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Article

THE ROLE OF CRYOTHERAPY IN CANCER TREATMENT – A REVIEW OF MECHANISMS, EFFICACY, AND FUTURE DIRECTIONS

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ABSTRACT

Cryotherapy, often called cryoablation or cryosurgery, is a minimally invasive treatment that uses extremely low temperatures to eliminate cancer cells. Using agents such as liquid nitrogen or argon gas, it achieves temperatures as low as −196°C, resulting in the development of intracellular ice crystals that destroy cellular structures and induce death. Its uses are many, ranging from dermatology to gynecology to oncology, with a rising interest in its ability to treat localized solid tumors, such as prostate, breast, and liver cancer. Cryotherapy has several advantages, including being less intrusive, protecting surrounding healthy tissues, and activating immunological responses. The hurdles include standardizing techniques, enhancing effectiveness in metastatic malignancies, and overcoming economic limitations. This study investigates cryotherapy's mechanics, therapeutic uses, and its interaction with immunotherapy.

Keywords: Cryotherapy, Cryoablation, Cancer treatment, Minimally invasive, Liquid nitrogen, Localized tumors, Immunological response, Metastatic malignancies.

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INTRODUCTION

Often called cryosurgery or cryoablation, cryotherapy is a minimally invasive technique that destroys cancer cells and other damaged or abnormal tissue using extremely low temperatures. This method uses liquid nitrogen or argon gas to achieve temperatures as low as −196°C [1,2]. This causes intracellular ice crystals to grow, disturb cellular architecture, and eventually cause cell death [3-5]. In dermatology, ophthalmology, and gynecology, cryotherapy is often used to treat both benign and malignant lesions [6-8]. Lately, there has been a lot of interest in the possible uses of cryotherapy as a cancer treatment [9]. Cryotherapy historical origins may be traced to ancient Egypt, when cold treatment was used to cure inflammation and injuries [10-13]. However, the development of contemporary cryotherapy procedures did not start until the middle of the 1800s [14-17]. British physician James Arnott was the first to treat uterine and breast tumors using a solution of crushed ice and salt in 1851 [18,19]. This was the initial stage of cancer cryotherapy. The advent of liquid nitrogen in the 1960s significantly improved cryosurgery, enabling more precise and effective treatment of a variety of illnesses, including cancers of the skin, prostate, liver, and kidneys [1,20,21]. Because of its exceptional capacity to eliminate cancer cells with little harm to the surrounding healthy tissues, cryotherapy is being investigated as a potential cancer treatment approach [15,22]. It may also be performed as an outpatient procedure. Precise freezing has shown significant potential in the management of localized solid tumors because it can identify and eradicate malignant cells while maintaining organ functionality [23-26]. Furthermore, the intriguing possibility of combining cryotherapy and immunotherapy to improve cancer treatment results stems from its capacity to elicit immune responses against cancer cells [1,26-28]. There is more and more evidence that cryotherapy can help treat different types of tumors [1,27,28]. This, along with the need to understand the challenges and possible future directions in its use, makes this review of the technology's current state in cancer treatment necessary [1,29]. This paper will thoroughly examine the mechanics of cryotherapy, its therapeutic uses, and its potential as a major component of modern cancer treatment regimens [24]. This study aims to shed light on how cryosurgery, a rapidly developing technique, could be optimized for therapeutic application in cancer in the future by examining its advances and limitations [17,26].

MECHANISM OF ACTION OF CRYOTHERAPY IN CANCER TREATMENT

Direct effects

Using extremely cold temperatures to target and kill cancer cells is called cryotherapy or cryoablation [30]. The primary mechanism is the formation of ice crystals within the cancer cells, which leads to:

Cellular death

The freezing process causes intracellular ice formation, which damages cell membranes, organelles, and structures essential for cellular function. This damage ultimately results in cell death. The temperature typically used in cryotherapy is between −40°C and −196°C, depending on the type of cancer and the treatment protocol [31-35].

Vascular damage

In addition, cryotherapy causes the tumor's blood arteries to be destroyed. The malignant tissue receives less blood as a result of this vascular damage, which exacerbates cellular death from a shortage of oxygen and nutrients [36-38].

Indirect effects

Cryotherapy's ability to destroy cancer cells has a number of unintended consequences that increase the treatment's overall efficacy.

Immune response

The death of cancer cells releases tumor antigens, which can stimulate the immune system. This immune response can help recognize and destroy remaining cancer cells that were not directly affected by the cryotherapy [39-41].

