

# Bölüm 27

## YENİ TEKNOLOJİLER IŞIĞINDA GİRİŞİMSEL ONKOLOJİK RADYOLOJİ

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### GİRİŞ

Son bir kaç dekatta tümör ablasyon yöntemleri kanser hastaları için ümit verici tedaviler olarak ortaya çıkmıştır. Bu tedaviler genellikle cerrahi rezeksiyonun mümkün olmadığı, kemoterapötiklerin etkisiz veya dirençli olduğu bölgelerdeki tümörleri tedavi etmek için kullanılmaktadır.

Girişimsel onkolojik radyolojide lokal bölgesel tedaviler ablatif ve intraarteriyel yönlendirmeli tedavilerden oluşur. Özellikle ablasyon teknolojisindeki gelişmeler ile daha büyük boyutlardaki tümörler daha güvenli bir şekilde ablate edilmektedir. Bu bölümde tedavi amacıyla kullanılan cihazların teknolojik olarak son ürünlerinden ve ürünlerin fizyolojik, mekanik, elektrik teknolojilerinden ve nano teknolojilerden söz edilecektir. Son olarak da bu tedavilerin sık görülen kanserlerdeki endikasyonlarından, uygulama şeklinden ve komplikasyonlarından bahsedilecektir.

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## SONUÇ

Girişimsel onkolojik radyoloji girişimsel tedavilerin en hızlı büyuen ve gelişen bölümünü oluşturmaktadır. Medikal onkologlar, cerrahi ve radyasyon onkologları dahil olmak üzere girişimsel radyologlar da tümör konseylerinde yer almaktı kanser hastalarının bakımına en iyi şekilde katkı sunmaktadır. Bu konseyler her hasta için kişiselleştirilmiş bakımı tedavi hakkında tartışma fırsatı sunmaktadır. Girişimsel radyoloğun hem işlemin teknik yönlerini bilmesi ve kanser tedavisi hakkında klinik bilgiye sahip olması hem de girişimsel onkolojik radyolojide kullanılan yeni teknolojilerden haberdar olması gerekmektedir.

Tüm teknolojik gelişmelere rağmen ablatif modalitelerdeki sınırlamalar ve dezavantajlar hekimler, mühendisler ve tasarımcıları işbirliği yapmaya zorlamaktadır. Güçlü yazılım programları ile ablasyon yapılacak tümörün gerçek geometride simülasyonunu yapılabilmelidir. Probların kullanımında daha fazla esneklik ve açlandırma sistemlerine ihtiyaç duyulmaktadır. Ablasyon tedavilerinin başarısı, donanım sistemleri, yazılım araçları, matematiksel modelleme ve ısının takibi vs gibi özelliklere dayandığından bu parametreler daha da iyileştirilmeli ve geliştirilmelidir.

## KAYNAKLAR

1. IMellal, A Oukaira, E Kengene. Thermal therapy modalities for cancer treatment: A review and future perspectives International Journal of Applied Science. 2017;4:2:14. Doi:10.21767/2394-9988.100064
2. Timothy Clark, Tarun Sabharwal. Interventional Radiology Techniques in Ablation-Springer-Verlag London. 2013.
3. Goldberg SN, Gazelle GS, Mueller PR. Thermal ablation therapy for focal malignancy: a unified approach to underlying principles, techniques, and diagnostic imaging guidance. AJR Am J Roentgenol. 2000;174:323–31. Doi: 10.2214/ajr.174.2.1740323.
4. LeVeen RF. Laser hyperthermia and radiofrequency ablation of hepatic lesions. Semin Interv Radiol. 1997;14:313–24. Doi: 10.2214/ajr.176.1.1760003.
5. Meijerink MR, van der Tol P, van Tilborg AA. Radiofrequency ablation of large size liver tumors using novel plan-parallel expandable bipolar electrodes: initial clinical experience. Eur J Radiol. 2011;77:167–71. Doi: 10.1016/j.ejrad.2009.06.025.
6. Daher S, Massarwa M, Ariel A. Benson . Current and Future Treatment of Hepatocellular Carcinoma: An Updated Comprehensive Review. J Clin Transl Hepatol. 2018;6: 69–78.doi: 10.14218/JCTH.2017.00031
7. Gelet A, Crouzet S, Rouviere O. High-Intensity Focused Ultrasound (HIFU) for Prostate Cancer. In: Bolla M and van Poppel H (eds) Management of Prostate Cancer: A Multidisciplinary Approach. Springer International Publishing. 2017; 251-72.

