and 2015, these investigators treated 79 patients for a distal tibia osteosarcoma without metastases. Of those, 52 were treated with microwave-induced hyperthermia, and 27 with amputation. Patients were considered eligible for microwave-induced hyperthermia if they had an at least 20-mm available distance from the tumor edge to the articular surface, good clinical and imaging response to neoadjuvant chemotherapy, and no pathologic fracture. Patients not meeting these indications were treated with amputation. In addition, if neither the posterior tibial artery nor the dorsalis pedis artery was salvageable, the patients were treated with amputation and were not included in any group in this study. A total of 13 other patients were treated with conventional limb-salvage resections and reconstructions (at the request of the patient, based on patient preference) and were not included in this study. All 79 patients were available for follow-up at a minimum of 12 months (mean follow-up in the hyperthermia group, 79 months, range of 12 to 158 months; mean follow-up in the amputation group, 95 months, range of 15 to 142 months). With the numbers available, the groups were no different in terms of sex, age, tumor grade, tumor stage, or tumor size. All statistical tests were 2-sided, and a probability less than 0.05 was considered statistically significant. Survival to death was evaluated using Kaplan-Meier analysis. Complications were recorded from the patients' files and graded using the classification of surgical complications described by Dindo et al. In the limb-salvage group, Kaplan Meier survival at 6 years was 80 % (95 % CI: 63 % to 90 %), and this was not different with the numbers available from survivorship in the amputation group at 6 years (70 %; 95 % CI: 37 % to 90 %; p = 0.301). With the numbers available, these researchers found no difference in local recurrence (6 versus 0; p = 0.066). However mean ± SD
MSTS functional scores were higher in patients who had microwave-induced hyperthermia compared with those who had amputations (85 % ± 6 % versus 66 % ± 5 %; p = 0.008). With the numbers available, these investigators found no difference in the proportion of patients experiencing complications between the 2 groups (6 of 52 [12 %] versus 3 of 27 [11 %]; p = 0.954). The authors were encouraged to find no early differences in survival, local recurrence, or serious complications between microwave-induced hyperthermia and amputation, and a functional advantage in favor of microwave-induced hyperthermia. However, they stated that these findings should be replicated in larger studies with longer mean duration of follow-up, and in studies that compare microwave-induced hyperthermia with conventional limb-sparing approaches. Level of Evidence = III.

Furthermore, National Comprehensive Cancer Network’s clinical practice guideline on “Bone cancer” (Version 2.2017) does not mention microwave thermotherapy as a therapeutic option.

Kidney Cancer

In a retrospective study, Gao and associates (2016) examined the safety and effectiveness of ultrasound (US)-guided percutaneous MWA for renal cell carcinoma (RCC) adjacent to renal sinus. This study included 41 patients who underwent US-guided percutaneous MWA of 41 RCCs adjacent to the renal sinus from April 2006 to December 2015. Contrast-enhanced images of US and CT or magnetic resonance (MR) imaging were performed at pre-ablation and 1 day, 1 month, 3 months, and every 6 months after ablation. Initial ablation success (IAS), disease-free survival (DFS), RCC-related survival (RRS), and OS were recorded at the follow-up visits; IAS was achieved in 92.7 % (38/41) of the study subjects. The IAS significantly differed between patients with RCCs less than or equal to 4 cm (100 %, 29/29) and RCCs greater than 4 cm (75 %, 9/12, p = 0.021). During the median follow-up of 37.6
(range of 3.0 to 97.3) months, the estimated 1-, 3-, and 5-year DFS of patients with an initial tumor of less than or equal to 4 cm were 100 %, 89.7 %, and 81.5 %, respectively. The 1-, 3-, and 5-year RRS were 100 %, 93.3 %, and 93.3 %, respectively. The 1-, 3-, and 5-year OS were 97.1 %, 87.8 %, and 83.6 %, respectively. The multivariate analysis using the Cox proportional hazard model revealed no independent predictor of recurrence among all the variables. There were no MWA-related deaths among the study subjects; 1 patient developed a retroperitoneal abscess after ablation. The authors concluded that US-guided percutaneous MWA appeared to be a promising method for RCCs adjacent to renal sinus, especially for tumors less than or equal to 4cm.

Furthermore, National Comprehensive Cancer Network’s clinical practice guideline on “Kidney cancer” (Version 2.2017) does not mention microwave thermotherapy as a therapeutic option.