Inflammatory response

The process induces a local inflammatory response that can further promote immune activation and assist in the elimination of residual tumor cells [42-44].

Cryoablation versus cryosurgery

Cryoablation

Cryoablation involves inserting a cryoprobe directly into the tumor, where it freezes the tissue. This method is minimally invasive and is often used for tumors that are not amenable to traditional surgical methods [26,44-46].

Cryosurgery

This is a more extensive surgical approach that involves freezing cancerous tissues either as a primary treatment or in conjunction with other treatments [1,17,30,47,48]. It is particularly useful for superficial tumors and can be employed to treat a variety of cancers, including skin cancer and precancerous lesions [6,31,49-51]. Cryosurgery often involves the use of cryoprobes or cryo-sprays to administer the freezing agent [52].

CLINICAL APPLICATIONS OF CRYOTHERAPY IN CANCER TREATMENT

Cryotherapy in solid tumors

Prostate cancer

Role and application

Cryotherapy is increasingly used for prostate cancer, especially in cases where patients are seeking alternatives to radiation or surgical removal [30,53-55]. Cryosurgery for prostate cancer involves the use of cryoprobes inserted into the prostate gland to freeze and destroy cancerous tissues [56,57]. It is particularly useful for localized prostate cancer and can be an option for patients who have failed other treatments or wish to avoid more invasive procedures.

Advantages

It offers a minimally invasive alternative to traditional surgery with reduced risk of incontinence and sexual dysfunction compared to radical prostatectomy. It also provides a viable option for patients who are not candidates for radiation therapy.

Breast cancer

Clinical trials and efficacy

As a primary therapy or as a supplement to surgery, cryoablation is being investigated as a potential therapeutic option for breast cancer [1,58,59]. Its efficacy in shrinking tumor size has been assessed in clinical trials, offering a viable substitute for women looking for less intrusive treatments.

Studies

Research indicates that cryoablation can be effective in treating early-stage breast cancer, showing promising results in terms of local control and cosmetic outcomes [60-62]. Studies also investigate its potential role in combination with other treatments to enhance overall efficacy.

Liver cancer

Application

Cryoablation is used in the treatment of liver cancer, especially for tumors that are small and localized [47,63-65]. It is particularly advantageous for patients with hepatocellular carcinoma or liver metastases who are not candidates for surgical resection [48,65-67].

Advantages

This method can be employed percutaneously or laparoscopically, allowing for precise targeting of tumors with minimal impact on surrounding healthy tissue [48,66].

Lung cancer

Application

Cryoablation is used for small, early-stage lung cancers and as a palliative treatment for inoperable cases [65,67,68]. It can also be applied to metastatic lung cancer [69,70].

Advantages

It offers a less invasive approach compared to surgery and can be an effective option for patients with comorbid conditions that contraindicate traditional surgical intervention [71,72].

Kidney cancer

Application

Cryoablation is used for renal cell carcinoma, particularly for patients with small tumors or those who are not candidates for nephrectomy [69,72-75]. It is typically performed percutaneously or laparoscopically [76-79].

Advantages

The procedure is minimally invasive and offers a good alternative for patients with localized tumors, with a lower risk of postoperative complications compared to traditional surgery [80].

Combination therapies

Cryotherapy and immunotherapy

Combining cryotherapy with immunotherapy can enhance the immune response against cancer [30,81,82]. The destruction of cancer cells by cryotherapy can release antigens and stimulate an immune response, which can be amplified by immunotherapy agents [83-85]. Cryotherapy and Chemotherapy: Cryotherapy can be used alongside chemotherapy to target residual cancer cells that are resistant to chemotherapy [86,87].

The localized destruction of cancer tissue can improve the effectiveness of chemotherapy by reducing tumor burden and potentially enhancing drug delivery [45,88,89]. Combining radiation therapy and cryotherapy may increase the overall effectiveness of cancer treatment [90-92]. Treatment results may be improved by cryotherapy since it can shrink the tumor and increase the radiation exposure to the cancer cells that are still there [84,93,94].

ADVANTAGES AND LIMITATIONS OF CRYOTHERAPY IN CANCER TREATMENT

Advantages

Minimally invasive

Cryotherapy is a minimally invasive procedure compared to traditional surgical methods [26,68]. It involves the application of extreme cold to target cancer cells, usually through small incisions or percutaneously, which limits the impact on surrounding healthy tissues [22,95].

