PREMERA HMO

An Independent Licensee of the Blue Cross Blue Shield Association

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.

POLICY CRITERIA | DOCUMENTATION REQUIREMENTS | CODING
RELATED INFORMATION | EVIDENCE REVIEW | REFERENCES | HISTORY

∞ 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.

References

1. Scheltema MJ, van den Bos W, de Bruin DM, et al. Focal vs extended ablation in localized prostate cancer with irreversible electroporation; a multi-center randomized controlled trial. BMC Cancer. May 05 2016; 16: 299. PMID 27150293
2. Rubinsky B, Onik G, Mikus P. Irreversible electroporation: a new ablation modality--clinical implications. Technol Cancer Res Treat. Feb 2007; 6(1): 37-48. PMID 17241099

3. Davalos RV, Mir IL, Rubinsky B. Tissue ablation with irreversible electroporation. Ann Biomed Eng. Feb 2005; 33(2): 223-31. PMID 15771276

4. Siegel RL, Giaquinto AN, Jemal A. Cancer statistics, 2024. CA Cancer J Clin. 2024; 74(1): 12-49. PMID 38230766

5. McGlynn KA, Petrick JL, El-Serag HB. Epidemiology of Hepatocellular Carcinoma. Hepatology. Jan 2021; 73 Suppl 1(Suppl 1): 4-13. PMID 32319693

6. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Hepatocellular Carcinoma. Version 2.2024. **https://www.nccn.org/professionals/physician_gls/pdf/hcc.pdf**. Accessed November 11, 2024

7. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Biliary Tract Cancers. Version 3.2024. **https://www.nccn.org/professionals/physician_gls/pdf/btc.pdf**. Accessed November 11, 2024

8. Kim HS, El-Serag HB. The Epidemiology of Hepatocellular Carcinoma in the USA. Curr Gastroenterol Rep. Apr 11 2019; 21(4): 17. PMID 30976932

9. Centers for Disease Control and Prevention (CDC). Hepatocellular carcinoma - United States, 2001-2006. MMWR Morb Mortal Wkly Rep. May 07 2010; 59(17): 517-20. PMID 20448528

10. Food and Drug Administration. NanoKnife System 510(k) Summary: K183385. **https://www.accessdata.fda.gov/cdrh_docs/pdf18/K183385.pdf**. Accessed November 11, 2024.

11. Geboers B, Scheffer HJ, Graybill PM, et al. High-Voltage Electrical Pulses in Oncology: Irreversible Electroporation, Electrochemotherapy, Gene Electrotransfer, Electrofusion, and Electroimmunotherapy. Radiology. May 2020; 295(2): 254-272. PMID 32208094

12. AngioDynamics. NanoKnife Patient Guide. **https://nanoknife.com/wp-content/uploads/2021/06/GL-ON-BR-911-REV-01-NanoKnife-Patient-Guide-WEB.pdf**. Accessed November 11 2024.

13. Brar G, Greten TF, Graubard BI, et al. Hepatocellular Carcinoma Survival by Etiology: A SEER-Medicare Database Analysis. Hepatol Commun. Oct 2020; 4(10): 1541-1551. PMID 33024922

14. Dhanasekaran R, Hemming AW, Zendejas I, et al. Treatment outcomes and prognostic factors of intrahepatic cholangiocarcinoma. Oncol Rep. Apr 2013; 29(4): 1259-67. PMID 23426976

15. Wade R, South E, Anwer S, et al. Ablative and non-surgical therapies for early and very early hepatocellular carcinoma: a systematic review and network meta-analysis. Health Technol Assess. Dec 2023; 27(29): 1-172. PMID 38149643

16. Cheung W, Kavnoudias H, Roberts S, et al. Irreversible electroporation for unresectable hepatocellular carcinoma: initial experience and review of safety and outcomes. Technol Cancer Res Treat. Jun 2013; 12(3): 233-41. PMID 23369152

17. Cannon R, Ellis S, Hayes D, et al. Safety and early efficacy of irreversible electroporation for hepatic tumors in proximity to vital structures. J Surg Oncol. Apr 2013; 107(5): 544-9. PMID 23090720

18. Frühling P, Nilsson A, Duraj F, et al. Single-center nonrandomized clinical trial to assess the safety and efficacy of irreversible electroporation (IRE) ablation of liver tumors in humans: Short to mid-term results. Eur J Surg Oncol. Apr 2017; 43(4): 751-757. PMID 28109674

19. Granata V, Fusco R, Catalano O, et al. Percutaneous ablation therapy of hepatocellular carcinoma with irreversible electroporation: MRI findings. AJR Am J Roentgenol. May 2015; 204(5): 1000-7. PMID 25905934