Breast Cancer Metastasis

Tian and colleagues (2017) noted that breast cancer is the leading cause of cancer related deaths in women and one of the most common cancers globally. The major obstacle in the management of breast cancer, especially at advanced stages, is metastasis. Metastasis in the advanced stages of breast cancer could decrease survival to approximately 5 years. The reasons could include lack of targeted receptors or chemotherapeutic agents for the management of advanced-stage breast cancer metastasis. The new emerging avenues for the management of this deadly pathological state include local manipulations like radiofrequency ablation (RFA), microwave thermotherapy, cryosurgery (cryotherapy), chemoembolization, radio-embolization, breast surgery, or metastasectomy. The authors stated that few single-institution reports showed improved survival in selected patients like those with oligo-metastatic stage IV breast cancer.
Dysmenorrhea

Perez Machado and colleagues (2017) described the clinical trial protocol that is designed to examine the effects of microwave diathermy (MWD) and transcutaneous electrical nerve stimulation (TENS) on primary dysmenorrhea. A total of 88 women, age range of 18 to 44 years, with no previous pregnancy, no practice physical activities, a body mass index (BMI) of less than or equal to 29.9 kg/m², a regular menstrual cycle and a diagnosis of primary dysmenorrhea, with menstrual pain ranging from mild-to-severe, will be selected. The participants will be randomized into 4 groups: MWD and TENS, MWD and placebo TENS, placebo MWD and TENS, and placebo MWD and placebo TENS. Pain will be measured using the visual numeric scale and the McGill Pain Questionnaire; the pressure pain threshold using a digital algometer and conditioned pain modulation using the cold pressor test.

Osteosarcoma

Han and colleagues (2017) stated that amputation has been the standard surgical treatment for distal tibia osteosarcoma owing to its unique anatomic features. Preliminary research suggested that microwave-induced hyperthermia may have a role in treating osteosarcoma in some locations of the body (such as the pelvis), but to the authors’ knowledge, no comparative study has evaluated its efficacy in a difficult-to-treat location like the distal tibia. These researchers examined if microwave-induced hyperthermia result in improved survival, decreased local recurrence, improved Musculoskeletal Tumor Society (MSTS) scores, or complications than amputation in patients with a distal tibial osteosarcoma. Between 2000 and 2015, these investigators treated 79 patients for a distal tibia osteosarcoma without metastases. Of those, 52 were treated with microwave-induced hyperthermia, and 27 with amputation. Patients were considered eligible for microwave-induced hyperthermia if they had an at least 20-mm available
distance from the tumor edge to the articular surface, good
clinical and imaging response to neoadjuvant chemotherapy,
and no pathologic fracture. Patients not meeting these
indications were treated with amputation. In addition, if neither
the posterior tibial artery nor the dorsalis pedis artery was
salvageable, the patients were treated with amputation and
were not included in any group in this study. A total of 13
other patients were treated with conventional limb-salvage
resections and reconstructions (at the request of the patient,
based on patient preference) and were not included in this
study. All 79 patients in this retrospective study were available
for follow-up at a minimum of 12 months (mean follow-up in
the hyperthermia group, 79 months, range of 12 to 158
months; mean follow-up in the amputation group, 95 months,
range of 15 to 142 months). With the numbers available, the
groups were no different in terms of sex, age, tumor grade,
tumor stage, or tumor size. All statistical tests were 2-sided,
and a probability less than 0.05 was considered statistically
significant. Survival to death was evaluated using Kaplan-
Meier analysis. Complications were recorded from the
patients’ files and graded using the classification of surgical
complications described by Dindo et al. In the limb-salvage
group, Kaplan Meier survival at 6 years was 80 % (95 % CI: 63
% to 90 %), and this was not different with the numbers
available from survivorship in the amputation group at 6 years
(70 %; 95 % CI: 37 % to 90 %; p = 0.301). With the numbers
available, these researchers found no difference in local
recurrence (6 versus 0; p = 0.066). However mean ± SD
MSTS functional scores were higher in patients who had
microwave-induced hyperthermia compared with those who
had amputations (85 % ± 6 % versus 66 % ± 5 %; p = 0.008).
With the numbers available, these investigators found no
difference in the proportion of patients experiencing
complications between the 2 groups (6 of 52 [12 %] versus 3
of 27 [11 %]; p = 0.954). The authors concluded that they
were encouraged to find no early differences in survival, local
recurrence, or serious complications between microwave-
induced hyperthermia and amputation, and a functional
advantage in favor of microwave-induced hyperthermia. However, they stated that these findings need to be replicated in larger studies with longer mean duration of follow-up, and in studies that compare microwave-induced hyperthermia with conventional limb-sparing approaches. Level of Evidence = III