Less painful than traditional surgery

Patients generally experience less pain with cryotherapy compared to conventional surgery [96,97]. The procedure is less invasive, which results in reduced discomfort and a more tolerable recovery process [98,99].

Shorter recovery time

Cryotherapy typically requires a shorter recovery period compared to traditional surgery. The minimal invasiveness of the procedure often translates to quicker postoperative recovery and less downtime.

imitations

May not be effective for all types of cancers or in all patients

Cryotherapy may not be suitable for all types of cancers or for all patients. Its effectiveness can vary based on the type, stage, and location of the tumor, and it may not be appropriate for large or deeply located tumors [99,100].

Requires precision to avoid damaging surrounding healthy tissues

The success of cryotherapy relies heavily on the precision of the procedure. Inaccurate placement or application can lead to damage to surrounding healthy tissues, which may result in complications or reduced efficacy [95,101].

Research is still in early stages for some types of cancer

Although cryotherapy is established for some cancers, research is still ongoing for others. The clinical application and efficacy of cryotherapy are not fully understood for all types of cancer, and more studies are needed to confirm its benefits and limitations [102-104].

CLINICAL TRIALS AND RESEARCH ON CRYOTHERAPY FOR CANCER TREATMENT

Key clinical trials

Prostate cancer cryotherapy trial

This trial assessed the efficacy of cryotherapy in patients with localized prostate cancer. Results demonstrated that cryotherapy provided comparable outcomes to other local treatments with a good safety profile [26,94,95,105].

Skin cancer cryotherapy trial

This study focused on the effectiveness of cryotherapy for basal cell carcinoma and squamous cell carcinoma. The trial found high success rates with cryotherapy, particularly for superficial lesions [57,106-109].

Cryotherapy for breast cancer

This trial explored the role of cryoablation in early-stage breast cancer. It evaluated tumor response and patient outcomes, finding that cryotherapy was effective in shrinking tumors before surgery [110-113].

META-ANALYSES AND SYSTEMATIC REVIEWS

Meta-analysis of cryotherapy for prostate cancer

This meta-analysis examined several studies on cryotherapy for prostate cancer, emphasizing how safe and effective it is in comparison to other forms of treatment. Cryotherapy was validated as a treatment option by the analysis [107,114-116].

Systematic review of cryotherapy for skin cancers

This review summarized data from multiple trials to investigate the efficacy of cryotherapy for different types of skin malignancies. It validated the high success rates of cryotherapy in treating squamous and basal cell carcinomas [117-119].

ONGOING STUDIES AND ADVANCED TECHNIQUES

MRI-guided cryotherapy for prostate cancer

This ongoing study investigates the use of MRI guidance to enhance cryotherapy precision for prostate cancer, aiming to improve targeting accuracy and treatment outcomes [120-124].

Combination of cryotherapy and immunotherapy

This study explores the potential benefits of combining cryotherapy with immunotherapy to enhance systemic immune responses against cancer [41,125-128].

Advanced imaging techniques for cryotherapy

Research is focusing on developing advanced imaging technologies, such as real-time ultrasound and advanced MRI, to improve cryotherapy monitoring and control [82,129].

Cryotherapy for liver tumors

With an emphasis on long-term survival and quality of life, this ongoing clinical trial evaluates the efficacy of cryotherapy for the treatment of primary and metastatic liver cancers [130-132].

Cryotherapy in combination with targeted therapies

This research evaluates the synergy between cryotherapy and targeted molecular therapies, aiming to improve treatment outcomes for various cancer types [133,134].

CHALLENGES AND FUTURE DIRECTIONS IN CRYOTHERAPY FOR CANCER TREATMENT

Challenges

Standardizing treatment protocols

One major obstacle is the absence of well recognized cryotherapy protocols. Different cryotherapy approaches, including those involving temperature settings, duration, and application procedures, might produce varying results [68,135]. In order to guarantee consistent and repeatable outcomes in many therapeutic contexts, standardizing these procedures is essential. To create thorough instructions for the application of cryotherapy in an efficient manner, research is required [136,137].

Overcoming limitations in cryotherapy for metastatic cancers

For localized tumors, cryotherapy works best; however, it is not very successful for treating metastatic cancers [136,137]. Addressing the spread of cancer cells that cryotherapy might not be able to reach is the difficult part [41]. It is required to conduct research on improving cryotherapy's efficacy for metastatic patients, potentially through combination therapies.

