02-40000-26

Original Effective Date: 02/15/16

Reviewed: 05/22/25

Revised: 06/15/25

Subject: Irreversible Electroporation (IRE)

THIS MEDICAL COVERAGE GUIDELINE IS NOT AN AUTHORIZATION, CERTIFICATION, EXPLANATION OF BENEFITS, OR A GUARANTEE OF PAYMENT, NOR DOES IT SUBSTITUTE FOR OR CONSTITUTE MEDICAL ADVICE. ALL MEDICAL DECISIONS ARE SOLELY THE RESPONSIBILITY OF THE PATIENT AND PHYSICIAN. BENEFITS ARE DETERMINED BY THE GROUP CONTRACT, MEMBER BENEFIT BOOKLET, AND/OR INDIVIDUAL SUBSCRIBER CERTIFICATE IN EFFECT AT THE TIME SERVICES WERE RENDERED. THIS MEDICAL COVERAGE GUIDELINE APPLIES TO ALL LINES OF BUSINESS UNLESS OTHERWISE NOTED IN THE PROGRAM EXCEPTIONS SECTION.

DESCRIPTION:

Irreversible electroporation (IRE) describes a process that uses application of brief, controlled, high-voltage direct current impulses to create multiple holes in cell membranes. This process irreversibly damages the cell's homeostasis mechanism, leading to instant cell death. IRE is most frequently performed in the liver, kidney, lung, prostate, and pancreas, and is also being used to treat metastatic disease in the liver.

The Nanoknife® Oncobionic System is a low-energy direct current thermal ablation system, which received initial Food and Drug Administration (FDA) 510K clearance in 2006, as a tissue ablation system indicated for surgical ablation of soft tissue, including cardiac and smooth muscle. Subsequent FDA clearance clarified the approved indications to "the surgical ablation of soft tissue". It has not received clearance for the therapy or treatment of any specific disease or condition.

Summary and Analysis of Evidence

George et al (2024) conducted an analysis to evaluate the safety and effectiveness of the NanoKnife System to ablate prostate tissue in patients with intermediate-risk prostate cancer (PCa) [PRESERVE study (NCT04972097)]. At the time of analysis, the trial had completed accrual with preliminary follow-up available. The median (IQR) age at screening was 67.0 (61.0–72.0) years and Gleason distribution 3 + 4 (80.2%) and 4 + 3 (19.8%). At 6 months, all patients with available data (n = 74) experienced a median (IQR) percent reduction in PSA of 67.6% (52.3–82.2%). Only ten subjects (8.3%) experienced a Grade 3 adverse event; five were procedure-related. No Grade ≥ 4 adverse events (AEs) were reported. The authors stated, "this study supports prior findings that IRE prostate ablation with the NanoKnife System can be performed safely. Final results are required to fully assess oncological, functional, and safety outcomes." The authors also acknowledged several study limitations, stating "first, AE data are reported before all patients have achieved 12 months of follow-up. It is possible that patients could experience

