Molina Clinical Policy
Focused Microwave Thermotherapy for Breast Cancer: Policy No. 381

Last Approval: 8/10/2022
Next Review Due By: August 2023

DISCLAIMER

This Molina Clinical Policy (MCP) is intended to facilitate the Utilization Management process. Policies are not a supplementation or recommendation for treatment; Providers are solely responsible for the diagnosis, treatment and clinical recommendations for the Member. It expresses Molina's determination as to whether certain services or supplies are medically necessary, experimental, investigational, or cosmetic for purposes of determining appropriateness of payment. The conclusion that a particular service or supply is medically necessary does not constitute a representation or warranty that this service or supply is covered (e.g., will be paid for by Molina) for a particular Member. The Member's benefit plan determines coverage – each benefit plan defines which services are covered, which are excluded, and which are subject to dollar caps or other limits. Members and their Providers will need to consult the Member's benefit plan to determine if there are any exclusion(s) or other benefit limitations applicable to this service or supply. If there is a discrepancy between this policy and a Member's plan of benefits, the benefits plan will govern. In addition, coverage may be mandated by applicable legal requirements of a State, the Federal government or CMS for Medicare and Medicaid Members. CMS's Coverage Database can be found on the CMS website. The coverage directive(s) and criteria from an existing National Coverage Determination (NCD) or Local Coverage Determination (LCD) will supersede the contents of this MCP and provide the directive for all Medicare members. References included were accurate at the time of policy approval and publication.

OVERVIEW

Microwave thermotherapy treats primary breast cancer with focused microwaves, based on the theory that heat can destroy microscopic carcinoma cells in the breast and reduce cancer recurrence. Microwave thermotherapy uses electromagnetic waves to expose the tumor to extremely high temperatures, causing tumor destruction. It uses localized heating caused by water molecules that move within tissues, and externally applied focused microwaves to cause tissue necrosis. This technique can heat and damage high-water-content tumor cells, while leaving tissues with lower-water-content such as adipose and breast glandular tissues unharmed. Heating the tumor and killing a large percentage or all of the tumor cells prior to surgery may improve the margins and reduce the possibility of inadvertently seeding viable cancer cells during the surgical procedure, resulting in fewer local recurrences in the breast. Microwave thermotherapy may shrink the tumor sufficiently to allow for a less invasive surgical procedure. In patients with locally advanced primary breast cancer, focused microwave thermotherapy (FMT) may sufficiently reduce the size of the tumor to allow a less invasive surgical procedure to be performed. Furthermore, 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. During this procedure, the breast to be treated is compressed between two microwave emitters, and a surgical probe is placed within the breast to monitor the temperature of the tissue. When the emitters are activated, microwave energy is delivered to a large volume of breast tissue. The tumor tissue in breast cancer, contains more water than the surrounding tissue. The cancerous tissue heats up faster and is destroyed while the healthy tissue remains relatively unaffected. At this time, however, there is insufficient evidence in the published literature to support the use of FMT as a treatment for breast cancer at this time.

Regulatory Status

No microwave thermotherapy device that is indicated for the treatment of breast cancer has received approval for marketing from the U.S. Food and Drug Administration (FDA) has been identified at the present time.

Several microwave ablation systems have received FDA 510(k) approval as a class II device for coagulation (e.g., ablation of soft tissue). The Microfocus™ APA 1000 System (Celsion, Columbia, MD) is currently undergoing clinical trials under the FDA investigational device exemption (IDE) process.

COVERAGE POLICY

Focused microwave thermotherapy as a treatment for breast cancer is considered **experimental, investigational, or unproven** due to insufficient evidence in peer reviewed medical literature that have not established safety, efficacy and effect on net health outcomes.

There is insufficient evidence in the peer-reviewed literature to support the safety and efficacy of microwave thermotherapy for the treatment of breast cancer. Microwave thermotherapy has not been shown to improve health outcomes in people with breast cancer in published clinical research. The evidence is insufficient to establish the effects of the technology on health outcomes.

DOCUMENTATION REQUIREMENTS. Molina Healthcare reserves the right to require that additional documentation be made available as part of its coverage determination; quality improvement; and fraud; waste and abuse prevention processes. Documentation required may include, but is not limited to, patient records, test results and credentials of the provider ordering or performing a drug or service. Molina Healthcare may deny reimbursement or take additional appropriate action if the documentation provided does not support the initial determination that the drugs or services were medically necessary, not investigational or experimental, and otherwise within the scope of benefits afforded to the member, and/or the documentation demonstrates a pattern of billing or other practice that is inappropriate or excessive.