Cost and availability of the technology

Cryotherapy techniques and equipment can be prohibitively expensive, particularly in places with limited resources [138,139]. This prevents cryotherapy from being widely used as a therapeutic alternative. For wider adoption, these financial obstacles must be removed and cryotherapy technology must become more widely available [140,141].

Future directions

Potential of combining cryotherapy with emerging treatments (e.g., immunotherapy)

The therapeutic efficacy may be increased by combining cryotherapy with cutting-edge therapies like immunotherapy [142,143]. Immunotherapy may strengthen the local immunological response that cryotherapy may elicit, improving overall results [144]. In order to optimize the advantages of these combined treatments, future research should investigate synergistic techniques.

Advances in precision technologies to improve outcomes

Technological developments in precision medicine and imaging could greatly enhance cryotherapy results. More precise tumor targeting is made possible by methods like MRI-guided cryotherapy, which may improve outcomes and reduce side effects. The integration of these technologies into clinical practice should be the main focus of future study [145].

Expanding its use for more cancer types

Nowadays, some diseases, such skin and prostate cancer, are the main targets of cryotherapy [41,146]. Its application to additional cancer types, such lung and breast malignancies, may open up new therapeutic avenues. To increase cryotherapy's therapeutic applicability, more research is required to determine how well it works for various malignancies and tumor types [56,147].

CONCLUSION

Because it is minimally invasive and can be used with other treatments like immunotherapy, cryotherapy is a good alternative for treating cancer. Although it has benefits over traditional surgery and is effective in treating localized tumors, issues like procedure standardization and its limited applicability in metastatic cases persist. Its use may be expanded by future developments in integrated therapeutic approaches and accurate imaging, which would make cryotherapy a more worthwhile cancer treatment option. To maximize its use and improve outcomes in general cancer practice, more research and clinical trials are essential.

CONFLICTS OF INTEREST

There are no conflicts of interest.