additional AEs; however, it is anticipated that many AEs, especially severe ones, and any related to treatment, would occur in the peri-operative period included in this analysis. Given that almost 90% of subjects completed their 3-month visit and delayed AEs are unlikely, conclusions regarding the safety of the procedure are unlikely to change. Second, as a single-arm trial, there is no randomized comparator and all patients received the treatment under study, and therefore only outcomes related to IRE were observed. Additionally, there was no central imaging or pathology review. Imaging and pathology interpretation are inherently subjective and there exists known variability. However, the current study represents real-world practice, as even interpretation among providers within a single clinical site can vary. Lastly, while this study included patients with intermediate-risk PCa, there is heterogeneity even within this subgroup. For example, intermediate risk could further be subdivided into favorable and unfavorable risk based on stage and/or Gleason score. A majority of subjects in this study had stage T1c PCa and a Gleason of 3 + 4, which may have limited the generalizability of the results to men with intermediate-risk PCa of other severities." Geboers et al (2024) prospectively compared systemic anti-tumour immune responses induced by irreversible electroporation (IRE) and robot-assisted radical prostatectomy (RARP) in patients with localised intermediate-risk prostate cancer (PCa). Between February 2021 and June 2022, before and after treatment (at 5, 14 and 30 days) peripheral blood samples of 30 patients with localised PCa were prospectively collected. Patient inclusion criteria were: International Society of Urological Pathologists Grade 2–3, clinical cancer stage ≤T2c, prostate-specific antigen level <20 ng/mL. Patients were treated with IRE (n = 20) or RARP (n = 10). Frequency and activation status of lymphocytic and myeloid immune cell subsets were determined using flow cytometry. PCa-specific T-cell responses to prostatic acid phosphatase (PSAP) and cancer testis antigen (New York oesophageal squamous cell carcinoma 1 [NY-ESO-1]) were determined by interferon-γ enzyme-linked immunospot assay (ELISpot). Repeated-measures analysis of variance and two-sided Student's t-tests were used to compare immune responses over time and between treatment cohorts. Patient and tumour characteristics were similar between the cohorts except for age (median 68 years [IRE] and 62 years [RARP]). IRE induced depletion of systemic regulatory T cells and a simultaneous increase in activated cytotoxic T-lymphocyte antigen 4 (CTLA-4)+ cluster of differentiation (CD)4+ ($P < 0.001$) and CD8+ ($P = 0.032$) T cells, consistent with reduction of systemic immune suppression allowing for effector T-cell activation, peaking 14 days after IRE. Effects were positively correlated with tumour volume/ablation size. Accordingly, IRE induced expansion of PSAP and/or NY-ESO-1 specific T-cell responses in four of the eight immune competent patients. The authors concluded, "irreversible electroporation induces a PCa-specific systemic immune response in patients with localised PCa, aiding conversion of the tumour microenvironment into a more immune permissive state. Therapeutic efficacy might be further enhanced by combination with CTLA-4 checkpoint inhibition, potentially opening up a new synergistic treatment paradigm for high-risk localised or (oligo)metastatic disease." Author acknowledged study limiltations included the relatively short follow-up time, restricting the number of events and the feasibility to associate immune parameters with long-term oncological outcome measures; and that tissue biopsies could have provided additional information about immune cell infiltration in the TME.

UpToDate review, "Nonsurgical local treatment strategies for colorectal cancer liver metastases" (Venook, Fidelman; 2025) states, "a systematic review included eight studies (five prospective phase II studies and three retrospective case cohorts) that included 162 patients with 283 CRC liver metastases <3 cm in size treated with IRE. Procedures were performed under general anesthesia with cardiac cycle synchronization and with the use of either CT or ultrasound for lesion localization. Probe spacing was

less than 3.2 cm for all ablations. Nonfatal cardiac arrhythmia occurred in nine (5.6 percent) patients. Six bile leaks and one late biliary stricture were reported. There were two procedure-related deaths. Procedure-related hemorrhage occurred in seven patients, with one patient requiring laparotomy to control bleeding. There were no reports of procedure-related liver failure. Local control lasted between zero months for patients with residual disease after IRE to up to 10 months. Progression-free survival ranged from 4 to 12 months. OS at 24 months was 61 to 62 percent for two of the studies and a third study reported a median OS of 2.7 years." Meijerink et al (2021) investigated the efficacy and safety of IRE for colorectal liver metastases (CRLMs) unsuitable for resection or thermal ablation because of proximity to critical structures and for further systemically administered treatments. A total of 51 participants (median age, 67 years [interquartile range, 62-75 years]; 37 men) underwent IRE. Of these 51 participants, 50 with a total of 76 CRLMs (median tumor size, 2.2 cm; range, 0.5-5.4 cm) were successfully treated in 62 procedures; in one participant, treatment was stopped prematurely because of pulse-induced cardiac arrhythmia. With a per-participant 1-year LTP-free survival of 68% (95% CI: 59, 84) according to competing risk analysis, the primary end point was met. Local control following repeat procedures was achieved in 74% of participants (37 of 50). Median overall survival from first IRE was 2.7 years (95% CI: 1.6, 3.8). The authors concluded that IRE was effective and relatively safe for colorectal liver metastases 5.0 cm or smaller that were unsuitable for partial hepatectomy, thermal ablation, or further systemic treatment. The reported results were limited by the lack of control group and blinding, as well as the use of concurrent procedures with IRE. In addition, the predefined threshold in the sample size calculation was chosen arbitrarily.