8. Lang BHH, Wu ALH. High Intensity Focused Ultrasound (HIFU) ablation of benign thyroid nodules – a systematic review. *J Ther Ultrasound*. 2017; 5: 11. Doi: 10.1186/s40349-017-0091-1.
9. Poissonnier L, Chapelon JY, Rouviere O, Curiel L, Bouvier R, et al. Control of prostate cancer by transrectal HIFU in 227 patients. *Eur Urol*. 2007;51:381-87.
10. Knavel EM, Brace CL. Tumor ablation: Common modalities and general practices. *Tech Vasc Interv Radiol*. 2013;16:192-200. Doi: 10.1053/j.tvir.2013.08.002.
11. Habash RW, Bansal R, Krewski D. Thermal therapy, Part III: ablation techniques. *Crit Rev Biomed Eng*. 2007;35:37-121.
12. Shi Y, Mao Y. Magnetic resonance thermometry-guided laser interstitial thermal therapy in neurosurgery, a promising tool for dural-based lesions? *World Neurosurgery*. 2017;98:836-838. Doi: 10.1016/j.wneu.2016.11.063.
13. Ansari MA, Erfanzadeh M, Mohajerani E. Mechanisms of Laser-Tissue Interaction: II. Tissue Thermal Properties. *J Lasers Med Sci*. 2013;4:99-106.
14. Schena E, Saccoccia P, Fong Y. Laser ablation for cancer: Past, present and future. *J Funct Biomater*. 2017;14; 8:19. Doi: 10.3390/jfb8020019.
15. Gassino R, Liu Y, Konstantaki M . A fiber optic probe for tumor laser ablation with integrated temperature measurement capability. *Journal of Lightwave Technology*. 2017;35:3447-3454.
16. Sung JY, Kim YS, Choi H, et al. Optimum first-line treatment technique for benign cystic thyroid nodules: ethanol ablation or radiofrequency ablation? *AJR Am J Roentgenol*. 2011; 196:210-4.
17. Goldberg SN, Grassi CJ, Cardella JF, et al. Image-guided tumor ablation: standardization of terminology and reporting criteria. *J Vasc Interv Radiol*. 2009;20:377-90.
18. Baust JG, Gage AA. The molecular basis of cryosurgery. *BJU Int*. 2005;95:1187-91.
19. Evonich 3rd RF, Nori DM, Haines DE. A randomized trial comparing effects of radiofrequency and cryoablation on the structural integrity of esophageal tissue. *J Interv Card Electrophysiol*. 2007;19:77-83.
20. Ablin RJ, Soanes WA, Gonder MJ. Elution of in vivo bound antiprostatic epithelial antibodies following multiple cryotherapy of carcinoma of prostate. *Urology*. 1973;2:276-9.
21. Den Brok MH, Sutmuller RP, Nierkens S, et al. Efficient loading of dendritic cells following cryo and radiofrequency ablation in combination with immune modulation induces anti-tumour immunity. *Br J Cancer*. 2006;95:896-905.
22. Chapman WC, Debelak JP, Blackwell TS, et al. Hepatic cryoablation-induced acute lung injury: pulmonary hemodynamic and permeability effects in a sheep model. *Arch Surg*. 2000;135:667-72.
23. Washington K, Debelak JP, Gobbell C, et al. Hepatic cryoablation-induced acute lung injury: histopathologic findings. *J Surg Res*. 2001;95:1-7. Doi.org/10.1006/jsre.2000.5976.
24. Seifert JK, Stewart GJ, Hewitt PM, Bolton EJ, Junginger T, Morris DL. Interleukin-6 and tumor necrosis factor-alpha levels following hepatic cryotherapy: association with volume and duration of freezing. *World J Surg*. 1999;23:1019-26.
25. Hruby G, Edelstein A, Karpf J, et al. Risk factors associated with renal parenchymal fracture during laparoscopic cryoablation. *BJU Int*. 2008;102:723-6. doi: 10.1111/j.1464-410X.2008.07735.x.
26. Lubner MG, Brace CL, Hinshaw JL, Lee Jr FT. Microwave tumor ablation: mechanism of action, clinical results, and devices. *J Vasc Interv Radiol*. 2010;21:192-203.

