LifeWise
Health Plan of Washington

MEDICAL POLICY – 6.01.68

Irreversible Electroporation of Tumors Located in the Liver, Pancreas, Kidney, or Lung

BCBSA Ref. Policy: 6.01.68

Effective Date:	Jan. 1, 2025
Last Revised:	Dec. 10, 2024
Replaces:	7.01.572

RELATED MEDICAL POLICIES:

7.01.92	Cryosurgical Ablation of Miscellaneous Solid Tumors Other than Liver, Prostate, or Dermatologic Tumors
7.01.95	Radiofrequency Ablation of Miscellaneous Solid Tumors Excluding Liver Tumors
7.01.133	Microwave Tumor Ablation
8.01.11	Transcatheter Arterial Chemoembolization (TACE) to Treat Primary or Metastatic Liver Malignancies
8.01.61	Focal Treatments for Prostate Cancer
8.01.521	Radioembolization for Primary and Metastatic Tumors of the Liver

Select a hyperlink below to be directed to that section.

∞ Clicking this icon returns you to the hyperlinks menu above.

Introduction

Irreversible electroporation (IRE) is a minimally invasive medical procedure used to treat tumors. The technique uses short, high-voltage electrical pulses to destroy tumor cells without using heat. These electrical pulses create tiny, permanent holes in the cell walls of the tumor, causing the cells to die. Unlike thermal ablation techniques, IRE avoids damaging nearby critical structures like blood vessels, nerves, and bile ducts. This makes it a good option for treating tumors located in hard-to-reach or sensitive areas, such as the liver, pancreas, kidney, or lung.

Note: The Introduction section is for your general knowledge and is not to be taken as policy coverage criteria. The rest of the policy uses specific words and concepts familiar to medical professionals. It is intended for providers. A provider can be a person, such as a doctor, nurse, psychologist, or dentist. A provider also can be a place where medical care is given, like a hospital, clinic, or lab. This policy informs them about when a service may be covered.

Policy Coverage Criteria

Service	Investigational
Irreversible electroporation	**Irreversible electroporation is considered investigational for treatment of primary or metastatic solid tumors including, but not limited to, tumors of the liver, pancreas, kidney or lung. (i.e. NanoKnife System).**

Coding

Code	Description
CPT	
0600T	Ablation, irreversible electroporation; 1 or more tumors per organ, including imaging guidance, when performed, percutaneous
0601T	Ablation, irreversible electroporation; 1 or more tumors, including fluoroscopic and ultrasound guidance, when performed, open

Note: CPT codes, descriptions and materials are copyrighted by the American Medical Association (AMA). HCPCS codes, descriptions and materials are copyrighted by Centers for Medicare Services (CMS).

Related Information

Other uses of Irreversible Electroporation

Pulsed field ablation is a form of irreversible electroporation energy used to treat individuals with atrial fibrillation. This use is not addressed in this policy.

Focal therapy with irreversible electropora5tion as treatment for prostate cancer is addressed separately. (See **Related Policies**.)

Evidence Review

Description

Irreversible electroporation produces high-frequency electric pulses to create an electric current that permanently damages cell membranes causing cell death due to the inability to maintain homeostasis. Irreversible electroporation produces no thermal effect and appears to preserve vessels, nerves and the extracellular matrix.

Background

Irreversible Electroporation

Electroporation generates high-frequency electrical pulses between two or more electrodes which produces an electric current that damages the cell membrane and allows molecules to pass into the cell passively. Electroporation can be temporary (reversible electroporation) or permanent (irreversible electroporation or IRE). In IRE the cell membrane is permanently damaged causing cell death due to the inability to maintain homeostasis. IRE achieves its action with no thermal effect. IRE appears to preserve vessels, nerves and the extracellular matrix.[1,2,3]