Seal et al (2025) evaluated the evidence for the use of IRE for treatment of pancreatic cancer and concluded "although the use of IRE opens up an interesting frontier in treating cases of locally advanced PanCa, further large-scale studies with appropriate controls and randomized control trials are needed before it can be adopted outside of research purposes. Prospective studies with significant sample sizes (we could not find any study with a sample size more than 10) are lacking for stage IV (metastatic) PanCa being treated with IRE. Therefore, evidence regarding improvement in overall survival in these patients is not available. Radiofrequency ablation remains the preferred ablation method for liver metastasis due to its relative safety and similar efficacy compared to IRE, except when metastasis is in close proximity to large vessels or bile ducts." Yang et al (2020) conducted a prospective trial for using IRE through surgical approaches for locally advanced pancreatic cancer (LAPC) in 11 medical centres in Asia, from 2012 to 2017. All related and treatment outcomes were analysed from a prospective database. 74 patients were enrolled. Thirty complications occurred in thirteen (17.6%) patients without mortality. The progression-free survival (PFS) rate at one year, three years, and five years were 69.1%, 48.7%, and 28.8%, and the overall survival (OS) rate at one year, three years, and five years were 97.2%, 53%, and 31.2%. The authors concluded that the study showed that combined induction chemotherapy and surgical IRE for LAPC is safe. For well-selected patients, IRE can achieve encouraging survival outcomes. However, the complication rate of 17.6% was not insignificant. Entry into this trial was limited to individuals who had responded to initial induction chemotherapy. Results may not apply to other individuals. Further prospective, randomized trials are warranted to fully understand the risks and benefits of IRE.

UpToDate review, "Localized hepatocellular carcinoma: Liver-directed therapies for nonsurgical candidates eligible for local ablation" (Curley et al, 2025) states. "where available, irreversible electroporation (IRE) represents a nonthermal ablation method that may be preferred over thermal

ablation techniques for lesions in a "risky" location, such as adjacent to blood vessels. However, in our view, further studies with more patients and longer follow-up durations are needed to assess the long-term efficacy of this ablation method before it can be applied with the same confidence as RFA or MWA. Few data are available for treatment of HCC; most series that describe IRE treatment for liver tumors include both primary liver tumors (HCC, cholangiocarcinoma) and hepatic metastases, and most suffer from limited numbers of HCC patients and short follow-up. The best data for HCC come from a retrospective single-center case series of 75 tumors treated with IRE in 58 patients. Patients were largely deemed poor candidates for other ablation procedures because of tumor location or poor general condition. Overall, 58 (77 percent), 67 (89 percent), and 69 (92 percent) of the 75 treated tumors were completely ablated after one, two, or three IRE procedures, respectively. At a median follow-up of nine months, the 6- and 12-month local progression-free survival rates were 87 and 70 percent, respectively. Complications occurred in 11 patients and included three patients with liver failure in the setting of Child-Turcotte-Pugh class B cirrhosis; one died." Verloh et al (2019) compared the frequency of adverse events of thermal microwave (MWA) and radiofrequency ablation (RFA) with non-thermal irreversible electroporation (IRE) in percutaneous ablation of hepatocellular carcinoma (HCC). 117 MWA/RFA and 47 IRE procedures (one tumor treated per procedure; 144 men and 20 women; median age, 66 years) were analyzed regarding adverse events, duration of hospital and intensive care unit (ICU) stays and occurrence of a post-ablation syndrome. 70.1% of the RFA/MWA and 63.8% of the IRE procedures were performed without complications. Shortcomings of this study included the retrospective nature, lack of randomization, and lack of blinding.

UpToDate review, "Image-guided ablation of lung tumors" (Dupuy, 2025) states, "irreversible electroporation (IRE) is a novel ablation technology being investigated for the treatment of solid malignancies. It utilizes direct electrical pulses to create nanoscale defects or pores in cell membranes; these defects disrupt cellular homeostasis leading to apoptotic cell death. Electroporation can either be reversible or irreversible, the latter leading to cell death. There is one IRE system approved for use in the United States. The system utilizes monopolar electrodes with a retractable sheath, which allows the active tip to be adjusted between 1 and 4 cm. The generator allows for the simultaneous use of up to six electrodes with a maximum delivery of 50 A and 3000 V. Since IRE is a non-thermal ablation technique, its purported benefits include overcoming the heat sink effect and the ability to treat near bronchovascular structures without causing structural injury. Theoretically, IRE would be a well-suited ablation modality for lung lesions close to the chest wall, hilum, and mediastinum due to the low potential for collateral structural damage. To date, there have been few published clinical studies evaluating electroporation of lung tissue in humans. One study was a prospective trial across two academic centers named the ALICE trial. This trial was stopped prematurely due to failing to meet expected efficacy at interim analysis based on high recurrence rates in 61 percent within one year of treatment."

POSITION STATEMENT:

Irreversible electroporation (IRE), including the use of the NanoKnife® system, is considered **experimental or investigational** for all indications, including, but not limited to, ablation of soft tissue or of solid organs, such as the liver, pancreas, and prostate.

There is insufficient clinical peer reviewed literature demonstrating the safety, efficacy, and the effects of irreversible electroporation (IRE), on long-term health outcomes.

