NOTE: This policy is not effective until October 1, 2017. To view the current policy, click here.

Medical Policy Manual Surgery, Policy No. 132

Cryosurgical Ablation of Miscellaneous Solid Organ, Pulmonary, and Breast Tumors

Effective: October 1, 2017

Next Review: November 2017
Last Review: June 2017

IMPORTANT REMINDER

Medical Policies are developed to provide guidance for members and providers regarding coverage in accordance with contract terms. Benefit determinations are based in all cases on the applicable contract language. To the extent there may be any conflict between the Medical Policy and contract language, the contract language takes precedence.

PLEASE NOTE: Contracts exclude from coverage, among other things, services or procedures that are considered investigational or cosmetic. Providers may bill members for services or procedures that are considered investigational or cosmetic. Providers are encouraged to inform members before rendering such services that the members are likely to be financially responsible for the cost of these services.

DESCRIPTION

Cryoablation kills cells freezing the tissue using a coolant that is circulated via a probe inserted into the tumor.

MEDICAL POLICY CRITERIA

Notes:

- This policy is limited to cryosurgery for the treatment of solid organ tumors, as well as breast and pulmonary tumors.
- This policy does not address liver tumors (primary or metastatic). See Cross References.

I. Cryosurgical ablation for the treatment of kidney, and prostate tumors may be considered medically necessary.
II. Cryosurgical ablation is considered **investigational** as a treatment of malignant or benign (fibroadenoma) breast tumors, pulmonary tumors, and all other solid organ tumors including but not limited to bone and pancreatic cancer.

**NOTE:** A summary of the supporting rationale for the policy criteria is at the end of the policy.

### POLICY GUIDELINES

It is critical that the list of information below is submitted for review to determine if the policy criteria are met. If any of these items are not submitted, it could impact our review and decision outcome.

- History and Physical
- Treatment plan including treatment area.

### CROSS REFERENCES

1. [Radioembolization for Primary and Metastatic Tumors of the Liver](#), Medicine, Policy No. 140
2. [Radiofrequency Ablation of Tumors (RFA)](#), Surgery, Policy No. 92
3. [Magnetic Resonance (MR) Guided Focused Ultrasound (MRgFUS) and High Intensity Focused Ultrasound (HIFU) Ablation, Surgery](#), Policy No. 139
4. [Microwave Tumor Ablation](#), Surgery, Policy No. 189
5. [Ablation of Primary and Metastatic Liver Tumors](#), Surgery, Policy No. 204

### BACKGROUND

Cryosurgical ablation (also called cryosurgery, cryotherapy, or cryoablation) kills cells (cancerous and normal) by freezing target tissues, most often by inserting a probe into the tumor through which coolant is circulated. Cryosurgery may be performed as an open surgical technique or as a closed procedure under laparoscopic or ultrasound guidance.

The goals of cryosurgery may include the following:

- Destruction or shrinkage of tumor tissue
- Controlling local tumor growth and preventing recurrence
- Palliating symptoms
- Extending survival duration for patients with certain tumors.

Potential complications associated with cryosurgery in any organ include the following:

- Hypothermic damage to normal tissue adjacent to the tumor (e.g., nerve damage)
- Structural damage along the probe track
- Secondary tumors if cancerous cells are seeded during probe removal.

### REGULATORY STATUS

There are several cryoablation devices cleared for marketing by the U.S. Food and Drug Administration (FDA) through the 510(k) process for use in open, minimally invasive or endoscopic surgical procedures in the areas of general surgery, urology, gynecology, oncology, neurology, dermatology, proctology, thoracic surgery and ear, nose and throat. Examples include:
- Cryocare® Surgical System by Endocare;
- CryoGen Cryosurgical System by Cryosurgical, Inc.;
- CryoHit® by Galil Medical;
- IceRod® CX, IcePearl® 2.1 CX and IceFORCE® 2.1 CX Cryoablation Needles by Galil Medical;
- SeedNet™ System by Galil Medical;
- Visica® System by Sanarus Medical;
- Visual-ICE® Cryoablation System by Galil;
- ERBECRYO 2® Cryosurgical Unit, ERBE USA Incorporated

**EVIDENCE SUMMARY**

In order to understand the impact of cryosurgical ablation on local or distant tumor recurrence and disease-free and overall survival in patients with solid tumors, randomized trials are needed that compare this technique with current standard treatments. The standard treatment for most solid tumors is surgical resection. For unresectable solid tumors, alternatives to resection depend on the tumor type and location, and may include thermal ablation, percutaneous ethanol injection, chemoembolization, chemotherapy, and radiation therapy.