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REFERENCES

1. Gage AA, Baust JG. Cryosurgery for tumors. J Am Coll Surg 2007;205:342-56.
2. Dobak J. A review of cryobiology and cryosurgery. In: Advances in Cryogenic Engineering. Boston, MA: Springer; 1998. p. 889-96. Jenning JW Sr. Production and control of low temperature in cryosurgery. AORN J 1968;7:41-6.
3. Xu K. Cryobiology: Mechanism of action and reaction to freezing. In: Modern cryosurgery for cancer. Singapore: World Scientific; 2012. p. 123-70.
4. Ismail M, Ahmed S, Davies J. Prostate cryotherapy. In: Prostate Cancer: A Comprehensive Perspective. London: Springer; 2012. p. 773-786.
5. Chu KF, Dupuy DE. Thermal ablation of tumours: Biological mechanisms and advances in therapy. Nat Rev Cancer 2014;14: 199-208.
6. Clebak KT, Mendez-Miller M, Croad J. Cutaneous cryosurgery for common skin conditions. Am Fam Physician 2020;101:399-406.
7. Bánvölgyi A, Görög A, Gadó K, Holló P. Common benign and malignant tumours of the aging skin: Characteristics and treatment options. Dev Health Sci 2022;4:86-90.
8. Zacarian SA. Cryosurgery in dermatology. In: Physical Modalities in Dermatologic Therapy: Radiotherapy, Electrosurgery, Phototherapy, Cryosurgery. New York: Springer; 1978. p. 270-81.
9. Gage AA. Selective cryotherapy. Cell Preserv Technol 2004;2:3-14.
10. Holt PJ. Cryotherapy for skin cancer: Results over a 5-year period using liquid nitrogen spray cryosurgery. Br J Dermatol 1988;119:231-40.
11. Levine D, Marcellin-Little DJ. Cryotherapy in small animal rehabilitation. Adv Small Anim Care 2021;2:11-8.
12. Trescot AM. Cryoneurolysis: Principles and practice. In: Weiner's Pain Management: A Practical Guide for Clinicians. United States: CRC Press; 2005. p. 1057-77.
13. Sobh HR, Elsherbiny OE, El-Refaay ER, Abd-Elghany SM. Effect of topical cryotherapy on clinical outcomes of patients with breast cancer related lymphedema. Tanta Sci Nurs J 2023;30:280-302.
14. Haslerud SI. Low-level laser therapy and cryotherapy in tendinopathy treatment. Clinical, biological, and biophysical effects of low-level laser therapy alone and in combination with cryotherapy.
15. Korpan NN. A history of cryosurgery: Its development and future. J Am Coll Surg 2007;204:314-24.
16. Xu K. History of cryosurgery. In: Modern Cryosurgery For Cancer. Singapore: World Scientific; 2012. p. 3-27.
17. Onik G. Cryosurgery. Crit Rev Oncol Hematol 1996;23:1-24.
18. Ullrick SR, Hebert JJ, Davis KW. Cryoablation in the musculoskeletal system. Curr Probl Diagn Radiol 2008;37:39-48.
19. Andrade JG, Khairy P, Dubuc M. Catheter cryoablation: Biology and clinical uses. Circ Arrhythm Electrophysiol 2013;6:218-27.
20. Gage AA. History of cryosurgery. Semin Surg Oncol 1998;14:99-109.
21. Cartwright AC, Armstrong NA. A History of the Medicines We Take: From Ancient Times to Present Day. England: Pen and Sword History; 2020.
22. Baust J, Gage AA, Ma H, Zhang CM. Minimally invasive cryosurgery-technological advances. Cryobiology 1997;34:373-84.
23. Rubinsky B. Cryosurgery. Ann Rev Biomed Eng 2000;2:157-87.
24. Vergnon JM, Huber RM, Moghissi K. Place of cryotherapy, brachytherapy and photodynamic therapy in therapeutic bronchoscopy of lung cancers. Eur Respir J 2006;28:200-18.
25. Riley P, Glenny AM, Worthington HV, Littlewood A, Clarkson JE, McCabe MG. Interventions for preventing oral mucositis in patients with cancer receiving treatment: Oral cryotherapy. Cochrane Database Syst Rev 2015;2015:CD011552.
26. Baust JG, Gage AA, Bjerklund Johansen TE, Baust JM. Mechanisms of cryoablation: Clinical consequences on malignant tumors. Cryobiology 2014;68:1-11.
27. Sun X, Cui B, Yuan B, Wang X, Fan L, Yu D, *et al*. Liquid metal microparticles phase change medicated mechanical destruction for enhanced tumor cryoablation and dual-mode imaging. Adv Funct Mater 2020;30:2003359.
28. Kepp O, Marabelle A, Zitvogel L, Kroemer G. Oncolysis without viruses - inducing systemic anticancer immune responses with local therapies. Nat Rev Clin Oncol 2020;17:49-64.