BILLING/CODING INFORMATION:

CPT Coding

0600T	Ablation, irreversible electroporation; 1 or more tumors per organ, including imaging guidance, when performed, percutaneous **(Investigational)**
0601T	Ablation, irreversible electroporation; 1 or more tumors per organ, including fluoroscopic and ultrasound guidance, when performed, open **(Investigational)**

REIMBURSEMENT INFORMATION:

Refer to section entitled **POSITION STATEMENT**.

PROGRAM EXCEPTIONS:

Federal Employee Program (FEP): Follow FEP guidelines.

State Account Organization (SAO): Follow SAO guidelines.

Medicare Advantage products: No National Coverage Determination (NCD) and/or Local Coverage Determination (LCD) were found at the time of the last guideline review date.

If this Medical Coverage Guideline contains a step therapy requirement, in compliance with Florida law 627.42393, members or providers may request a step therapy protocol exemption to this requirement if based on medical necessity. The process for requesting a protocol exemption can be found at Coverage Protocol Exemption Request

DEFINITIONS:

Electroporation: a cell is subjected to a powerful electrical field using high-voltage direct current (up to 3 kV); this creates multiple holes in the cell membrane and irreversibly damages the cell's homeostasis mechanism, leading to instant cell death.

RELATED GUIDELINES:

Radiofrequency and Microwave Ablation of Liver Tumors, 02-40000-23

Radiofrequency Ablation of Solid Tumors Other Than Liver Tumors, 02-99221-13

OTHER:

Index terms:

Note: The use of specific product names is illustrative only. It is not intended to be a recommendation of one product over another, and is not intended to represent a complete listing of all products available.

IRE
NanoKnife®
Oncobionic System
Soft tissue ablation

REFERENCES:

1. Akinwande O, Ahmad SS, Van Meter T, Schulz B, Martin RC. CT Findings of Patients Treated with Irreversible Electroporation for Locally Advanced Pancreatic Cancer. J Oncol. 2015;2015:680319.
2. Blue Cross Blue Shield Association Evidence Positioning System®. 6.01.68 - Irreversible Electroporation of Tumors Located in the Liver, Pancreas, Kidney, or Lung, 12/24.
3. Chen X, et al. Electric Ablation with Irreversible Electroporation (IRE) in Vital Hepatic Structures and Follow-up Investigation. Sci Rep. 2015 Nov 9;5:16233.
4. Centers for Medicare and Medicaid (CMS). Local Coverage Article: Billing and Coding: Noncovered Services (A57743) (10/03/18) (revised 02/20/20).
5. Centers for Medicare and Medicaid (CMS). Local Coverage Determination (LCD): Noncovered Services (L33777) (Retired 07/01/20).
6. Chan G, Pua U. Irreversible Electroporation of the Pancreas. Semin Intervent Radiol. 2019;36(3):213–220. doi:10.1055/s-0039-1693980. PMID: 31435129.
7. ClinicalTrials.gov. NCT01442324: Pilot Study of Irreversible Electroporation (IRE) to Treat Metastatic Liver Cancer & Cholangiocarcinoma. Azienda Ospedaliera di Padova (July 2012).
8. ClinicalTrials.gov. NCT01078415: Pilot Study of Irreversible Electroporation (IRE) to Treat Early-Stage Primary Liver Cancer (HCC). Angiodynamics, Inc. (September 2011).
9. ClinicalTrials.gov. NCT02335827: Irreversible Electroporation (IRE) For Unresectable Renal Tumors (IRE). Fuda Cancer Hospital, Guangzhou. (March 2016)
10. ClinicalTrials.gov. NCT02425059: Irreversible Electroporation (IRE) For Unresectable Rectal Neoplasms. Fuda Cancer Hospital, Guangzhou. (March 2016).
11. Cribbs KA, Manning EF, Zhou J, Lahue BJ, Polascik TJ. Real-World Comparative Safety and Effectiveness of Irreversible Electroporation and High-Intensity Focused Ultrasound for Prostate Cancer Ablation. Urology. 2023 Apr;174:7-17. doi: 10.1016/j.urology.2023.01.024. Epub 2023 Feb 2.
12. Fang C, Kibriya N, et al. Safety and efficacy of irreversible electroporation treatment in hepatobiliary and pancreatic tumours: a single-centre experience. Clin Radiol. 2021 Aug;76(8):599-606. doi: 10.1016/j.crad.2021.03.020. Epub 2021 Apr 29.
13. First Coast Service Options, Inc. (FCSO). Local Coverage Determination (LCD) L33777, Noncovered Services. 10/01/15. Revised 01/01/19.
14. Frühling P, Nilsson A, Duraj F, Haglund U, Norén A. 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. 2017 Apr;43(4):751-757. doi: 10.1016/j.ejso.2016.12.004. Epub 2017 Jan 11.
15. Gajewska-Naryniecka A, Szwedowicz U, Łapińska Z, Rudno-Rudzińska J, Kielan W, Kulbacka J. Irreversible Electroporation in Pancreatic Cancer-An Evolving Experimental and Clinical Method. Int J Mol Sci. 2023 Feb 23;24(5):4381. doi: 10.3390/ijms24054381.
16. Geboers B, Scheltema MJ, Jung J, Bakker J, Timmer FEF, Cerutti X, Katelaris A, Doan P, Gondoputro W, Blazevski A, Agrawal S, Matthews J, Haynes AM, Robertson T, Thompson JE, Meijerink MR, Clark SJ, de Gruijl TD, Stricker PD. Irreversible electroporation of localised prostate cancer downregulates immune suppression and induces systemic anti-tumour T-cell activation - IRE-IMMUNO study. BJU Int. 2025 Feb;135(2):319-328. doi: 10.1111/bju.16496. Epub 2024 Aug 5.
17. George AK, Miocinovic R, Patel AR, Lomas DJ, Correa AF, Chen DYT, Rastinehad AR, Schwartz MJ, Uchio EM, Sidana A, Helfand BT, Gahan JC, Yu A, Vourganti S, Barqawi AB, Brisbane WG, Wysock JS, Polascik TJ, McClure TD, Coleman JA. A Description and Safety Overview of Irreversible