SUMMARY OF MEDICAL EVIDENCE

Focused microwave thermotherapy has been investigated in a number of settings, including as a treatment for primary breast cancer in conjunction with lumpectomy for early-stage breast cancer and as a cytoreductive technique in conjunction with preoperative chemotherapy in locally advanced breast cancer. There is limited published clinical trial data on FMT for the treatment of breast cancer. Additional randomized studies with a larger number of subjects are needed to evaluate the safety and efficacy of these treatments. Further investigation of 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 (Dooley et al., 2010; Vargas et al., 2004; Gardner et al., 2002). The key published literature to date, includes case series, a systematic review of feasibility and pilot studies conducted prior to 2010.

Gardner et al. (2002) published 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).

Vargas et al. (2004) reported a dose-finding study in 25 subjects conducted as part of an Investigational Device Exemption (IDE) trial. Study subjects underwent microwave thermotherapy at various doses before undergoing surgical resection of breast cancer to determine whether the use of thermotherapy before breast conserving surgery (BCS) could potentially reduce the incidence of positive surgical margins, and thus the need for re-excision. The authors 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.

Preoperative Focused-Microwave Thermotherapy

Two small studies with early, intermediate outcomes were noted. However, these studies provide insufficient data due to the limited numbers of patients and duration. Longer follow-up of clinical outcomes is required to evaluate the clinical benefit of therapy.

Vargas et al. (2007) reported on a study of 15 patients who received preoperative FMT in combination with neoadjuvant anthracycline-based chemotherapy for invasive (T2, T3) breast cancer. Compared with 13 patients who received only the anthracycline-based regimen, there was greater (88% verses 59%) tumor volume reduction in the experimental group.

Dooley et al. (2008) reported on a randomized study of preoperative focused-microwave thermotherapy for early-stage breast cancer. In this study, 34 patients received thermotherapy before surgery and 41 received only surgery. Positive margins were found in 10% (4 of 41 controls) compared with 0% (0 of 34) in the experimental group (p=0.13).

Dooley et al. (2010) reviewed results of four clinical studies evaluating FMT for preoperative treatment of invasive breast cancer.

- In the initial phase 1 study, 8 of 10 (80%) participants receiving one low dose of FMT prior to mastectomy had a partial tumor response. Partial tumor response was identified by ultrasound measurements of tumor volume reduction or by pathologic cell kill.
- In the phase 2 study, the FMT dose was increased to stimulate 100% pathologic tumor cell kill for invasive carcinoma prior to BCS.

- In a randomized trial comprised of participants with early-stage invasive breast cancer. In this study, 34 patients received thermotherapy before surgery and 41 received only surgery. Positive margins were found in 10% (4 of 41 controls) compared with 0% (0 of 34) in the experimental group (p=0.13). These studies provide insufficient data to change the coverage statement. Studies involving larger numbers of patients with longer follow-up of clinical outcomes are needed.
- In a randomized trial of participants with large breast tumors, the median reduction of tumor volume based on ultrasound measurements was 88.4% (n=14) for those who received FMT and chemotherapy, as compared with 58.8% (n=10) reduction in those who received chemotherapy alone. Study limitations include small numbers of participants.
- The authors concluded that wide-field adaptive phased-array FMT can be safely administered in a preoperative 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; larger randomized studies are required to verify these conclusions.

Systematic Reviews

Outcomes Comparison of Types of Minimally Invasive Breast Cancer Treatment
Mauri et al. (2017) published a systematic review of 45 studies (n=1,156) that included radiofrequency (n=577), microwaves (n=78), laser (n=227), cryoablation (n=156), and high-intensity focused ultrasound (n=129). The following are the findings of the review:

- Pooled technical success was 96 % (microwave = 93%);
- Pooled technique efficacy was 75% (67 – 81), not reported for microwaves;
- Differences between techniques were not significant for technical success (P =0.449), major complications (P =0.181) or minor complications (P =0.762), but significant for technique efficacy (P =0.009).

The study concluded that techniques are technically successful, but efficacy remains suboptimal.

Comparison of Breast Cancer Treatment with and without Thermotherapy
Datta et al. (2016) performed a systematic review of 34 studies (n=2100) divided locally recurrent breast cancer subjects into single- and double-arm groups. Subjects were divided into single-arm (only combination therapy) and double-arm (randomized to radiation therapy only and radiation plus thermotherapy) studies. In the eight two-arm studies, complete response achieved in 60.2% of patients with both treatments versus 38.1% of those with radiation therapy only (P <.0001). In the 26 one-arm studies, the 63.4% complete response was comparable to that in two-arm studies (60.2%). Acute and late grade 3/4 toxicities with combination therapy were 14.4 and 5.2%. The authors concluded that treatment is more effective when thermotherapy is added to radiation therapy for breast cancer patients.