29. Shields JA, Parsons H, Shields CL, Giblin ME. The role of cryotherapy in the management of retinoblastoma. Am J Ophthalmol 1989;108:260-4.
30. Korpan NN, editor. Basics of Cryosurgery. Germany: Springer Science & Business Media; 2012.
31. Baust JG, Santucci KL, Snyder KK, Robilotto A, Baust JM. Mechanisms of tissue injury in cryosurgery. The Application of Heat in Oncology: Principles and Practice. United States: John Wiley & Sons; 2023. p. 45-71.
32. Agarwal V, Singh M. Cryopreservation of cell lines. In: Animal Cell Culture: Principles and Practice. Cham: Springer International Publishing; 2023. p. 147-61.
33. Thomsen S. Measuring thermal damage with gross and microscopic pathology. In: The Application of Heat in Oncology: Principles and Practice. United States: John Wiley & Sons; 2023. p. 217-50.
34. Aggarwal N, Ahuja K, Pal N, Pannu R, Berwal V. Cryosurgery: A therapeutic modality for oro-facial lesions. Int J Commu Health Med Res 2017;3:66.
35. Chato JC, Lee RC. The future of biothermal engineering. Ann N Y Acad Sci 1998;858:1-20.
36. Pasquali P, Trakatelli MG. Cryotherapy. In: Hyperpigmentation. United States: CRC Press; 2017. p. 258-65.
37. Gonçalves JC. Fractional cryosurgery for skin cancer. Dermatol Surg 2009;35:1788-96.
38. Debela DT, Muzazu SG, Heraro KD, Ndalama MT, Mesele BW, Haile DC, et al. New approaches and procedures for cancer treatment: Current perspectives. SAGE Open Med 2021;9:20503121211034366.
39. Schacht V, Becker K, Szeimies RM, Abels C. Apoptosis and leucocyte-endothelium interactions contribute to the delayed effects of cryotherapy on tumours *in vivo*. Arch Dermatol Res 2002;294:341-8.
40. Hoffmann NE, Bischof JC. The cryobiology of cryosurgical injury. Urology 2002;60:40-9.
41. Abdo J, Cornell DL, Mittal SK, Agrawal DK. Immunotherapy plus cryotherapy: Potential augmented abscopal effect for advanced cancers. Front Oncol 2018;8:85.
42. Sabel MS. Cryo-immunology: A review of the literature and proposed mechanisms for stimulatory versus suppressive immune responses. Cryobiology 2009;58:1-11.
43. Hoffmann NE, Bischof JC. Mechanisms of injury caused by *in vivo* freezing. In: Life in the Frozen State. United States: CRC Press; 2004. p. 481-508.
44. Wu F. Heat-based tumor ablation: Role of the immune response. Adv Exp Med Biol 2016;880:131-53.
45. Tranberg KG. Local destruction of tumors and systemic immune effects. Front Oncol 2021;11:708810.
46. Moioli EK, Krunic AL. Immunological aspects of cryosurgery. In: Skin Cancer: A Practical Approach. New York: Springer; 2013. p. 397-407.
47. Habrawi Z, Melkus MW, Khan S, Henderson J, Brandi L, Chu V, *et al.* Cryoablation: A promising non-operative therapy for low-risk breast cancer. Am J Surg 2021;221:127-33.
48. Aghayev A, Tatli S. The use of cryoablation in treating liver tumors. Expert Rev Med Devices 2014;11:41-52.
49. Gage AA, Baust JM, Baust JG. Experimental cryosurgery investigations *in vivo*. Cryobiology 2009;59:229-43.
50. Goel R, Anderson K, Slaton J, Schmidlin F, Vercellotti G, Belcher J, *et al.* Adjuvant approaches to enhance cryosurgery. J Biomech Eng 2009;131:074003.
51. Sinclair RD, Dawber RP. Cryosurgery of malignant and premalignant diseases of the skin: A simple approach. Australas J Dermatol 1995;36:133-42.
52. Neel HB 3rd. Cryosurgery for the treatment of cancer. Laryngoscope 1980;90:1-48.
53. Zimmerman EE, Crawford P. Cutaneous cryosurgery. Am Fam Physician 2012;86:1118-24.
54. Karow AM. Organ cryopreservation. In: Clinical Applications of Cryobiology. London: CRC Press; 199. p. 191-217.
55. Tsivian M, Polascik TJ. Focal cryotherapy for prostate cancer. Curr Urol Rep 2010;11:147-51.
56. Babaian RJ, Donnelly B, Bahn D, Baust JG, Dineen M, Ellis D, *et al.* Best practice statement on cryosurgery for the treatment of localized prostate cancer. J Urol 2008;180:1993-2004.
57. Jung JH, Risk MC, Goldfarb R, Reddy B, Coles B, Dahm P. Primary cryotherapy for localised or locally advanced prostate cancer. Cochrane Database Syst Rev 2018;5:CD005010.
58. Onik G. Percutaneous image-guided prostate cancer treatment: Cryoablation as a successful example. Tech Vasc Interv Radiol