27. Brace CL. Radiofrequency and microwave ablation of the liver, lung, kidney, and bone: what are the differences? *Curr Probl Diagn Radiol.* 2009b;38:135–43. Doi: 10.1067/j.cpradiol.2007.10.001.
28. S.Young, M.Rivard, R.KimyonT. et al. Accuracy of liver ablation zone prediction in a single 2450 MHz 100 Watt generator model microwave ablation system: An in human study.*Diagnostic and Interventional Imaging.* 2020;101:225-33. Doi.org/10.1016/j.diii.2019.10.007.
29. Jourabchi N, Beroukhim K, Tafti BA et al. Irreversible electroporation (nanoknife) in cancer treatment. *Gastrointest Interv.* 2014;3:8-18. Doi:10.1016/j.gii.2014.02.002.
30. Savic LJ, Chapiro J, Hamm B at al. Irreversible electroporation in interventional oncology: where we stand and where we go. *Rofo.* 2016;188:735-45. Doi:10.1055/s0042-104203.
31. Thomson KR, Cheung W, Ellis SJ, et al. Investigation of the safety of irreversible electroporation in humans. *J Vasc Interv Radiol.* 2011;22:611-21. Doi:10.1016/j.jvir.2010.12.014.
32. Li D, Kang J, Golas BJ, Yeung VW, Madoff DC. Minimally invasive local therapies for liver cancer. *Cancer Biol Med* 2014; 11:217-36. Doi:10.7497/j.issn.2095-3941.2014.04.001.
33. Dollinger M, Jung EM, Beyer L, et al. Irreversible electroporation ablation of malignant hepatic tumors: subacute and follow-up ct appearance of ablation zones. *J Vasc Interv Radiol.* 2014;25: 1589-94. Doi:10.1016/j.jvir.2014.06. 026.
34. Bart Geboers , Hester J. Scheffer, Philip M. Graybill at al. High-Voltage Electrical Pulses in Oncology: Irreversible Electroporation, Electrochemotherapy, Gene Electrotransfer, Electrifusion, and Electroimmunotherapy. *Radiology.* 2020;295: 254-272. Doi.org/10.1148/radiol.2020192190.
35. Stephen T.KeeEdward W.Lee Irreversible electroporation (NanoKnife) in cancer treatment. *Gastrointestinal Intervention.* 2014;3:8-18. Doi.org/10.1016/j.gii.2014.02.002.
36. Govindarajan Narayanan. Irreversible Electroporation. *Semin Intervent Radiol.* 2015;32:349–55. Doi.org/10.3389/fonc.2020.01235.
37. Rebecca M. Brock, Natalie Beitel-White, Rafael V. Davalos et al. Starting a Fire Without Flame: The Induction of Cell Death and Inflammation in Electroporation-Based Tumor Ablation Strategies. *Front. Oncol.* 2020;10:1-9. Doi.org/10.3389/fonc.2020.01235.
38. Hofmann F, Ohnimus H, Scheller C et al. Electric field pulses can induce apoptosis. *J Memb Biol.* 1999;169:103–9. Doi: 10.1007/s002329900522.
39. Golstein P, Kroemer G. Cell death by necrosis: towards a molecular definition. *Trends Biomed Sci.*2007;32:37–43. Doi: 10.1016/j.tibs.2006.11.001.
40. Sahay A, Sahay N, Kapoor A et al. A. Percutaneous image-guided radiofrequency ablation of tumors in inoperable patients - immediate complications and overall safety. *Indian J Palliat Care.* 2016; 22:67–73. Doi: 10.4103/0973-1075.173951.
41. Jacobson LS, Lima H, Goldberg MF et al. Cathepsin-mediated necrosis controls the adaptive immune response by Th2 (T helper type 2)-associated adjuvants. *J Biol Chem.* 2013; 288:7481–91. Doi: 10.1074/jbc.m112.400655.
42. Festjens N, Vanden Berghe T, Vandenebeele P. Necrosis, a well-orchestrated form of cell demise: signalling cascades, important mediators and concomitant immune response. *Biochim Biophys Acta.* 2006;1757:1371–87. Doi: 10.1016/j.bbabi.2006.06.014.
43. Frank D, Vince JE. Pyroptosis versus necroptosis: similarities, differences, and crosstalk. *Cell Death Differ.* 2019;26:99–114. Doi: 10.1038/s41418-018-0212-6.
44. Esmaeili N, Friebel M. Electrochemotherapy: a review of current status, alternative IGP approaches, and future perspectives. *J Healthcare Eng.* 2019;2019:1-11. Doi: 10.1155/2019/2784516.