Electroporation for Prostate Tissue Ablation in Intermediate-Risk Prostate Cancer Patients: Preliminary Results from the PRESERVE Trial. Cancers (Basel). 2024 Jun 8;16(12):2178. doi: 10.3390/cancers16122178.

18. Guenther E, Klein N, Zapf S, et al. Prostate cancer treatment with Irreversible Electroporation (IRE): Safety, efficacy and clinical experience in 471 treatments. PLoS One. 2019;14(4):e0215093. Published 2019 Apr 15. doi:10.1371/journal.pone.0215093.
19. Guo X, Du F, et al. Immunological effect of irreversible electroporation on hepatocellular carcinoma. BMC Cancer. 2021 Apr 21;21(1):443. doi: 10.1186/s12885-021-08176-x.
20. Gupta P, Maralakunte M, et al. Efficacy and safety of irreversible electroporation for malignant liver tumors: a systematic review and meta-analysis. Eur Radiol. 2021 Sep;31(9):6511-6521. doi: 10.1007/s00330-021-07742-y. Epub 2021 Feb 27.
21. Hamdy FC, Donovan JL, Lane JA, Metcalfe C, Davis M, Turner EL, Martin RM, Young GJ, Walsh EI, Bryant RJ, Bollina P, Doble A, Doherty A, Gillatt D, Gnanapragasam V, Hughes O, Kockelbergh R, Kynaston H, Paul A, Paez E, Powell P, Rosario DJ, Rowe E, Mason M, Catto JWF, Peters TJ, Oxley J, Williams NJ, Staffurth J, Neal DE; ProtecT Study Group. Fifteen-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Prostate Cancer. N Engl J Med. 2023 Apr 27;388(17):1547-1558. doi: 10.1056/NEJMoa2214122. Epub 2023 Mar 11.
22. Jarm T, Krmac T, et al. Investigation of safety for electrochemotherapy and irreversible electroporation ablation therapies in patients with cardiac pacemakers. Biomed Eng Online. 2020 Nov 16;19(1):85. doi: 10.1186/s12938-020-00827-7.
23. Jiang T, Zhao Q, Tian G, Chen X, Wu L. Irreversible electroporation ablation of end-stage metastatic retroperitoneal lesions: Report on three cases and literature review. Exp Ther Med. 2019;18(3):2243–2249. doi:10.3892/etm.2019.7780.
24. Labarbera N. Uncertainty Quantification in Irreversible Electroporation Simulations. Bioengineering (Basel). 2017 May 6;4(2). pii: E41. doi: 10.3390/bioengineering4020041.
25. Lee EW, Thai S, Kee ST. Irreversible electroporation: a novel image-guided cancer therapy. Gut Liver. 2010 Sep;4 Suppl 1(Suppl 1):S99-S104. doi: 10.5009/gnl.2010.4.S1.S99. Epub 2010 Sep 10.
26. Liu X, Wang H, Zhao Z, Zhong Q, Wang X, Liu X, Chen J, Han C, Shi Z, Liang Q. Advances in irreversible electroporation for prostate cancer. Discov Oncol. 2024 Nov 26;15(1):713. doi: 10.1007/s12672-024-01570-4.
27. Lyu T, Wang X, et al. Irreversible electroporation in primary and metastatic hepatic malignancies: A review. Medicine (Baltimore). 2017 Apr;96(17):e6386. doi: 10.1097/MD.0000000000006386.
28. Meijerink MR, Ruarus AH, et al. Irreversible Electroporation to Treat Unresectable Colorectal Liver Metastases (COLDFIRE-2): A Phase II, Two-Center, Single-Arm Clinical Trial. Radiology. 2021 May;299(2):470-480. doi: 10.1148/radiol.2021203089. Epub 2021 Mar 16.
29. Narayanan G. Irreversible Electroporation for Treatment of Liver Cancer. Gastroenterol Hepatol (N Y). 2011 May; 7(5): 313–316.
30. Narayanan G, Gentile NT, Eyshi J, Schiro BJ, Gandhi RT, Peña CS, Ucar A, Aparo S, de Zarraga FI, Joseph SN, Asbun HJ, Dijkstra M. Irreversible Electroporation in Treating Colorectal Liver Metastases in Proximity to Critical Structures. J Vasc Interv Radiol. 2024 Dec;35(12):1806-1813. doi: 10.1016/j.jvir.2024.08.021. Epub 2024 Aug 30.
31. National Institute for Health and Care Excellence (NICE). Interventional procedure guidance 441: Irreversible electroporation for treating primary lung cancer and metastases in the lung (June 2015). Accessed at http://www.nice.org.uk/.