Summary of Evidence

For individuals being treated with locoregional therapy for tumors in the liver who receive irreversible electroporation, the evidence includes primarily single-arm studies. Relevant outcomes are overall survival, disease-specific survival, symptoms, morbid events, functional outcomes, and quality of life. Irreversible electroporation may be an option for locoregional therapy that is less damaging to nearby blood vessels, bile ducts, and nerves than thermal ablation therapies. Most studies of IRE for liver tumors lack a comparator arm. One comparative study was identified reporting health outcomes, but the study is retrospective and included 18 individuals treated with IRE. Therefore, there is insufficient data to determine how survival or adverse events compare to other methods for locoregional therapy. There is a lack of standardization on appropriate use. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals with locally advanced pancreatic cancer who receive irreversible electroporation, the evidence includes single-arm studies. Relevant outcomes are overall survival, disease-specific survival, symptoms, morbid events, functional outcomes, and quality of life. Thermal ablation therapies are not commonly used to treat pancreatic cancer due to the increased risk of trauma to the adjacent major anatomical structures. IRE may be an alternative that does not cause thermal injury to nearby sensitive structures. However, there is a lack of consensus on the optimal IRE treatment protocol. Studies of IRE for pancreatic tumors are single-arm. There is insufficient data to determine whether survival is improved with chemotherapy followed by IRE compared to chemotherapy alone. Two RCTs are underway. Prospective, single arm studies suggest a high complication rate. There are no studies reporting functional or quality of life outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals being treated with locoregional therapy for tumors in the kidneys who receive irreversible electroporation, the evidence includes single-arm studies. Relevant outcomes are overall survival, disease-specific survival, symptoms, morbid events, functional outcomes, and quality of life. Studies of IRE for kidney tumors are single-arm. Only one study included more than 10 participants. No comparative data are available. Therefore, there is no data to determine how survival or adverse events compare to other methods for locoregional therapy. There are no studies reporting functional or quality of life outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

For individuals being treated with locoregional therapy for tumors in the lungs who receive irreversible electroporation, the evidence includes single-arm studies. Relevant outcomes are overall survival, disease-specific survival, symptoms, morbid events, functional outcomes, quality of life. Irreversible electroporation may be an option for locoregional therapy that is less damaging to nearby bronchovascular structures. Studies of IRE for lung tumors are single-arm. The ALICE study was a prospective, single-arm study conducted at two centers that was stopped early (n=23) due to failing to meet expected efficacy at an interim analysis based on high recurrence rates of 61% at a median follow-up of 1 year. No comparative data are available. Therefore, there is no data to determine how survival or adverse events compare to other methods for locoregional therapy. There are no studies reporting functional or quality of life outcomes. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

Ongoing and Unpublished Clinical Trials

Some ongoing and unpublished trials that might influence this policy are listed in **Table 1**.

Table 1. Summary of Key Trials

NCT No.	Trials Name	Planned Enrollment	Completion Date
Ongoing			
NCT03899636[a]	A Pivotal Study of Safety and Effectiveness of NanoKnife IRE for Stage 3 Pancreatic Cancer (DIRECT)	528	Dec 2023
NCT03899649[a]	A Registry Study of NanoKnife IRE for Stage 3 Pancreatic Cancer (DIRECT)	532	Dec 2024
NCT05170802	AHPBA Registry Database (Collection of Clinical Data Related to Pancreatic Cancer & Treatment - Irreversible Electroporation (IRE))	30	Dec 2024
ISRCTN14986389[b]	Investigating the feasibility of a clinical trial to test using irreversible electroporation to treat locally advanced pancreatic cancer following initial chemotherapy (LAP-PIE)	50	Nov 2024

NCT: national clinical trial.

[a] Denotes industry-sponsored or cosponsored trial.

[b] ISRCTN registry

Practice Guidelines and Position Statements

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

National Comprehensive Cancer Network

The National Comprehensive Cancer Network (NCCN) guidelines for Hepatocellular Carcinoma (v2.2024)[6]states that 'Irreversible electroporation (IRE) is an emerging modality for tumor

ablation' and that 'Larger studies are needed to determine the effectiveness of IRE for local HCC treatment.'

The National Comprehensive Cancer Network (NCCN) guidelines for Biliary Tract Cancers (v3.2024)[7]states that ablation is a reasonable alternative to surgical resection for intrahepatic CCA, particularly in individuals with high-risk disease and 'Options for ablation include cryoablation, radiofrequency ablation, microwave ablation, and irreversible electroporation' for treatment of small, single intrahepatic cholangiocarcinoma tumors (<3cm) amenable to complete ablation, whether recurrent or primary.

The National Comprehensive Cancer Network (NCCN) guidelines for Pancreatic Adenocarcinoma (v3.2024)[29]states that 'Irreversible electroporation (IRE) is an ablative technique in which electric pulses are used to create nanopores to induce cell death. This technique has been used in individuals with locally advanced pancreatic cancer and may be safe and feasible and improve survival. However, due to concerns about complications and technical expertise, the Panel does not currently recommend IRE for treatment of locally advanced pancreatic cancer.'