45. Kalal BS, Upadhyia D, Pai VR. Chemotherapy resistance mechanisms in advanced skin cancer. *Oncol Rev.* 2017;11:326–26. Doi: 10.4081/oncol.2017.326.
46. Longo F, Perri F, Pavone E et al. Electrochemotherapy as palliative treatment in patients with advanced head and neck tumours: outcome analysis in 93 patients treated in a single institution. *Oral Oncol.* 2019; 92:77–84. Doi: 10.1016/j.oraloncology.2019.03.016.
47. Mir LM, Orlowski S. Mechanisms of electrochemotherapy. *Adv Drug Deliv Rev.* 1999;35:107–18. Doi: 10.1016/S0169-409X(98)00066-0.
48. Frandsen SK, Gissel H, Hojman P et al. Direct therapeutic applications of calcium electroporation to effectively induce tumor Necrosis. *2012;72:1336–41.* Doi: 10.1158/0008-5472. can11-3782.
49. Falk H, Matthiessen LW, Wooler G et al. Calcium electroporation for treatment of cutaneous metastases; a randomized doubleblinded phase II study, comparing the effect of calcium electroporation with electrochemotherapy. *Acta Ocol.* 2017;57:311–9. Doi: 10.1080/0284186X.2017.1355109.
50. Miller L, Leor J, Rubinsky B. Cancer cells ablation with irreversible electroporation. *Technol Cancer Res Treat.* 2005;4:699–705. Doi: 10.1177/153303460500400615.
51. Beitel-White N, Bhonsle S, Martin RCG et al. Electrical characterization of human biological tissue for irreversible electroporation treatments. *Conf Proc IEEE Eng Med Biol Soc.* 2018; 2018:4170–3. doi: 10.1109/EMBC.2018.8513341.
52. Brock RM, Beitel-White N, Coutermarsh-Ott S, Grider DJ, et al. Cell Death Electroporation Mini Review 98. Patient derived xenografts expand human primary pancreatic tumor tissue availability for ex vivo irreversible electroporation testing. *Front Oncol.* 2020;10:843. Doi: 10.3389/fonc.2020.00843.
53. Partridge BR, O'Brien TJ, Lorenzo MF et al. High-frequency irreversible electroporation for treatment of primary liver cancer: a proof-of-principle study in canine hepatocellular carcinoma. *J Vasc Interv Radiol.* 2020;31:482–91. Doi: 10.1016/j.jvir.2019.10.015.
54. Mercadal B, Beitel-White N, Aycock K, et al. A.Dynamics of cell death after conventional IRE and H-FIRE treatments. *Ann Biomed Eng.* 2020;48:1451–62. Doi: 10.1007/s10439-020-02462-8
55. Beebe SJ, Fox PM, Rec LJ et al. Nanosecond pulsed electric field (nsPEF) effects on cells and tissues: apoptosis induction and tumor growth inhibition. *IEEE Transac Plasma Scie.* 2002; 30:286–92. Doi: 10.1109/TPS.2002.1003872.
56. Guo S, Burcus NI, Hornef J et al. Nano-pulse stimulation for the treatment of pancreatic cancer and the changes in immune profile. *Cancers.* 2018; 10:217. Doi: 10.3390/cancers10070217.
57. Novickij V, Cesna R, Perminaite E et al. Antitumor response and immunomodulatory effects of submicrosecond irreversible electroporation and its combination with calcium electroporation. *Cancers.* 2019;11:1763. Doi: 10.3390/cancers11111763.
58. Kessel D. *Transcatheter Embolization and Therapy.* United Kingdom. 2010.
59. Malogolowkin MH , Stanley P , Steele DA., et al. Feasibility and Toxicity of Chemoembolization for Children With Liver Tumors. *Journal of Clinical Oncology.* 2016;18:1279-1284. Doi: 10.1200/JCO.2000.18.6.1279
60. Jean-Luc Raoul, Alejandro Forner, Luigi Bolondi. Updated use of TACE for hepatocellular carcinoma treatment: How and when to use it based on clinical evidence. *Cancer Treat Rev.* 2019;72:28–36. Doi: 10.1016/j.ctrv.2018.11.002.
61. [www.nccn.org](http://www.nccn.org). NCCN Guidelines version 5.2020. Hepatocellular Carcinoma.