32. National Institute for Health and Care Excellence (NICE). Interventional procedure guidance 442: Irreversible electroporation for treating pancreatic cancer (June 2015). Accessed at http://www.nice.org.uk/.
33. National Institute for Health and Care Excellence (NICE). Interventional procedure guidance 443: Irreversible electroporation for treating renal cancer (June 2015). Accessed at http://www.nice.org.uk/.
34. National Institute for Health and Care Excellence (NICE). Interventional procedure guidance 444: Irreversible electroporation for treating primary liver cancer (June 2015). Accessed at http://www.nice.org.uk/.
35. National Institute for Health and Care Excellence (NICE). Interventional procedure guidance 445: Irreversible electroporation for treating liver metastases (June 2015). Accessed at http://www.nice.org.uk/.
36. National Institute for Health and Care Excellence (NICE). Interventional procedure guidance 572: Irreversible electroporation for treating prostate cancer (December 2016). Accessed at http://www.nice.org.uk/.
37. National Institute for Health and Care Excellence (NICE). Interventional procedure guidance 579: Irreversible electroporation for treating pancreatic cancer (May 2017). Accessed at http://www.nice.org.uk/.
38. National Institute for Health and Care Excellence (NICE). Interventional procedure guidance 664: Irreversible electroporation for primary liver cancer (November 2019). Accessed at http://www.nice.org.uk/.
39. Orcutt S, Kis B, Malafa M. Case report: Irreversible electroporation for locally advanced pancreatic cancer. Int J Surg Case Rep. 2017;40:54-57.
40. Qin Z, et al. Irreversible Electroporation Ablation of an Unresectable Fibrous Sarcoma With 2 Electrodes: A Case Report. Technol Cancer Res Treat. 2017 Jan 1:1533034617711530.
41. Rombouts SJ, et al. Irreversible Electroporation of the Pancreas Using Parallel Plate Electrodes in a Porcine Model: A Feasibility Study. PLoS One. 2017 Jan 4;12(1):e0169396.
42. Salati U, et al. State of the ablation nation: a review of ablative therapies for cure in the treatment of hepatocellular carcinoma. Future Oncol. 2017 Jul;13(16):1437-1448.
43. Scheffer HJ, et al. Colorectal liver metastatic disease: efficacy of irreversible electroporation-a single-arm phase II clinical trial (COLDFIRE-2 trial). BMC Cancer. 2015 Oct 24;15:772.
44. Scheltema MJ, Geboers B, Blazevski A, Doan P, Katelaris A, Agrawal S, Barreto D, Shnier R, Delprado W, Thompson JE, Stricker PD. Median 5-year outcomes of primary focal irreversible electroporation for localised prostate cancer. BJU Int. 2023 Jun;131 Suppl 4:6-13. doi: 10.1111/bju.15946. Epub 2022 Dec 28. PMID: 36495481.
45. Seal R, Bararia A, Chattopadhyay BK, Sikdar N. Irreversible electroporation for metastatic pancreatic carcinoma with liver metastasis: What does the evidence say. World J Clin Cases. 2025 Jan 26;13(3):98452. doi: 10.12998/wjcc.v13.i3.98452.
46. Sivaraman A, Barret E. Focal Therapy for Prostate Cancer: An "À la Carte" Approach. Eur Urol. 2016 Jun;69(6):973-5. doi: 10.1016/j.eururo.2015.12.015. Epub 2016 Jan 6. PMID: 26778462.
47. Spiliopoulos S, Reppas L, Filippiadis D, Delvecchio A, Conticchio M, Memeo R, Inchingolo R. Irreversible electroporation for the management of pancreatic cancer: Current data and future directions. World J Gastroenterol. 2023 Jan 14;29(2):223-231. doi: 10.3748/wjg.v29.i2.223.
48. Sugimoto K, Abe M, et al. Irreversible electroporation of hepatocellular carcinoma: the role of ultrasonography. Ultrasonography. 2020 Jul;39(3):229-237. doi: 10.14366/usg.20023. Epub 2020 Apr 2.