20. Padia SA, Johnson GE, Yeung RS, et al. Irreversible Electroporation in Patients with Hepatocellular Carcinoma: Immediate versus Delayed Findings at MR Imaging. Radiology. Jan 2016; 278(1): 285-94. PMID 26523493

21. Niessen C, Beyer LP, Pregler B, et al. Percutaneous Ablation of Hepatic Tumors Using Irreversible Electroporation: A Prospective Safety and Midterm Efficacy Study in 34 Patients. J Vasc Interv Radiol. Apr 2016; 27(4): 480-6. PMID 26922979

22. Scheffer HJ, Nielsen K, van Tilborg AA, et al. Ablation of colorectal liver metastases by irreversible electroporation: results of the COLDFIRE-I ablate-and-resect study. Eur Radiol. Oct 2014; 24(10): 2467-75. PMID 24939670

23. Narayanan G, Gentile NT, Eyshi J, et al. Irreversible Electroporation in Treating Colorectal Liver Metastases in Proximity to Critical Structures. J Vasc Interv Radiol. Aug 30 2024. PMID 39218213

24. Belfiore MP, Reginelli A, Maggialetti N, et al. Preliminary results in unresectable cholangiocarcinoma treated by CT percutaneous irreversible electroporation: feasibility, safety and efficacy. Med Oncol. Apr 09 2020; 37(5): 45. PMID 32270353

25. Sugimoto K, Kakimi K, Takeuchi H, et al. Irreversible Electroporation versus Radiofrequency Ablation: Comparison of Systemic Immune Responses in Patients with Hepatocellular Carcinoma. J Vasc Interv Radiol. Jun 2019; 30(6): 845-853.e6. PMID 31126596

26. Blaise L, Pereira H, Vilgrain V, et al. Percutaneous ablation for locally advanced hepatocellular carcinoma with tumor portal invasion. Clin Res Hepatol Gastroenterol. Nov 2021; 45(6): 101731. PMID 34139320

27. Ruarus AH, Barabasch A, Catalano O, et al. Irreversible Electroporation for Hepatic Tumors: Protocol Standardization Using the Modified Delphi Technique. J Vasc Interv Radiol. Nov 2020; 31(11): 1765-1771.e15. PMID 32978054

28. Balaban EP, Mangu PB, Khorana AA, et al. Locally Advanced, Unresectable Pancreatic Cancer: American Society of Clinical Oncology Clinical Practice Guideline. J Clin Oncol. Aug 01 2016; 34(22): 2654-68. PMID 27247216

29. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Pancreatic Adenocarcinoma. Version 3.2024. **https://www.nccn.org/professionals/physician_gls/pdf/pancreatic.pdf**. Accessed November 11, 2024

30. Klein AP. Pancreatic cancer epidemiology: understanding the role of lifestyle and inherited risk factors. Nat Rev Gastroenterol Hepatol. Jul 2021; 18(7): 493-502. PMID 34002083

31. van Roessel S, Kasumova GG, Verheij J, et al. International Validation of the Eighth Edition of the American Joint Committee on Cancer (AJCC) TNM Staging System in Patients With Resected Pancreatic Cancer. JAMA Surg. Dec 01 2018; 153(12): e183617. PMID 30285076

32. Ellis LM, Bernstein DS, Voest EE, et al. American Society of Clinical Oncology perspective: Raising the bar for clinical trials by defining clinically meaningful outcomes. J Clin Oncol. Apr 20 2014; 32(12): 1277-80. PMID 24638016

33. Charalambous P, Moris D, Karachaliou GS, et al. The efficacy and safety of the open approach irreversible electroporation in the treatment of pancreatic cancer: A systematic review. Eur J Surg Oncol. Sep 2020; 46(9): 1565-1572. PMID 32536525

34. Martin RC, McFarland K, Ellis S, et al. Irreversible electroporation therapy in the management of locally advanced pancreatic adenocarcinoma. J Am Coll Surg. Sep 2012; 215(3): 361-9. PMID 22726894

35. Martin RC, Kwon D, Chalikonda S, et al. Treatment of 200 locally advanced (stage III) pancreatic adenocarcinoma patients with irreversible electroporation: safety and efficacy. Ann Surg. Sep 2015; 262(3): 486-94; discussion 492-4. PMID 26258317

36. Månsson C, Bergenfeldt M, Brahmstaedt R, et al. Safety and preliminary efficacy of ultrasound-guided percutaneous irreversible electroporation for treatment of localized pancreatic cancer. Anticancer Res. Jan 2014; 34(1): 289-93. PMID 24403476