62. Salem R, Gordon AC, Mouli S et al. Y90 radioembolization significantly prolongs time to progression compared with chemoembolization in patients with hepatocellular carcinoma. *Gastroenterology*. 2016; 151:1155–1163. Doi: 10.1053/j.gastro.2016.08.029
63. Shantanu Warhadpande, Alex Lionberg, Kyle J. Cooper. *Pocketbook of Clinical IR. A Concise Guide to Interventional Radiology*. Thieme Medical Publishers, New York. 2019
64. www.esmo.org. Guidelines. Gastrointestinal cancers.
65. D. Rohan Jeyarajah, Maria B. Majella Doyle, N. Joseph Espat. Role of yttrium-90 selective internal radiation therapy in the treatment of liver-dominant metastatic colorectal cancer: an evidence-based expert consensus algorithm. *Journal Gastrointestinal Oncology*. 2020;11: 443–60. Doi: 10.21037/jgo.2020.01.09.
66. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Colon Cancer. Version 4.2018. [NCCN Category 2A Recommendation: Based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate]
67. Cucchetti A, Cappelli A, Ercolani G et al. Selective internal radiation therapy (SIRT) as conversion therapy for unresectable primary liver malignancies. *Liver Cancer*. 2016;5:303-11. Doi.org/10.1159/000449341.
68. Shah JL, Zendejas-Ruiz IR, Thornton LM et al. Neoadjuvant transarterial radiation lobectomy for colorectal hepatic metastases: a small cohort analysis on safety, efficacy, and radiopathologic correlation. *J Gastrointest Oncol* 2017;8:43–51. Doi: 10.21037/jgo.2017.01.26.
69. Garlipp B, de Baere T, Damm R et al. Left-liver hypertrophy after therapeutic right-liver radioembolization is substantial but less than after portal vein embolization. *Hepatology* 2014;59:1864-73. Doi: 10.1002/hep.26947.
70. Sonntag PD, Hinshaw JL, Lubner MG, et al. Thermal ablation of lung tumors. *Surg Oncol Clin N Am*. 2011;20:369–87. Doi: 10.1016/j.soc.2010.11.008.
71. Bojarski JD, Dupuy DE, Mayo-Smith WW. CT imaging findings of pulmonary neoplasms after treatment with radiofrequency ablation: results in 32 tumors. *AJR Am J Roentgenol*. 2005;185(2):466–71.
72. Chan VO, McDermott S, Malone DE, Dodd JD. Percutaneous radiofrequency ablation of lung tumors: evaluation of the literature using evidence-based techniques. *J Thorac Imaging*. 2011;26(1):18–26.
73. Anderson EM, Lees WR, Gillams AR. Early indicators of treatment success after percutaneous radiofrequency of pulmonary tumors. *Cardiovasc Intervent Radiol*. 2009;32(3):478–83.
74. Kaltsas G, Grossman AB. The expanding role of somatostatin analogues in the treatment of neuroendocrine tumours: the clarinet study. *Clin Endocrinol*. 2015;83:759–61. Doi: 10.1111/cen.12831.
75. Rinke A, Müller HH, Schade-Brittinger C et al. Placebo-controlled, double-blind, prospective, randomized study on the effect of octreotide LAR in the control of tumor growth in patients with metastatic neuroendocrine midgut tumors: a report from the Promid Study Group. *J Clin Oncol*. 2009;27:4656–63. Doi: 10.1200/JCO.2009.22.8510.
76. Stump R, Haueis S, Kalt N, Tschauder C et al. Transplantation and surgical strategies in patients with neuroendocrine liver metastases: protocol of four systematic reviews. *JMIR Res Protoc*. 2013;2:58. Doi: 10.2196/resprot.2891.
77. Saxena A, Chua TC, Sarkar A et al. Progression and survival results after radical hepatic metastasectomy of indolent advanced neuroendocrine neoplasms (NENs) supports an aggressive surgical approach. *Surgery*. 2011;149:209–20. Doi: 10.1016/j.surg.2010.06.008.