2007;10:149-58.
59. Franco L. Cryosurgery for prostate cancer. In: Modern Cryosurgery for Cancer. Singapore: World Scientific; 2012. p. 715-56.
60. Pigg N, Ward RC. Cryoablation for the treatment of breast cancer: A review of the current landscape and future possibilities. Acad Radiol 2023;30:3086-100.
61. Carriero S, Lanza C, Pellegrino G, Ascenti V, Sattin C, Pizzi C, *et al.* Ablative therapies for breast cancer: State of art. Technol Cancer Res Treat 2023;22:15330338231157193.
62. Sharma R, Wagner JL, Hwang RF. Ablative therapies of the breast. Surg Oncol Clin N Am 2011;20:317-39, viii.
63. Zhao Z, Wu F. Minimally-invasive thermal ablation of early-stage breast cancer: A systemic review. Eur J Surg Oncol 2010;36:1149-55.
64. Habrawi Z, Melkus MW, Khan S, Henderson J, Brandi L, Chu V, *et al.* Cryoablation: A promising non-operative therapy for low-risk breast cancer. Am J Surg 2021;221:127-33.
65. Hinshaw JL, Lee FT Jr. Cryoablation for liver cancer. Tech Vasc Interv Radiol 2007;10:47-57.
66. Shafir M, Shapiro R, Sung M, Warner R, Sicular A, Klipfel A. Cryoablation of unresectable malignant liver tumors. Am J Surg 1996;171:27-31.
67. Mala T. Cryoablation of liver tumours-a review of mechanisms, techniques and clinical outcome. Minim Invasive Ther Allied Technol 2006;15:9-17.
68. Kwak K, Yu B, Lewandowski RJ, Kim DH. Recent progress in cryoablation cancer therapy and nanoparticles mediated cryoablation. Theranostics 2022;12:2175-204.
69. Inoue M, Nakatsuka S, Jinzaki M. Cryoablation of early-stage primary lung cancer. Biomed Res Int 2014;2014:521691.
70. Chou HP, Chen CK, Shen SH, Sheu MH, Wu MH, Wu YC, *et al.* Percutaneous cryoablation for inoperable malignant lung tumors: Midterm results. Cryobiology 2015;70:60-5.
71. Niu L, Xu K, Mu F. Cryosurgery for lung cancer. J Thorac Dis 2012;4:408-19.
72. Eiken PW, Welch BT. Cryoablation of lung metastases: Review of recent literature and ablation technique. Semin Intervent Radiol 2019;36:319-25.
73. Desai MM, Aron M, Gill IS. Laparoscopic partial nephrectomy versus laparoscopic cryoablation for the small renal tumor. Urology 2005;66:23-8.
74. Maria T, Georgiades C. Percutaneous cryoablation for renal cell carcinoma. J Kidney Cancer VHL 2015;2:105-13.
75. Zargar H, Atwell TD, Cadeddu JA, de la Rosette JJ, Janetschek G, Kaouk JH, *et al.* Cryoablation for small renal masses: Selection criteria, complications, and functional and oncologic results. Eur Urol 2016;69:116-28.
76. Lehman DS, Landman J. Cryoablation and radiofrequency for kidney tumor. Curr Urol Rep 2008;9:128-34.
77. Williams SK, de la Rosette JJ, Landman J, Keeley FX Jr. Cryoablation of small renal tumors. EAU-EBU Update Ser 2007;5:206-18.
78. Finley DS, Beck S, Box G, Chu W, Deane L, Vajgrt DJ, *et al.* Percutaneous and laparoscopic cryoablation of small renal masses. J Urol 2008;180:492-8.
79. Kim EH, Tanagho YS, Saad NE, Bhayani SB, Figenshau RS. Comparison of laparoscopic and percutaneous cryoablation for treatment of renal masses. Urology 2014;83:1081-7.
80. Gill IS, Novick AC, Soble JJ, Sung GT, Remer EM, Hale J, *et al.* Laparoscopic renal cryoablation: Initial clinical series. Urology 1998;52:543-51.
81. Hinshaw JL, Lubner MG, Ziemlewicz TJ, Lee FT Jr., Brace CL. Percutaneous tumor ablation tools: Microwave, radiofrequency, or cryoablation-what should you use and why? Radiographics 2014;34:1344-62.
82. Yakkala C, Denys A, Kandalaft L, Duran R. Cryoablation and immunotherapy of cancer. Curr Opin Biotechnol 2020;65:60-4.
83. Sidana A. Cancer immunotherapy using tumor cryoablation. Immunotherapy 2014;6:85-93.
84. Ho AY, Tabrizi S, Dunn SA, McArthur HL. Current advances in immune checkpoint inhibitor combinations with radiation therapy or cryotherapy for breast cancer. Breast Cancer Res Treat 2022;191:229-41.
85. Yuanying Y, Lizhi N, Feng M, Xiaohua W, Jianying Z, Fei Y, *et al.* Therapeutic outcomes of combining cryotherapy, chemotherapy and DC-CIK immunotherapy in the treatment of metastatic non-small cell lung cancer. Cryobiology 2013;67:235-40.
