



Cigna Medical Coverage Policy

Subject Microwave Thermotherapy for Breast Cancer

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Coverage Policy

Cigna does not cover microwave thermotherapy for the treatment of breast cancer, because it is considered experimental, investigational or unproven.

General Background

Breast cancer is the most common form of cancer among women. In situ breast cancer is confined within the ducts (i.e., ductal carcinoma in situ) or lobules (i.e., lobular carcinoma in situ). Invasive or infiltrating carcinomas start in the ducts or lobules and invade the surrounding fatty tissue.

Treatment of breast cancer will depend upon the type and stage of cancer, patient's age and comorbidities, and the risks and benefits associated with the various treatment options. Surgical intervention is the standard of care for most breast cancers. Surgical options include breast-sparing surgery (e.g., lumpectomy, segmental mastectomy, partial mastectomy) and total mastectomy. Surgical treatment may be combined with other therapies, such as chemotherapy, radiation therapy, immunotherapy and/or monoclonal antibody therapy.

Microwave Thermotherapy

Less invasive breast cancer treatment modalities are currently being studied (National Comprehensive Cancer Network [NCCN], 2014; American Cancer Society [ACS], 2013). Some of these modalities include breast cancer

ablation as part of the initial treatment regimen. One cancer ablation technique that is currently under investigation involves the use of microwave heating or thermotherapy of the tumor.

Microwave thermotherapy or microwave therapy is a type of treatment in which body tissue is exposed to high temperatures to damage and kill cancer cells or to make cancer cells more sensitive to the effects of radiation and certain anticancer drugs (NCI, 2013).

Microwave thermotherapy is being proposed as a possible first-line treatment in lieu of conservative breast surgery (i.e., lumpectomy) with postsurgical radiation, and also as an adjunct to chemotherapy as a pre- or postoperative measure. Because breast carcinomas have higher water content than normal breast tissue, they absorb more heat and incur more damage than the surrounding tissue when the area is precisely targeted with regulated microwave heat for a consistent period of time. Researchers have proposed that tumor cell heating alone for 60 minutes at 43°C (Centigrade) or 109°F (Fahrenheit) is tumoricidal and that the period of time necessary to kill tumor cells decreases by a factor of two for each degree of increase in temperature above approximately 43°C (Varga, et al., 2004; Gardner, et al., 2002).

To heat the breast, two microwave phased-array waveguide applicators are placed a few millimeters from the patient's skin. These applicators contain fans that assist in cooling the skin's surface during the heat application. The patient is placed in a prone position, and the breast is compressed approximately four to eight centimeters (cm) between the microwave applicators. Five surface temperature sensors are attached to the skin for continuous monitoring. Two probes are inserted into the breast: one acts as a thermal sensor to monitor the internal tumor temperature, while the other assists in focusing the directed microwave energy into the tumor. Computer-controlled display monitoring occurs throughout the therapy session. Treatment is considered complete when the desired thermal dose is delivered to the tumor or a maximum treatment time (i.e., 40 minutes) is reached. To assist in preventing skin damage from the redundant heat, additional auxiliary fans are used to cool the air surrounding the patient. Once the desired thermal dose is achieved, the microwave power is reduced to zero, and the breast compression is maintained during a five-minute cool-down period. During this period, because of the thermal insulation of the surrounding breast tissues, the thermal dose continues to accumulate in the tumor (Gardner, et al., 2002).

U.S. Food and Drug Administration (FDA)

To date, the FDA has not approved the use of microwave thermotherapy device(s) for the intended treatment of breast cancer.

Several microwave ablation systems have received 510(k) approval from the FDA as Class II devices for the intended use of coagulation (i.e., ablation of soft tissue). These include the VivaTip™ Microwave ablation probe and accessories approved in 2003 (Vivant Medical, Inc., Mountain View, CA), the VivaWave™ Microwave ablation system approved in 2006 (Valleylab, Boulder, CO) and Tri-Loop™ Microwave ablation probe approved in 2006 (Vivant Medical, Inc., Mountain View, CA) (this list may not be all-inclusive).