78. Osborne DA, Zervos EE, Strosberg J et al. Improved outcome with cytoreduction versus embolization for symptomatic hepatic metastases of carcinoid and neuroendocrine tumors. *Ann Surg Oncol.* 2006;13:572–81. Doi: 10.1245/ASO.2006.03.071.
79. Fiore F, Del Prete M, Franco R et al. Transarterial embolization (TAE) is equally effective and slightly safer than transarterial chemoembolization (TACE) to manage liver metastases in neuroendocrine tumors. *Endocrine.* 2014;47:177–82. Doi: 10.1007/s12020-013-0130-9.
80. Cao CQ, Yan TD, Bester L et al. Radioembolization with yttrium microspheres for neuroendocrine tumour liver metastases. *Br J Surg.* 2010;97:537–43. Doi: 10.1002/bjs.6931.
81. Vogl TJ, Naguib NN, Zangos S et al. Liver metastases of neuroendocrine carcinomas: interventional treatment via transarterial embolization, chemoembolization and thermal ablation. *Eur J Radiol.* 2009;72:517–28. Doi: 10.1016/j.ejrad.2008.08.008.
82. Memon K, Lewandowski RJ, Riaz A et al. Chemoembolization and radioembolization for metastatic disease to the liver: available data and future studies. *Curr Treat Options Oncol.* 2012;13:403–15.
83. Da Silva TN, Van Velthuysen MLF, Van Eijck CHJ et al. Successful neoadjuvant peptide receptor radionuclide therapy for an inoperable pancreatic neuroendocrine tumour. *Endocrinol Diabetes Metab Case Rep.* 2018;2018:0–15.
84. Tuba Kendi, Thorvardur R. Halldanarson, Annie Packard. Therapy With 177Lu-DOTATATE: Clinical Implementation and Impact on Care of Patients With Neuroendocrine Tumors. *American Journal Of Roentgenology.* 2019;213:309–17. Doi: 10.2214/AJR.19.21123.
85. Cazzato RL, Garnon J, Ramamurthy N et al. 18F-FDOPA PET/CT-Guided Radiofrequency Ablation of Liver Metastases from Neuroendocrine Tumours: Technical Note on a Preliminary Experience. *Cardiovasc Intervent Radiol.* 2016;39:1315–21.
86. Lubner MG, Brace CL, Ziemlewicz TJ et al. Microwave ablation of hepatic malignancy. *Semin Intervent Radiol.* 2013;30:56–66.
87. Uhlig J, Strauss A, Rücker G. Partial nephrectomy versus ablative techniques for small renal masses: a systematic review and network meta-analysis. *Eur Radiol.* 2019;29:1293–1307. Doi: 10.1007/s00330-018-5660-3.
88. Christopher S. Morris, Mark O. Baerlocher, Sean R. Dariushnia. Society of Interventional Radiology Position Statement on the Role of Percutaneous Ablation in Renal Cell Carcinoma. *J Vasc Interv Radiol* 2020; 31:189–94. Doi.org/10.1016/j.jvir.2019.11.001
89. Volpe A, Panzarella T, Rendon RA et al. The natural history of incidentally detected small renal masses. *Cancer* 2004;100:738–45.
90. Capitanio U, Bensalah K, Bex A, et al. Epidemiology of renal cell carcinoma. *Eur Urol* 2019; 75:74–84.
91. Campbell S, Uzzo RG, Allaf ME et al. Renal mass and localized renal cancer: AUA guideline. *J Urol* 2017;198:520–29.
92. Dabestani S, Marconi L, Hofmann F et al. Local treatments for metastases of renal cell carcinoma: a systematic review. *Lancet Oncol* 2014;15:e549–e561.
93. Choueiri TK, Motzer RJ. Systemic therapy for metastatic renal-cell carcinoma. *N Engl J Med* 2017;376:354–66.
94. Motzer RJ, Jonasch E, Agarwal N et al. NCCN Clinical Practice Guidelines in Oncology: Kidney Cancer Version 2.2020. 2019. [www.nccn.org](http://www.nccn.org)