49. Tameez Ud Din A, Tameez-Ud-Din A, Chaudhary FMD, Chaudhary NA, Siddiqui KH. Irreversible Electroporation For Liver Tumors: A Review Of Literature. Cureus. 2019;11(6):e4994. Published 2019 Jun 25. doi:10.7759/cureus.4994.
50. Tasu JP, Vesselle G, et al. Irreversible electroporation for locally advanced pancreatic cancer. Diagn Interv Imaging. 2016 Dec;97(12):1297-1304. doi: 10.1016/j.diii.2016.10.001. Epub 2016 Nov 14.
51. Tasu JP, Tougeron D, Rols MP. Irreversible electroporation and electrochemotherapy in oncology: State of the art. Diagn Interv Imaging. 2022 Nov;103(11):499-509. doi: 10.1016/j.diii.2022.09.009. Epub 2022 Oct 17. PMID: 36266192.
52. Tian G, et al. Ablation of hepatic malignant tumors with irreversible electroporation: A systematic review and meta-analysis of outcomes. Oncotarget. 2016 Dec 20.
53. UpToDate. Image-guided ablation of lung tumors. 2025. Accessed at uptodate.com.
54. UpToDate. Localized hepatocellular carcinoma: Liver-directed therapies for nonsurgical candidates who are eligible for local ablation. 2025. Accessed at uptodate.com.
55. UpToDate. Nonsurgical local treatment strategies for colorectal cancer liver metastases. 2025. Accessed at uptodate.com.
56. UpToDate. Nonsurgical therapies for localized hepatocellular carcinoma: Radiofrequency ablation, laser and microwave thermal ablation, percutaneous injection therapies, cryoablation, high-intensity focused ultrasound, and irreversible electroporation. 2021. Accessed at uptodate.com.
57. UpToDate. Radiofrequency ablation, cryoablation, and other ablative techniques for renal cell carcinoma. 2025. Accessed at uptodate.com.
58. U.S. Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH). Oncobionic System with six probe output (Oncobionic, Inc., Rancho Santa Margarita, CA). Summary of Safety and Effectiveness. No. K080376. April 2, 2008. Accessed at http://www.accessdata.fda.gov/cdrh_docs/pdf8/K080376.pdf.
59. U.S. Food and Drug Administration (FDA) Center for Devices and Radiological Health (CDRH). The NanoKnife® System (AngioDynamics, Inc. Fremont, CA). Summary of Safety and Effectiveness. No. K102329. October 24, 2011. Accessed at http://www.accessdata.fda.gov/cdrh_docs/pdf10/K102329.pdf.
60. Verloh N, Jensch I, Lürken L, Haimerl M, Dollinger M, Renner P, Wiggermann P, Werner JM, Zeman F, Stroszczynski C, Beyer LP. Similar complication rates for irreversible electroporation and thermal ablation in patients with hepatocellular tumors. Radiol Oncol. 2019 Mar 3;53(1):116-122. doi: 10.2478/raon-2019-0011. Erratum in: Radiol Oncol. 2023 Mar 22;57(1):116-122.
61. Vos DJW, Ruarus AH, Timmer FEF, Geboers B, Bagla S, Belfiore G, Besselink MG, Leen E, Martin Ii RCG, Narayanan G, Nilsson A, Paiella S, Weintraub JL, Wiggermann P, Scheffer HJ, Meijerink MR. Consensus Guidelines of Irreversible Electroporation for Pancreatic Tumors: Protocol Standardization Using the Modified Delphi Technique. Semin Intervent Radiol. 2024 Jul 10;41(2):176-219. doi: 10.1055/s-0044-1787164.
62. Vroomen LGPH, Petre EN, et al. Irreversible electroporation and thermal ablation of tumors in the liver, lung, kidney and bone: What are the differences? Diagn Interv Imaging. 2017 Sep;98(9):609-617. doi: 10.1016/j.diii.2017.07.007. Epub 2017 Aug 30.
63. Wagstaff PG, Buijs M, van den Bos W, de Bruin DM, Zondervan PJ, de la Rosette JJ, Laguna Pes MP. Irreversible electroporation: state of the art. Onco Targets Ther. 2016 Apr 22;9:2437-46. doi: 10.2147/OTT.S88086.
64. Wagstaff PG, et al. The efficacy and safety of irreversible electroporation for the ablation of renal masses: a prospective, human, in-vivo study protocol. BMC Cancer. 2015 Mar 22;15:165.
65. Wang Z, Lu J, et al. A retrospective study of CT-guided percutaneous irreversible electroporation (IRE) ablation: clinical efficacy and safety. BMC Cancer. 2021 Feb 5;21(1):124. doi: 10.1186/s12885-021-07820-w.