Despite the weaknesses in the published clinical evidence, cryosurgical ablation has become a recognized standard of care for tumors of the kidney, liver (addressed in Ablation of Primary and Metastatic Liver Tumors, Surgery, Policy No. 204), and prostate.\[1-48\]

The following literature appraisal focuses on the investigational indications noted in medical policy criterion II above.

**BREAST TUMORS**

The standard treatment for breast cancer is surgical excision by lumpectomy or mastectomy, with or without adjuvant radiation therapy, chemotherapy, and/or hormone therapy. Fibroadenomas, benign tumors of the breast, generally do not require treatment. If treated, they are typically surgically excised.

**SYSTEMATIC REVIEWS**

One systematic review was found that included cryoablation along with other minimally-invasive thermal ablation techniques (i.e., radiofrequency, microwave, cryoablation and high-intensity focused ultrasound) for treatment of early-stage breast cancer.\[^{49}\] Zhao et al. reported that studies on cryoablation for breast cancer were primarily limited to pilot and feasibility studies conducted in the research setting. A wide range of 36-83% was reported for complete ablation of tumors. The authors concluded that, while promising, large randomized controlled trials are needed to further evaluate patient selection criteria, techniques to ensure complete tumor ablation, and long-term outcomes compared with surgical excision of breast tumors.

**RANDOMIZED CONTROLLED TRIALS (RCTS)**

There are no prospective, randomized controlled trials comparing survival and recurrence rates following cryoablation of breast tumors with surgical excision or, for unresectable tumors, with nonoperative therapies.

**NONRANDOMIZED STUDIES**
The remaining nonrandomized evidence does not permit reliable conclusions concerning the impact of cryosurgical ablation on breast cancer survival or recurrence due to a number of methodological limitations, including: heterogeneous or unreported patient selection criteria, the use of varied cryoablation techniques, nonrandomized allocation of treatment, lack of an appropriate surgical excision control group for comparison, small subject population, and limited data on long-term outcomes.[50-63]

**PULMONARY TUMORS**

**SYSTEMATIC REVIEWS**

Ratko et al. conducted a systematic review for the Agency for Healthcare Research and Quality (AHRQ) on the comparative effectiveness and harms of nonsurgical therapies for non-small cell lung cancer (NSCLC).[64] Patients were divided into the following 3 populations: 1) patients with stage I NSCLC who were not surgical candidates, 2) patients with stage I NSCLC who were surgical candidates but declined surgery, and 3) patients with inoperable endoluminal NSCLC causing obstruction. Only group 3 received therapies other than conformal radiotherapy or radiofrequency ablation including brachytherapy, laser and mechanical debridement, cryoablation, endoluminal stents, and photodynamic therapy. Five of the 17 studies related to group 3 were randomized controlled trials (RCTs), 1 was a nonrandomized comparative study, and 11 were single-arm studies. All five RCTs were rated as poor in quality. The authors concluded that the evidence was insufficient to permit conclusions on the comparative effectiveness of local nonsurgical therapies for any patients with inoperable endoluminal NSCLC causing obstruction.

Lee et al (2011) conducted a systematic review of endoscopic cryoablation of lung and bronchial tumors.[65] Included in the review were 15 case studies and 1 comparative observational study. Cryoablation was performed for inoperable, advanced lung and bronchial cancers in most studies. Some studies included patients with comorbid conditions and poor general health who would not be considered surgical candidates. Complications occurred in 11.1% of patients (10 studies) and consisted of hemorrhage, mediastinal emphysema, atrial fibrillation, and dyspnea. Within 30 days of the procedure, death from hemoptysis and respiratory failure, considered to be most likely related to disease progression, occurred in 7.1% of patients. Improvements in pulmonary function and clinical symptoms occurred in studies reporting these outcomes. One published review reported the outcomes of 15 case series and one comparative observational study for endoscopic cryotherapy of endobronchial tumors. Most studies were for inoperable, advanced lung and bronchial cancers. A critical analysis of the studies was not provided. However, the authors noted the significant limitations in the available evidence due to lack of control groups, lack of random treatment allocation, and heterogeneity in study methodologies, participants’ characteristics (e.g., comorbid conditions, general health, cancer grade), treatment protocols, operative techniques, and outcome measures. Complications occurred in 11.1% of patients from ten studies and consisted of hemorrhage, mediastinal emphysema, atrial fibrillation, and dyspnea. Within 30 days of the procedure, death from hemoptysis and respiratory failure, considered to be most likely related to disease progression, occurred in 7.1% of patients. Improvements in pulmonary function and clinical symptoms occurred in studies reporting these outcomes. Because the studies in the review did not include control groups or compare outcomes of cryosurgery to alternative strategies for managing similar patients, no conclusions can be made on the net health outcomes of cryosurgery for lung cancer.
NONRANDOMIZED STUDIES