95. A Fares, MH Shaaban, RM Reyad. Combined percutaneous radiofrequency ablation and cementoplasty for the treatment of extraspinal painful bone metastases: a prospective study. *Journal of the Egyptian* 2018;30:117-22. Doi.org/10.1016/j.jnci.2018.05.002
96. Jack W. Jennings . Is Percutaneous Bone Cryoablation Safe? *Radiology* 2019;291:529–30. Doi. org/10.1148/radiol.2019190212
97. Gerard Deib, Benyamin Deldar, Ferdinand Hui. Percutaneous Microwave Ablation and Cementoplasty: Clinical Utility in the Treatment of Painful Extraspinal Osseous Metastatic Disease and Myeloma. *American Journal of Roentgenology*. 2019;212:1377-84. Doi: 10.2214/ AJR.18.20386
98. Edward Chow , Yvette Mvan der Linden, Daniel Roos. Single versus multiple fractions of repeat radiation for painful bone metastases: a randomised, controlled, non-inferiority trial. *The Lancet Oncology* . 2014;2:164-71. Doi: 10.1016/S1470-2045(13)70556-4.
99. Jessica L.Conway, Emily Yurkowski, Justin Glazierd. Comparison of patient-reported outcomes with single versus multiple fraction palliative radiotherapy for bone metastasis in a population-based cohort. *Radiotherapy and Oncology*. 2016;2:202-07. doi.10.1016/j.randonc.2016.03.025
100. M Distelmaier, A Barabasch, P Heil et al. Midterm safety and efficacy of irreversible electroporation of malignant liver tumors located close to major portal or hepatic veins. *Radiology*. 2017;285:1023-1031. Doi.org/10.1148/radiol.2017161561.
101. A. Giorgio, F. Amendola, A. Calvanese. Ultrasound-guided percutaneous irreversible electroporation of hepatic and abdominal tumors not eligible for surgery or thermal ablation: a western report on safety and efficacy. *Journal of Ultrasound* 2019;22:53–8.
102. Md Sharjis Ibne Wadud, Rafid Ayman. Prospects of Irreversible Electroporation in Malignant Tissue or Tumour Ablation *International Journal for Research in Applied Science & Engineering Technology*. 2020;8:2921-26. Doi.org/10.22214/ijraset.2020.5491 .
103. Laurien GPH Vroomen. Electroporation in interventional oncology. 2019 L.G.P.H. Vroomen.