The FDA granted Premarket Approval (PMA) in 1989 for the two-channel, 915-MHz (megahertz) microwave adaptive phased-array thermotherapy system Microfocus-1000™ APA (Celsion® Corporation; Columbia, Maryland). In 1997, the FDA granted PMA approval for a design change to enhance the heat focusing capabilities of the Microfocus 1000™ hyperthermia system (FDA, 2010).

Literature Review

The studies that have been conducted on microwave thermotherapy for the treatment of breast cancer have been small in sample size and have used various treatment protocols to determine the most effective temperature and the length of treatment sessions that are needed for tumoricidal effects to be obtained. Total ablation of all tumor/cancer cells has yet to be obtained while numerous adverse events have occurred. It is unknown at this time what long-term effect microwave thermotherapy will have on breast tissue conservation and effective cancer ablation.

In a recent review of clinical studies, Dooley et al. (2010) reported the results of four clinical studies of preoperative microwave thermotherapy for treating invasive carcinomas in the intact breast. The authors concluded that further investigation in larger randomized clinical studies for the use of microwave thermotherapy both as a preoperative heat-alone treatment to reduce positive margins for early-stage breast cancer and as a

preoperative combination heat and chemotherapy treatment to reduce tumor volume for large breast cancer tumors to improve breast conservation are needed.

In 2002, Gardner et al. reported on a case series FDA-approved Phase I pilot study using thermotherapy for the treatment of primary breast cancer. The purpose of this study was to measure thermal effectiveness on the local lesion and to determine whether heat could eradicate all cancer cells within the breast. Ten volunteers with breast cancer lesions that varied in size from one to eight centimeters (cm) (mean = 4.3 cm) each received one thermotherapy treatment prior to mastectomy. A FDA Investigational Device Exemption–approved two-channel 915-MHz microwave adaptive phased array thermotherapy system Microfocus-1000™ APA (Celsion Corporation, Columbia, MD) was used in this study. The mastectomy specimens were histologically evaluated to document the impact of the thermotherapy. Eight specimens showed tumor shrinkage or ischemic necrosis, while six histological stainings documented 82–97% tumor cell destruction (mean = 89.7%). Pretreatment imaging did not reveal ischemic necrosis to be present in any patient. When ultrasound imaging and the pathology results were compared, the ultrasound images showed that in six of the 10 patients, tumor size reduction ranged from 29–60% (mean = 41%) in 18 days or less. The mastectomy specimens showed that in four of the 10 patients, significant ischemic tumor necrosis estimated at 40–60% (mean = 48%) had occurred, and in six of eight patients, tumor cell destruction was estimated at 82–97% (mean = 87%), based on apoptosis measurements. Adverse events included rapid elevation of surface temperature, flap necrosis after mastectomy for three patients, and one skin blister. The researchers concluded that it is possible that a longer observation time between thermotherapy and surgery could have increased tumor cell destruction and tumor size reduction. The pathology data of this study suggest that achieving a 60-minute thermal dose and a peak temperature of >45°C may correlate with the onset of ischemic tumor necrosis, but higher peak temperatures would most likely be required to increase tumor necrosis of advanced breast carcinomas.