**CPT Codes / HCPCS Codes / ICD-10 Codes**

Information in the [brackets] below has been added for clarification purposes. Codes requiring a 7th character are represented by "+":

<table>
<thead>
<tr>
<th>Code</th>
<th>Code Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>CPT codes not covered for indications listed in the CPB:</td>
<td></td>
</tr>
<tr>
<td>Microwave thermotherapy - no specific code:</td>
<td></td>
</tr>
<tr>
<td>Other CPT codes related to the CPB:</td>
<td></td>
</tr>
<tr>
<td>77280 - 77295</td>
<td>Radiation therapy</td>
</tr>
<tr>
<td>HCPCS codes not covered for indications listed in the CPB:</td>
<td></td>
</tr>
<tr>
<td>C9751</td>
<td>Bronchoscopy, rigid or flexible, transbronchial ablation of lesion(s) by microwave energy, including fluoroscopic guidance, when performed, with computed tomography acquisition(s) and 3-d rendering, computer-assisted, image-guided navigation, and endobronchial ultrasound (ebus) guided transtracheal and/or transbronchial sampling (eg, aspiration[s]/biopsy[ies]) and all mediastinal and/or hilar lymph node stations or structures and therapeutic intervention(s)</td>
</tr>
<tr>
<td>ICD-10 codes not covered for indications listed in the CPB:</td>
<td></td>
</tr>
<tr>
<td>C11.0 - C11.9</td>
<td>Malignant neoplasm of nasopharynx</td>
</tr>
<tr>
<td>Code</td>
<td>Code Description</td>
</tr>
<tr>
<td>---------</td>
<td>------------------------------------------------------</td>
</tr>
<tr>
<td>C25.0 - C25.9</td>
<td>Malignant neoplasm of pancreas</td>
</tr>
<tr>
<td>C33 - C34.92</td>
<td>Malignant neoplasm of trachea, bronchus and lung</td>
</tr>
<tr>
<td>C40.00 - C41.9</td>
<td>Malignant neoplasm of bone and articular cartilage of limbs</td>
</tr>
<tr>
<td>C64.1 - C64.9</td>
<td>Malignant neoplasm of kidney, except renal pelvis</td>
</tr>
<tr>
<td>C67.0 - C67.9</td>
<td>Malignant neoplasm of bladder</td>
</tr>
<tr>
<td>C50.011 - C50.929</td>
<td>Malignant neoplasm of breast</td>
</tr>
<tr>
<td>C64.1 - C64.9</td>
<td>Malignant neoplasm of kidney, except renal pelvis</td>
</tr>
<tr>
<td>C79.81</td>
<td>Secondary malignant neoplasm of breast</td>
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<tr>
<td>D05.00 - D05.92</td>
<td>Carcinoma in situ of breast</td>
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<tr>
<td>H18.601 - H18.629</td>
<td>Keratoconus</td>
</tr>
<tr>
<td>M54.2</td>
<td>Cervicalgia</td>
</tr>
<tr>
<td>M54.5</td>
<td>Low back pain</td>
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<tr>
<td>N41.1</td>
<td>Chronic prostatitis</td>
</tr>
<tr>
<td>N86</td>
<td>Erosion and ectropion of cervix uteri</td>
</tr>
<tr>
<td>N94.4 - N94.6</td>
<td>Dysmenorrhea</td>
</tr>
<tr>
<td>R10.2</td>
<td>Pelvic and perineal pain</td>
</tr>
</tbody>
</table>
The above policy is based on the following references:

Breast Cancer

10. van Esser S, van den Bosch MA, van Diest PJ, et al. Minimally invasive ablative therapies for invasive breast...


5. Babjuk M, Burger M, Zigeuner R, et al; European Association of Urology. EAU guidelines on non-muscle-


20. Pontari M. Chronic prostatitis/chronic pelvic pain syndrome, UpToDate [online serial]. Waltham, MA: UpToDate; reviewed May 2016.


Amendment to
Aetna Clinical Policy Bulletin Number: 0682 Microwave Thermotherapy

There are no amendments for Medicaid.