37. Scheffer HJ, Vroomen LG, de Jong MC, et al. Ablation of Locally Advanced Pancreatic Cancer with Percutaneous Irreversible Electroporation: Results of the Phase I/II PANFIRE Study. Radiology. Feb 2017; 282(2): 585-597. PMID 27604035

38. Ruarus AH, Vroomen LGPH, Geboers B, et al. Percutaneous Irreversible Electroporation in Locally Advanced and Recurrent Pancreatic Cancer (PANFIRE-2): A Multicenter, Prospective, Single-Arm, Phase II Study. Radiology. Jan 2020; 294(1): 212-220. PMID 31687922

39. Narayanan G, Hosein PJ, Arora G, et al. Percutaneous irreversible electroporation for downstaging and control of unresectable pancreatic adenocarcinoma. J Vasc Interv Radiol. Dec 2012; 23(12): 1613-21. PMID 23177107

40. Narayanan G, Hosein PJ, Beulaygue IC, et al. Percutaneous Image-Guided Irreversible Electroporation for the Treatment of Unresectable, Locally Advanced Pancreatic Adenocarcinoma. J Vasc Interv Radiol. Mar 2017; 28(3): 342-348. PMID 27993507

41. Martin RC, McFarland K, Ellis S, et al. Irreversible electroporation in locally advanced pancreatic cancer: potential improved overall survival. Ann Surg Oncol. Dec 2013; 20 Suppl 3: S443-9. PMID 23128941

42. Kluger MD, Epelboym I, Schrope BA, et al. Single-Institution Experience with Irreversible Electroporation for T4 Pancreatic Cancer: First 50 Patients. Ann Surg Oncol. May 2016; 23(5): 1736-43. PMID 26714959

43. Leen E, Picard J, Stebbing J, et al. Percutaneous irreversible electroporation with systemic treatment for locally advanced pancreatic adenocarcinoma. J Gastrointest Oncol. Apr 2018; 9(2): 275-281. PMID 29755766

44. Liu S, Qin Z, Xu J, et al. Irreversible electroporation combined with chemotherapy for unresectable pancreatic carcinoma: a prospective cohort study. Onco Targets Ther. 2019; 12: 1341-1350. PMID 30863100

45. Holland MM, Bhutiani N, Kruse EJ, et al. A prospective, multi-institution assessment of irreversible electroporation for treatment of locally advanced pancreatic adenocarcinoma: initial outcomes from the AHPBA pancreatic registry. HPB (Oxford). Aug 2019; 21(8): 1024-1031. PMID 30737097

46. Martin RC, Durham AN, Besselink MG, et al. Irreversible electroporation in locally advanced pancreatic cancer: A call for standardization of energy delivery. J Surg Oncol. Dec 2016; 114(7): 865-871. PMID 27546233

47. Surveillance, Epidemiology, and End Results Program (SEER). SEER Stat Fact Sheets: Kidney and Renal Pelvis. **http://seer.cancer.gov/statfacts/html/kidrp.html**. Accessed November 11, 2024.

48. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Kidney Cancer. Version 1.2025. **https://www.nccn.org/professionals/physician_gls/pdf/kidney.pdf**. Accessed November 11, 2024

49. Cheungpasitporn W, Thongprayoon C, O'Corragain OA, et al. The risk of kidney cancer in patients with kidney stones: a systematic review and meta-analysis. QJM. Mar 2015; 108(3): 205-12. PMID 25208892

50. Argani P, Laé M, Ballard ET, et al. Translocation carcinomas of the kidney after chemotherapy in childhood. J Clin Oncol. Apr 01 2006; 24(10): 1529-34. PMID 16575003

51. Cho E, Curhan G, Hankinson SE, et al. Prospective evaluation of analgesic use and risk of renal cell cancer. Arch Intern Med. Sep 12 2011; 171(16): 1487-93. PMID 21911634

52. Mandel JS, McLaughlin JK, Schlehofer B, et al. International renal-cell cancer study. IV. Occupation. Int J Cancer. May 29 1995; 61(5): 601-5. PMID 7768630

53. Lowrance WT, Ordoñez J, Udaltsova N, et al. CKD and the risk of incident cancer. J Am Soc Nephrol. Oct 2014; 25(10): 2327-34. PMID 24876115

54. Adams KF, Leitzmann MF, Albanes D, et al. Body size and renal cell cancer incidence in a large US cohort study. Am J Epidemiol. Aug 01 2008; 168(3): 268-77. PMID 18544571