The National Comprehensive Cancer Network (NCCN) guidelines for Kidney Cancer (v1.2025)[48]do not refer to irreversible electroporation. The guidelines state that 'Thermal ablation (e.g., cryosurgery, radiofrequency ablation, microwave ablation) is an option for the management of clinical stage T1 renal lesions. Thermal ablation is suitable for renal masses ≤3 cm. Thermal ablation is an option for clinical T1b masses in select individuals not eligible for surgery.'

The National Comprehensive Cancer Network (NCCN) guidelines for Non-Small Cell Lung Cancer (v8.2024)[68]do not refer to irreversible electroporation. With respect to ablation therapies, the guidelines state that:

- 'Image-guided thermal ablation (IGTA) therapy (e.g., cryotherapy, microwave, radiofrequency) may be an option for select individuals' for initial treatment for stage 1A disease.
- 'IGTA may be considered for those individuals who are deemed "high risk"—those with tumors that are for the most part surgically resectable but rendered medically inoperable due to comorbidities. In cases where IGTA is considered for high-risk or borderline operable individuals, a multidisciplinary evaluation is recommended.'
- 'IGTA is an option for the management of NSCLC lesions <3 cm. Ablation for NSCLC lesions >3 cm may be associated with higher rates of local recurrence and complications.'

- 'There is evidence on the use of IGTA for selected individuals with stage 1A NSCLC, those who present with multiple lung cancers, or those who present with locoregional recurrence of symptomatic local thoracic disease.'
- 'In the setting of progression at a limited number of sites on a given line of systemic therapy (oligoprogression), local ablative therapy to the oligoprogressive sites may extend the duration of benefit of the current line of systemic therapy.'

National Institute for Health and Care Excellence (NICE)

The National Institute for Health and Care Excellence (NICE) published an interventional procedures guidance in 2017 on irreversible electroporation for treating pancreatic cancer.[71] The guidance stated that 'Current evidence on the safety and efficacy of irreversible electroporation for treating pancreatic cancer is inadequate in quantity and quality. Therefore, this procedure should only be used in the context of research.

Medicare National Coverage

There is no national coverage determination.

Regulatory Status

The NanoKnife System (Angiodynamics) was originally cleared through the 510(k) process (K102329) in 2011 for the surgical ablation of soft tissue. NanoKnife has not received clearance for the treatment of any specific disease. FDA product code: OAB.

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History

Date	Comments
10/01/19	New policy, approved September 10, 2019, effective January 3, 2020. Add to Surgery section. The use of irreversible electroporation (IRE) (i.e., NanoKnife System) is considered investigational for all indications.
07/01/20	Coding update. Added codes 0600T and 0601T. Removed 32999, 47399, 48999, and 53899.
10/01/20	Annual Review, approved September 1, 2020. Policy updated with literature review. References added. Policy statement unchanged.
11/01/21	Annual Review, approved October 5, 2021. Policy reviewed. References added. Policy statement unchanged.
10/01/22	Annual Review, approved September 26, 2022. Policy updated with literature review. References added. Policy statement unchanged. Changed the wording from "patient" to "individual" throughout the policy for standardization.
08/01/23	Annual Review, approved July 24, 2023.Policy updated with literature review. References updated. No references added. Policy statement unchanged.

Date	Comments
01/01/25	Policy renumbered from 7.01.572 Irreversible Electroporation (NanoKnife System) to 6.01.68 Irreversible Electroporation of Tumors Located in the Liver, Pancreas, Kidney, or Lung, approved December 10, 2024. Policy revised with literature review through August 8, 2024. Irreversible electroporation is investigational for treatment of liver, pancreatic, kidney and lung cancer. The use of this technology for the treatment of prostate cancer moved to policy 8.01.61 Focal Treatments for Prostate Cancer. No other changes.

Scope: Medical policies are systematically developed guidelines that serve as a resource for Company staff when determining coverage for specific medical procedures, drugs or devices. Coverage for medical services is subject to the limits and conditions of the member benefit plan. Members and their providers should consult the member benefit booklet or contact a customer service representative to determine whether there are any benefit limitations applicable to this service or supply. This medical policy does not apply to Medicare Advantage.