VHA Office of Integrated Veteran Care
Clinical Determination and Indication
Cryoablation for Malignant Breast Tumors

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I. Disclaimer

This document is currently in draft and is intended to be used as a reference for non-VA providers and not intended to replace clinical judgment when determining care pathways. These guidelines do not guarantee benefits or constitute medical advice.

II. Clinical Determinations and Indications

a. Indications for Cryoablation

Cryoablation is considered investigational and experimental for the following indications:

- Treatment of malignant breast tumors

There is insufficient evidence from peer-reviewed medical literature to support the safety and efficacy of this treatment. Therefore, cryoablation for the treatment of malignant breast tumors is considered **not medically necessary**.

III. Background and Supporting Information

The following information is for reference purposes only in accordance with the medical benefits package outlined in 38 C.F.R. § 17.38 (b). Each subsection supports VA's determinations for medical necessity and alignment with generally accepted standards of medical practice.

a. Background Information

Breast Tumors

A breast tumor is a collection of cells that grow rapidly, forming an abnormal mass in the breast. Once diagnosed, it is categorized as either benign or malignant. Benign tumors are generally harmless and do not spread and invade other areas of the body. Malignant tumors may grow quickly and are more likely to travel to other areas of the body, making them potentially more dangerous. Please note that some individuals may not prefer the term breast and may prefer to use the term chest.

Diagnosis and Management

Four main techniques are used to identify potential breast cancer, including mammography, ultrasound, clinical exam, and magnetic resonance imaging (MRI). Diagnosis of breast cancer is confirmed by biopsy. Imaging techniques utilize specialized equipment to visualize areas within the breast to assess differences in tissue density and architecture. If a difference is detected, further techniques may be used to confirm diagnosis.

Pathologists grade breast tumors by looking at tumor cell characteristics via microscopy and determining the level of mutation. Characteristics of the cancer cells are compared to normal cells and graded on a scale of 1-3, with three being the least characteristic of a normal cell. Staging is the process of determining the size of the tumor and whether it has spread to other parts of the body. The Tumor Lymph Node Metastasis (TNM) system is the most widely used cancer staging system.

Treatment plans are determined after a tumor has been graded and staged. Oncology providers partner with patients to determine the best treatment plan. Therapies for treating cancer include, but are not limited to the following: chemotherapy, radiation therapy, hormonal therapy, surgical removal, and tumor-specific targeted therapies.

Cryoablation of Breast Tumors

Cryoablation is a minimally invasive procedure performed in the outpatient setting with minimal anesthetics used at the insertion sites only. The cooling effect produced by the probes (cryoprobe) provides some pain relief. With guided imagery (e.g., ultrasound), an ablation probe needle applies an extremely cold liquid or gas (e.g., Argon) and targets the breast tumor tissue. The treatment creates an ice ball around the targeted tumor with a freeze, passive thaw (allowing the frozen tissue to thaw) and refreeze (using cryoablation again on the same tissue) process. The procedure takes approximately 45 minutes to perform.

The freezing technique causes a cytotoxic effect to the targeted site and the surrounding tissue, resulting in cellular dehydration. During the passive thaw phase, targeted cells begin to swell, and eventually rupture, destroying the cell. Additionally, ice crystals form and damage structures within the cell. Cryoablation may also cause very small blood clots, blocking blood flow to targeted cells resulting in their death.

b. Research, Clinical Trials, and Evidence Summaries

Fine et al. (2021) conducted the ICE3 Trial - Cryoablation of Low-Risk Breast Cancer- “ICE3” (NCT02200705). It is the largest controlled multilocation

clinical trial performed for liquid nitrogen (LN2)-based cryoablation of small, low-risk, early-stage malignant breast tumors without subsequently removing them. The trial began in 2014 and recruited 206 patients across 19 hospitals and medical centers across the U.S. During the ICE3 Trial, 188 of 194 patients that were eligible to receive treatment with the cryoablation did not have recurrence. The team also found that only 2.06% of patients (mean age of 75) who received breast cryoablation for low-risk early-stage breast cancers had an ipsilateral breast tumor recurrence (IBTR). Cryoablation has not been compared to surgical excision of breast tumors as a viable alternative. This trial was non-randomized, and authors noted that further studies should be performed to evaluate cryoablation as a viable treatment alternative.

Regen-Tuero et al. (2021) discussed the rationale for conducting immunotherapy in combination with cryoablation on small metastatic breast cancers in patients that were considered poor candidates for surgery. The combined therapies were reviewed for potential immune response effects. The authors theorized that combined therapies could enhance the immune response of the body after the cryoablation and therefore be more receptive to the immunotherapy drugs. This immune activation response could help the tumor-specific immune response and thereby improve the patient outcome. It was recommended that specific clinical trials were needed to determine which combination approach would best treat breast cancers.

Current studies on cryoablation for malignant breast tumors are insufficient in demonstrating a treatment benefit relative to standard therapy. Trials are limited and there are no randomized studies to determine outcomes.

c. Medicare Coverage Determinations

There are no available Medicare coverage determinations for this service. VA and Medicare are governed by separate laws and regulations; thus, VA coverage determinations may be different.

IV. Definitions

Term	Definition
Argon	A colorless, odorless, gaseous element found in the air used especially in lasers and electric bulbs
Carcinoma	A type of cancer that forms in epithelial tissue
Cryoablation	A procedure using an instrument called a cryoprobe to freeze and destroy targeted tissue
Cryoprobe	A chilled instrument used to freeze tissues in cryosurgery
Cytotoxic	Toxic or destructive to cells

Term	Definition
Endothelial Cell	The main type of cell found in the inside lining of blood vessels, lymph vessels, and the heart
Extracellular	Situated or occurring outside a cell or the cells of the body
Fibroadenoma	A benign (non-cancerous) tumor that most often forms in the breast and is made up of fibrous (connective) tissue and glandular tissue
Intracellular	Inside or within a cell
Invasive Ductal Carcinoma	The most common type of invasive breast cancer. It begins in the lining of the milk ducts (thin tubes that carry milk from the lobules of the breast to the nipple) and spreads outside the ducts to surrounding normal tissue
Ipsilateral	Situated, appearing on, or affecting the same side of the body
Ischemia	Inadequate blood supply to an organ or part of the body
Malignant	Diseases in which abnormal cells divide without control and can invade nearby tissues or spread to distant sites
Milieu	Surroundings or environment
Organelles	Tiny structures that perform particular tasks in a cell's cytoplasm
Tumor Lymph Node Metastasis	Used to stage tumors by their size, number of lymph nodes that have cancer, and spread of the cancer to other parts of the body

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VI. CDI History/Revision Information

- Explanation of changes to the CDI

Revision Type	Date of Revision	Update(s) Made to CDI
	MM/DD/YYYY	
	MM/DD/YYYY	