55. Hidayat K, Du X, Zou SY, et al. Blood pressure and kidney cancer risk: meta-analysis of prospective studies. J Hypertens. Jul 2017; 35(7): 1333-1344. PMID 28157813

56. Chin AI, Lam JS, Figlin RA, et al. Surveillance strategies for renal cell carcinoma patients following nephrectomy. Rev Urol. 2006; 8(1): 1-7. PMID 16985554

57. Hilton A, Kourounis G, Georgiades F. Irreversible electroporation in renal tumours: A systematic review of safety and early oncological outcomes. Urologia. Aug 2022; 89(3): 329-337. PMID 35139717

58. Buijs M, Zondervan PJ, de Bruin DM, et al. Feasibility and safety of irreversible electroporation (IRE) in patients with small renal masses: Results of a prospective study. Urol Oncol. Mar 2019; 37(3): 183.e1-183.e8. PMID 30509869

59. Canvasser NE, Sorokin I, Lay AH, et al. Irreversible electroporation of small renal masses: suboptimal oncologic efficacy in an early series. World J Urol. Oct 2017; 35(10): 1549-1555. PMID 28255621

60. Xing M, Kokabi N, Zhang D, et al. Comparative Effectiveness of Thermal Ablation, Surgical Resection, and Active Surveillance for T1a Renal Cell Carcinoma: A Surveillance, Epidemiology, and End Results (SEER)-Medicare-linked Population Study. Radiology. Jul 2018; 288(1): 81-90. PMID 29737950

61. Thomson KR, Cheung W, Ellis SJ, et al. Investigation of the safety of irreversible electroporation in humans. J Vasc Interv Radiol. May 2011; 22(5): 611-21. PMID 21439847

62. Pech M, Janitzky A, Wendler JJ, et al. Irreversible electroporation of renal cell carcinoma: a first-in-man phase I clinical study. Cardiovasc Intervent Radiol. Feb 2011; 34(1): 132-8. PMID 20711837

63. Diehl SJ, Rathmann N, Kostrzewa M, et al. Irreversible Electroporation for Surgical Renal Masses in Solitary Kidneys: Short-Term Interventional and Functional Outcome. J Vasc Interv Radiol. Sep 2016; 27(9): 1407-1413. PMID 27292599

64. Vroomen LGPH, Scheffer HJ, Melenhorst MCAM, et al. Irreversible Electroporation to Treat Malignant Tumor Recurrences Within the Pelvic Cavity: A Case Series. Cardiovasc Intervent Radiol. Oct 2017; 40(10): 1631-1640. PMID 28470395

65. Liu B, Clark J, Domes T, et al. Percutaneous irreversible electroporation for the treatment of small renal masses: The first Canadian case series. Can Urol Assoc J. Sep 2019; 13(9): E263-E267. PMID 30763229

66. Wendler JJ, Pech M, Fischbach F, et al. Initial Assessment of the Efficacy of Irreversible Electroporation in the Focal Treatment of Localized Renal Cell Carcinoma With Delayed-interval Kidney Tumor Resection (Irreversible Electroporation of Kidney Tumors Before Partial Nephrectomy [IRENE] Trial-An Ablate-and-Resect Pilot Study). Urology. Apr 2018; 114: 224-232. PMID 29305201

67. Wendler JJ, Pech M, Köllermann J, et al. Upper-Urinary-Tract Effects After Irreversible Electroporation (IRE) of Human Localised Renal-Cell Carcinoma (RCC) in the IRENE Pilot Phase 2a Ablate-and-Resect Study. Cardiovasc Intervent Radiol. Mar 2018; 41(3): 466-476. PMID 28929209

68. National Comprehensive Cancer Network (NCCN). NCCN Clinical Practice Guidelines in Oncology: Non-Small Cell Lung Cancer. Version 7.2024. **https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf**. Accessed November 11, 2024

69. Centers for Disease Control and Prevention. Lung Cancer Risk Factors. **https://www.cdc.gov/lung-cancer/risk-factors/index.html**. Accessed November 11, 2024.

70. Ricke J, Jürgens JH, Deschamps F, et al. Irreversible electroporation (IRE) fails to demonstrate efficacy in a prospective multicenter phase II trial on lung malignancies: the ALICE trial. Cardiovasc Intervent Radiol. Apr 2015; 38(2): 401-8. PMID 25609208

71. National Institute for Health and Care Excellence (NICE). Irreversible electroporation for treating pancreatic cancer: Interventional procedures guidance [IPG579]. 2017. **https://www.nice.org.uk/guidance/ipg579**. Accessed November 11, 2024.

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.