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

Last Approval: 8/9/2023
Next Review Due By: August 2024

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

Focused microwave thermotherapy (FMT) or Microwave ablation therapy (MWA) is a hyperthermic ablative therapy that 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. FMT utilizes electromagnetic waves to induce localized heating caused by the movement of water molecules. Given that tumor cells have higher water content than the surrounding adipose and breast glandular tissue, this allows the FMT technique to heat and kill the tumor cells while leaving the surrounding healthy tissue largely intact. Inducing tumor necrosis via FMT prior to surgery may improve surgical outcomes and reduce the possibility of inadvertently seeding viable cancer cells during the surgical procedure thus resulting in fewer local recurrences in the breast. In patients with locally advanced primary breast cancer, FMT may sufficiently reduce the size of the tumor to allow a less invasive surgical procedure. Furthermore, if a sufficient thermal dose is applied, thermotherapy treatment of early-stage breast cancer may destroy the tumor and eliminate the need for any further breast surgery or radiation therapy.

During FMT, 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. FMT has been investigated for multiple 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.

Regulatory Status

No microwave thermotherapy device 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.

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

Clinical Studies

Zhou et al. (2021) conducted a single arm multicenter clinical study that enrolled 35 participants with early-stage breast cancer. All 35 patients underwent microwave ablation therapy prior to surgical resection. Thirteen patients who underwent surgery alone with a diagnosis of breast cancer at a similar stage to the 35 participants were used at the control group. Of the 35 participants, 32 achieved complete tumor ablation. In addition to the ablation, MWA achieved a significant antitumor immune response that was still present post-surgery.

Yu et al. (2020) conducted a single institution retrospective study comparing nipple sparing mastectomy versus MWA. Twenty-one patients were included in the MWA group, and forty-three patients were in the nipple sparking mastectomy group. All participants in both groups achieved technique effectiveness and there was no significant difference in tumor progression between the two groups. In the MWA group there was one local tumor progression at 42 months post treatment, and one ipsilateral breast recurrence at 28 months post treatment. In the nipple sparing mastectomy group there was one ipsilateral breast recurrence at 31 months post-surgery, and two bone metastases at 30- and 34-months post treatment. Neither group had any cancer related deaths or major complications. The MWA group required less hospital time and achieved better cosmetic results. This study revealed MWA could achieve similar short-term results as nipple sparing mastectomy, and further research is needed to discover if it can be a viable alternative for patients who are not appropriate surgical candidates.

Vargas et al. (2007) studied 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.

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.

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 (based on tumor shrinkage measured by ultrasound) or tumor cell kill (based on necrosis and apoptosis measurements).

Systematic Reviews

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).
- 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.

Zhao and Wu (2010) published a systematic review of minimally invasive thermal ablation of early-stage breast cancer. The analyzed studies were all feasibility or pilot studies using different energy sources, patients, tumor characteristics, and ablation settings. Complete tumor ablation could be achieved in 0-8% of patients treated with microwave ablation. The authors concluded that minimally invasive thermal ablation is a promising new tool for the local destruction of small breast carcinomas; however large, randomized control studies are needed to assess the long-term benefits of minimally invasive thermal ablation techniques.

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 (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.

Microwave Thermotherapy in Treating Women with Stage I or Stage II Breast Cancer (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.

Randomized Study of Combination Chemotherapy With or Without Focused Microwave Thermotherapy Before Surgery in Treating Women With Large Breast Cancer Tumors (ClinicalTrials 2015)
Randomized phase III study to determine whether preoperative focused microwave heat treatment and chemotherapy combined are more effective than chemotherapy alone. The study aimed to enroll 238 participants and began in November 2010. The primary outcome measure is ultrasound measured tumor shrinkage. At this time, the recruitment status is unknown, and the study has not been updated since 2015.

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 investigational and are not currently FDA approved and are therefore not recommended, except in clinical trials.

The National Comprehensive Cancer Network (NCCN) (2023) Clinical Practice Guidelines for breast cancer does not address does not address the use of FMT as a treatment option for breast cancer (V.4.2023).

The National Cancer Institute (NCI) (2023) does not mention microwave thermotherapy as a treatment option for breast cancer in the NCI Breast Cancer Treatment PDQ Health Professional Version.

CODING & BILLING INFORMATION

CPT (Current Procedural Terminology) Code

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

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APPROVAL HISTORY

8/09/2023	Policy reviewed and updated. No changes in coverage criteria. Updated references.
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 by practicing physician board-certified in Oncology/Hematology 09/08/2020.

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APPENDIX

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