Vargas et al. (2004) reported on an uncontrolled, prospective, multicenter, nonrandomized dose escalation study of 25 patients. A FDA Investigational Device Exemption–approved two-channel 915-MHz microwave adaptive phased array thermotherapy system Microfocus-1000™ APA (Celsion Corporation, Columbia, MD) was used in this study. Tumoricidal temperatures (i.e., > 43°C or 109.4°F [Fahrenheit]) were reached in 23 patients. Prior to thermotherapy, the mean ultrasound measurement of the lesions was 17.6 millimeters (mm) (range = 7–25 mm), but after thermotherapy there was no significant change in tumor size (i.e., 18.4 mm). After an average of 17 days, all patients underwent breast-conserving surgery. The surgical pathology reports showed tissue necrosis in 17 patients. Although complete ablation occurred in two patients, carcinoma in situ was still present at the borders of their surgical specimens. Another patient had one remaining cluster of cancer cells with a 99.9% ablation of the remaining tumor. Cumulative thermal results for 14 of 15 patients showed a peak tumor temperature of 46.9°C (i.e., 116°F) and a range of 25–100% tumor necrosis. Adverse events that occurred in the 80 and 100 cumulative equivalent minutes (CEMs) groups included erythema, mild pain and first-degree burns. In the cohort receiving 120 CEMs, there were 19 adverse events, including severe pain, mild erythema, edema, and second- and third-degree burns. Although this study showed that pathological tumor necrosis occurred, the presurgical diagnostic films showed no uniform decrease in tumor response to thermotherapy. Additional studies are needed to determine the cause of tissue edema, the exact treatment time needed, and the safety measures that need to be in place for the use of thermotherapy.

Professional Societies/Organizations

The National Comprehensive Cancer Network (NCCN) national guidance that is published for the treatment of breast cancer does not include the use of microwave thermotherapy as a standalone or adjuvant treatment option (NCCN, 2014).

According to the American Cancer Society (ACS), hyperthermia may be a promising way to enhance cancer treatment; however, it remains largely an experimental technique at this time and not commonly used in cancer treatment. Many clinical trials of hyperthermia are now under way to try to determine the best way to use this technique. Current studies are determining its usefulness against several cancers, including its possible use in the treatment of breast cancer (ACS, 2013).

The American Society of Breast Surgeons (ASBS) published the following statement: “Ablative and minimally invasive percutaneous excisional treatments for early stage breast cancer are being investigated by various groups involved with breast cancer research. At this time, these include ablation by laser, cryotherapy, microwave, and radiofrequency. These techniques raise a number of questions about efficacy and patient safety, staging, margin analysis, and follow-up. Until such a time that safety and efficacy of these techniques are

ascertained, ablative and percutaneous excisional treatments for breast cancer are investigational and should not be performed outside the realm of clinical research trials” (ASBS, 2002). This position statement is still current.

The National Cancer Institute (NCI) has indicated that a number of challenges must be overcome for hyperthermia to be considered a standard treatment for cancer. Many clinical trials are underway to determine the effectiveness of this therapy as a standalone or in combination with other therapies for the treatment of cancers (NCI, 2011).

Use Outside of the US

No relevant information.

Summary

Studies to date have failed to prove the efficacy of microwave thermotherapy as a substitute for surgical excision or as an adjuvant treatment for breast cancers. Supporting data from well-designed randomized clinical trials regarding the effectiveness of this modality are needed. No consistent method has been developed to calculate either the amount of thermal heat that would be needed to treat a breast cancer of given size and depth or the total treatment times required. Patient safety parameters need to be developed to decrease the potential for thermal burns as a result of this therapy. Definitive patient selection criteria have not been established. There is insufficient evidence in published, peer-reviewed literature that documents the effectiveness of microwave thermotherapy in the treatment of breast cancer. Studies have not demonstrated that using microwave thermotherapy improves short- or long-term patient treatment outcomes and survival rates.

Coding/Billing Information

Note: 1) This list of codes may not be all-inclusive.

2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Experimental/Investigational/Unproven/Not Covered when used to report microwave thermotherapy for the treatment of breast cancer.

CPT* Codes	Description
19499	Unlisted procedure, breast
0301T	Destruction/reduction of malignant breast tumor with externally applied focused microwave, including interstitial placement of disposable catheter with combined temperature monitoring probe and microwave focusing sensocatheter under ultrasound thermotherapy guidance

*Current Procedural Terminology (CPT®) © 2013 American Medical Association: Chicago, IL.

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