The ECLIPSE trial is prospective, multicenter trial of cryoablation for metastatic disease in the lungs, interim results at 1-year follow-up were published in 2015.[66] The trial enrolled 40 patients with 60 metastatic lung lesions who were treated with cryoablation and had at least 12 months of follow-up. Outcomes included survival, local tumor control, quality of life, and complications. Local tumor control was achieved in 94.2% (49/52) of treated lesions, and 1-year OS was 97.5% (39/40). There were no significant changes in quality of life over the 12-month study. The most common adverse event was pneumothorax requiring chest tube insertion in 18.8% (9/48 procedures).

OTHER TUMORS

Cryoablation for the treatment of other solid tumors has not been well-studied.

SYSTEMATIC REVIEWS

In 2014, Keane et al. reported on a systematic review of ablation therapies, including cryoablation, for locally advanced pancreatic cancer.[67] The review noted studies have demonstrated ablative therapies, including cryoablation, are feasible but larger studies are needed. No conclusions could be made on whether ablation resulted in better oncologic outcomes than best supportive care.

In 2012, Tao and colleagues reported on a systematic review of cryoablation for pancreatic cancer.[68] The authors identified 29 studies from the literature search and included 5 of these studies in the review. The 5 studies were all case series and considered to be of low quality. Adverse events, when mentioned in the studies, included delayed gastric emptying (0% to 40.9% in 3 studies), pancreatic leak (0% to 6.8% in 4 studies), biliary leak (0% to 6.8% in 3 studies), and one instance of upper gastrointestinal hemorrhage. Pain relief was reported in 3 studies and ranged from 66.7% to 100%. Median survival times reported in 3 studies ranged from 13.4 to 16 months. One-year total survival rates reported in 2 studies were 57.5% and 63.6%.

RANDOMIZED CONTROLLED TRIALS

One preliminary randomized trial studied 36 female patients with NSCLC who also had epidermal growth factor receptor gene mutations.[69] All patients received 6 months treatment with molecular target therapy gefitinib, an epidermal growth factor receptor-tyrosine kinase inhibitor. Patients were randomized to either an experimental group and underwent cryoablation prior to receiving gefitinib, or to a control group in which cryoablation was not performed. At 1-year follow-up, the survival rate in the cryoablation group was significantly higher than that of the control group. The findings of this preliminary study suggest that cryoablation may improve the effects of gefitinib in this patient population. Additional larger, long-term randomized trials are needed to validate these findings.

NONRANDOMIZED STUDIES

The remaining published literature is limited to case series and retrospective reviews.[70-79] As discussed above, these studies do not permit reliable conclusions concerning the impact of cryoablation on health outcomes.
Clinical practice guidelines from U.S. professional associations consistently list cryoablation as a treatment option for tumors of the kidney or prostate.[80-84]

No clinical practice guidelines or position statements from U.S. professional societies were identified that recommend cryoablation for the treatment of solid tumors other than kidney and prostate tumors.[85-93]

**SUMMARY**

Cryosurgical ablation has become a recognized standard of care in the management of tumors of the kidney and prostate. Therefore, this technique may be considered medically necessary in the treatment of these tumors.

There is not enough research to show that cryosurgical ablation for the treatment of solid organ, pulmonary, bone, and breast tumors other than tumors of the kidney or prostate improves health outcomes. In addition, there are no clinical practice guidelines that recommend the use of cryosurgical ablation of those tumors. Therefore, cryosurgical ablation as a treatment for solid organ, pulmonary, bone, and breast tumors other than those of the kidney or prostate is considered investigational.

**REFERENCES**


94. BlueCross BlueShield Association Medical Policy Reference Manual "Cryosurgical Ablation of Miscellaneous Solid Tumors Other Than Liver, Prostate, or Dermatologic Tumors." 7.01.92

95. BlueCross BlueShield Association Medical Policy Reference Manual "Cryosurgical Ablation of Primary or Metastatic Liver Tumors." Policy No. 7.01.75

96. BlueCross BlueShield Association Medical Policy Reference Manual "Whole Gland Cryoablation of Prostate Cancer." Policy No. 7.01.79

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<th>Number</th>
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<td>20983</td>
<td>Ablation therapy for reduction or eradication of 1 or more bone tumors (eg, metastasis) including adjacent soft tissue when involved by tumor extension, percutaneous, including imaging guidance when performed; cryoablation</td>
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Date of Origin: March 2004