Minimally Invasive Treatment to Destroy Breast Cancer
Zhou et al. (2010) conducted a systematic review of minimally invasive thermal treatment for small breast cancers. All studies were feasibility or pilot studies. The systematic review determined that minimally invasive thermal treatment to destroy small breast cancers was promising, despite the fact that all studies were feasibility or pilot studies, and the percentage of patients achieving complete tumor ablation using microwave ablation was only 0 to 8.

Minimally Invasive Thermal Ablation of Early-Stage Breast Cancer
Zhao and Wu (2010) published a systematic review of minimally invasive thermal ablation of early-stage breast cancer (search: Pubmed, Embase and the Cochrane databases between January 1990 and December 2009). The clinical outcomes of the pertinent articles were compiled and assessed. 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 76-100% of breast cancer patients treated with radiofrequency ablation, 13-76% in laser ablation, 0-8% in microwave ablation, 36-83% in cryoablation, and 20-100% in high-intensity focused ultrasound ablation. The authors concluded that minimally invasive thermal ablation is a promising new tool for the local destruction of small breast carcinomas; large, randomized control studies are needed to assess the long-term benefits of minimally invasive thermal ablation techniques compared to current breast conserving therapies.

Randomized Clinical Trials

The following clinical trials are ongoing with the first update posted in 2003 and the last updated posted in 2013. There is no estimated date of completion for these trials:

Combination Chemotherapy with or without Microwave Thermotherapy Before Surgery in Treating Women with Locally Advanced Breast Cancer ([1]ClinicalTrials, 2013)

A total of 228 female patients with locally advanced primary breast cancer will be randomized (ratio 1:1) either to chemotherapy plus thermotherapy or chemotherapy alone. The primary endpoints include downsizing from mastectomy to partial mastectomy and determining the percentage of patients with ≥85% pathological cell death. Trials are ongoing but are no longer recruiting new patients. This study is ongoing, but not actively recruiting participants.

Microwave Thermotherapy in Treating Women with Stage I or Stage II Breast Cancer ([2]ClinicalTrials, 2013)

Randomized phase II trial to compare the effectiveness of microwave thermotherapy before surgery to that of surgery alone in treating women who have stage I or stage II breast cancer. A total of 222 female patients with early-stage primary breast cancer will be randomized (ratio 1:1) either to thermotherapy (at one of two different doses) plus surgery or surgery alone. The primary endpoints include reduction of tumor cells at surgical margins and reduction of second incision rates due to unclean surgical margins. No additional study details are available at the time of this writing.

National and Specialty Organizations

The American Society of Breast Surgeons (ASBS) (2018) published a consensus guideline on transcutaneous and percutaneous methods of treating breast cancer. The guidelines indicated that these treatments are being investigated and not currently FDA approved by the FDA; therefore, these treatments are not recommended, except in clinical trials.

The National Comprehensive Cancer Network (NCCN) (2022) Clinical Practice Guidelines for breast cancer does not address does not address the use of FMT as a treatment option for breast cancer (V.3.2022).

The National Cancer Institute (NCI) (2022) does not mention microwave thermotherapy as a treatment option for breast cancer in the NCI Breast Cancer Treatment PDQ Health Professional Version.

SUPPLEMENTAL INFORMATION

None.

CODING & BILLING INFORMATION

CPT Code

CPT	Description
19499	Unlisted procedure, breast [when specified as focused microwave thermotherapy]

HCPCS Codes – Any / All

CODING DISCLAIMER. Codes listed in this policy are for reference purposes only and may not be all-inclusive. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement. Listing of a service or device code in this policy does not guarantee coverage. Coverage is determined by the benefit document. Molina adheres to Current Procedural Terminology (CPT®), a registered trademark of the American Medical Association (AMA). All CPT codes and descriptions are copyrighted by the AMA; this information is included for informational purposes only. Providers and facilities are expected to utilize industry standard coding practices for all submissions. When improper billing and coding is not followed, Molina has the right to reject/deny the claim and recover claim payment(s). Due to changing industry practices, Molina reserves the right to revise this policy as needed.

APPROVAL HISTORY

8/10/2022	Policy reviewed and updated. No changes in coverage criteria. Updated references.
8/11/2021	Policy reviewed and updated. No changes in coverage criteria. Updated references.
9/16/2020	New Policy. IRO Peer Review Sep 8 -2020: Policy reviewed by practicing physician board-certified in Oncology/Hematology.