66. Yang PC, Huang KW, Pua U, Kim MD, Li SP, Li XY, Liang PC. Prognostic factor analysis of irreversible electroporation for locally advanced pancreatic cancer - A multi-institutional clinical study in Asia. Eur J Surg Oncol. 2020 May;46(5):811-817. doi: 10.1016/j.ejso.2019.12.006. Epub 2019 Dec 10. PMID: 31839436.

67. Yao C, Lv Y, et al. Irreversible electroporation ablation area enhanced by synergistic high- and low-voltage pulses. PLoS One. 2017 Mar 2;12(3):e0173181. doi: 10.1371/journal.pone.0173181. eCollection 2017.

68. Zager Y, et al. Optimization of Irreversible Electroporation Protocols for In-vivo Myocardial Decellularization. PLoS One. 2016 Nov 28;11(11):e0165475.

69. Zeng J, Liu G, et al. The Safety and Efficacy of Irreversible Electroporation for Large Hepatocellular Carcinoma. Technol Cancer Res Treat. 2017 Feb;16(1):120-124.

70. Zhang N, Li Z, Han X, Zhu Z, Li Z, Zhao Y, Liu Z, Lv Y. Irreversible Electroporation: An Emerging Immunomodulatory Therapy on Solid Tumors. Front Immunol. 2022 Jan 7;12:811726. doi: 10.3389/fimmu.2021.811726.

71. Zhang K, Teoh J, Zhu G, Ng CF, Suberville M, Laguna P, de la Rosette J. Irreversible Electroporation for the Focal Treatment of Prostate Cancer: A Systematic Review. World J Mens Health. 2025 Apr;43(2):321-332. doi: 10.5534/wjmh.240012. Epub 2024 Jul 3.

72. Zhou L, Yin S, et al. Irreversible electroporation in patients with liver tumours: treated-area patterns with contrast-enhanced ultrasound. World J Surg Oncol. 2020 Nov 23;18(1):305. doi: 10.1186/s12957-020-02083-4.

73. Zimmerman A, Grand D, Charpentier KP. Irreversible electroporation of hepatocellular carcinoma: patient selection and perspectives. J Hepatocell Carcinoma. 2017 Mar 13;4:49-58.

COMMITTEE APPROVAL:

This Medical Coverage Guideline (MCG) was approved by the Florida Blue Medical Policy and Coverage Committee on 05/22/25.

GUIDELINE UPDATE INFORMATION:

02/15/16	New Medical Coverage Guideline.
03/15/17	Scheduled review. Maintained position statement. Updated references.
03/15/18	Scheduled review. Position statement maintained; updated references.
04/15/19	Scheduled review. Position statement maintained; updated references.
04/15/20	Scheduled review. Maintained position statement and updated references.
07/01/20	Quarterly CPT/HCPCS coding update. Added codes 0600T, 0601T.
01/01/21	Annual CPT/HCPCS coding update. Revised 0601T.
06/15/21	Scheduled review. Maintained position statement and updated references.
12/15/21	Revision. Updated references and maintained position statement.
06/15/23	Scheduled review. Maintained position statement and updated references.
06/15/24	Scheduled review. Revised description. Maintained position statement and updated references.
06/15/25	Scheduled review. Updated references, revised description and maintained position statement (added specific indication of prostate cancer).