REFERENCES

Government Agencies

1. Centers for Medicare and Medicaid Services (CMS). Medicare coverage database. Available from CMS. Accessed July 2022.
2. [1] ClinicalTrials.gov. Combination Chemotherapy with or without microwave thermotherapy before surgery in treating women with locally advanced breast cancer (NCT00036985). Available from ClinicalTrials.gov. Updated December 19, 2013.
3. [2] ClinicalTrials.gov. Microwave thermotherapy in treating women with stage I or stage II breast cancer (NCT00036998). Available from ClinicalTrials.gov. Updated November 6, 2013. Accessed July 2022.

Peer Reviewed Publications

1. Datta NR, Puric E, Klingbiel D, Gomez S, Bodis S. Hyperthermia and radiation therapy in locoregional recurrent breast cancers: A systematic review and meta-analysis. Int J Radiat Oncol Biol Phys. 2016;94(5):1073-1087. doi: 10.1016/j.ijrobp.2015.12.361. Accessed July 2022.
2. Dooley WC, Vargas HI, Fenn AJ, et al. Focused microwave thermotherapy for preoperative treatment of invasive breast cancer: A review of clinical studies. Ann Surg Oncol. 2010; 17(4):1076-1093. doi: 10.1245/s10434-009-0872-z. Accessed July 2022.
3. Dooley WC, Vargas HI, Fenn AJ, et al. Randomized study of preoperative focused microwave phased array thermotherapy for early-stage invasive breast cancer. Cancer Therapy. 2008; 6(2):395-408. Available from EBSCO. Accessed July 2022.
4. Gardner RA, Vargas HI, Block JB, et al. Focused microwave phased array thermotherapy for primary breast cancer. Ann Surg Oncol. 2002 May;9(4):326-32. doi: 10.1007/BF02573866. Accessed July 2022.
5. Mauri G, Sconfienza LM, Pescatori LC, et al. Technical success, technique efficacy and complications of minimally-invasive imaging-guided percutaneous ablation procedures of breast cancer: A systematic review and meta-analysis. Eur Radiol. 2017 Aug;27(8):3199-3210. doi: 10.1007/s00330-016-4668-9. Accessed July 2022.
6. Vargas HI, Dooley WC, Gardner RA, et al. Focused microwave phased array thermotherapy for ablation of early-stage breast cancer: Results of thermal dose escalation. Ann Surg Oncol. 2004 Feb;11(2):139-46. doi: 10.1245/aso.2004.03.059. PMID 14761916. Accessed July 2022.
7. Vargas HI, Dooley WC, Fenn AJ, et al. Study of preoperative focused microwave phased array thermotherapy in combination with neoadjuvant anthracycline-based chemotherapy for large breast carcinomas. Cancer Therapy. 2007; 5(2):401-8. Available here.
8. Zhao Z, Wu F. Minimally-invasive thermal ablation of early-stage breast cancer: A systemic review. Eur J Surg Oncol. 2010 Dec;36(12):1149-55. doi: 10.1016/j.ejso.2010.09.012. Accessed July 2022.

National and Specialty Organizations

1. American Society of Breast Surgeons. Consensus guideline on the use of transcutaneous and percutaneous methods for the treatment of benign and malignant tumors of the breast. Available from ASBS. Published October 16, 2018. Accessed July 2022.
2. National Cancer Institute (NCI). Breast cancer treatment (adult) (PDQ) health professional version. Available from NCI. Updated May 27, 2022. Accessed June 2022.
3. NCCN Comprehensive Cancer Network (NCCN). NCCN guidelines: Breast cancer (V.4.2022). Available from NCCN. Updated June 21, 2022. Accessed June 2022.

Other Peer Reviewed and National Organization Publications (used in the development of this policy)

1. Huston TL, Simmons RM. Ablative therapies for the treatment of malignant diseases of the breast. Am J Surg. 2005 Jun;189(6):694-701. doi: 10.1016/j.amjsurg.2005.03.011. Accessed July 2022.
2. National Cancer Institute (NCI). Hyperthermia to treat cancer. Available from NCI. Updated June 17, 2021. Accessed June 2022.
3. Zhou W, Jiang Y, Chen L, et al. Image and pathological changes after microwave ablation of breast cancer: A pilot study. Eur J Radiol. 2014 Oct;83(10):1771-7. doi: 10.1016/j.ejrad.2014.06.015. Accessed July 2022.
4. Zhou W, Zha X, Liu X, et al. US-guided percutaneous microwave coagulation of small breast cancers: A clinical study. Radiology. 2012 May;263(2):364-73. doi: 10.1148/radiol.12111901. Accessed June 2022.

APPENDIX

Reserved for State specific information. *Information includes, but is not limited to, State contract language, Medicaid criteria and other mandated criteria.*