86. Agrawal DK. Immunotherapy plus cryotherapy: Potential augmented abscopal effect for advanced cancers. Front Oncol 2018;8:85.
87. Peng P, Hu H, Liu P, Xu LX. Neoantigen-specific CD4(+) T-cell response is critical for the therapeutic efficacy of cryo-thermal therapy. J Immunother Cancer 2020;8:e000421.
88. Clarke DM, Baust JM, Van Buskirk RG, Baust JG. Chemo-cryo combination therapy: An adjunctive model for the treatment of prostate cancer. Cryobiology 2001;42:274-85.
89. Ci T, Li H, Chen G, Wang Z, Wang J, Abdou P, *et al.* Cryo-shocked cancer cells for targeted drug delivery and vaccination. Sci Adv 2020;6:eabc3013.
90. Wei G, Wang Y, Yang G, Wang Y, Ju R. Recent progress in nanomedicine for enhanced cancer chemotherapy. Theranostics 2021;11:6370-92.
91. Ding Y, Li W, Zhang F, Liu Z, Zanjanizadeh Ezazi N, Liu D, *et al*. Electrospun fibrous architectures for drug delivery, tissue engineering and cancer therapy. Adv Funct Mater 2019;29:1802852.
92. Tang L, He S, Yin Y, Liu H, Hu J, Cheng J, *et al.* Combination of nanomaterials in cell-based drug delivery systems for cancer treatment. Pharmaceutics 2021;13:1888.
93. Williams SB, Lei Y, Nguyen PL, Gu X, Lipsitz SR, Yu HY, *et al.* Comparative effectiveness of cryotherapy vs brachytherapy for localised prostate cancer. BJU Int 2012;110:E92-8.
94. Donnelly BJ, Saliken JC, Brasher PM, Ernst SD, Rewcastle JC, Lau H, *et al.* A randomized trial of external beam radiotherapy versus cryoablation in patients with localized prostate cancer. Cancer 2010;116:323-30.
95. Littrup PJ, Jallad B, Chandiwala-Mody P, D'Agostini M, Adam BA, Bouwman D. Cryotherapy for breast cancer: A feasibility study without excision. J Vasc Interv Radiol 2009;20:1329-41.
96. Singletary SE. Minimally invasive techniques in breast cancer treatment. Semin Surg Oncol 2001;20:246-50.
97. Otsuka I. Cutaneous metastasis after surgery, injury, lymphadenopathy, and peritonitis: Possible mechanisms. Int J Mol Sci 2019;20:3286.
98. Ahmed M, Rubio IT, Klaase JM, Douek M. Surgical treatment of nonpalpable primary invasive and *in situ* breast cancer. Nat Rev Clin Oncol 2015;12:645-63.
99. Knavel EM, Brace CL. Tumor ablation: Common modalities and general practices. Tech Vasc Interv Radiol 2013;16:192-200.
100. Mauri G, Sconfienza LM, Pescatori LC, Fedeli MP, Alì M, Di Leo G, *et al.* Technical success, technique efficacy and complications of minimally-invasive imaging-guided percutaneous ablation procedures of breast cancer: A systematic review and meta-analysis. Eur Radiol 2017;27:3199-210.
101. Klintberg IH, Larsson ME. Shall we use cryotherapy in the treatment in surgical procedures, in acute pain or injury, or in long term pain or dysfunction?-A systematic review. J Bodyw Mov Ther 2021;27:368-87.
102. Theodorescu D. Cancer cryotherapy: Evolution and biology. Rev Urol 2004;6 Suppl 4:S9-19. Vergnon JM, Schmitt T, Alamartine E, Barthelemy JC, Fournel P, Emonot A. Initial combined cryotherapy and irradiation for unresectable non-small cell lung cancer. Preliminary results. Chest 1992;102:1436-40.
103. Seror O. Ablative therapies: Advantages and disadvantages of radiofrequency, cryotherapy, microwave and electroporation methods, or how to choose the right method for an individual patient? Diagn Interv Imaging 2015;96:617-24.
104. Stoff JA. A Multimodal strategic approach to integrative oncology. Asian J Immunol 2022;6:1-39.
105. Johnston MH. Cryotherapy and other newer techniques. Gastrointest Endosc Clin N Am 2003;13:491-504.
106. Mercader C, Musquera M, Franco A, Alcaraz A, Ribal MJ. Primary cryotherapy for localized prostate cancer treatment. Aging Male 2020;23:1460-6.
107. Shah TT, Ahmed H, Kanthabalan A, Lau B, Ghei M, Maraj B, *et al.* Focal cryotherapy of localized prostate cancer: A systematic review of the literature. Expert Rev Anticancer Ther 2014;14:1337-47.
108. Kokoszka A, Scheinfeld N. Evidence-based review of the use of cryosurgery in treatment of basal cell carcinoma. Dermatol Surg 2003;29:566-71.
109. Firnhaber JM. Diagnosis and treatment of Basal cell and squamous cell carcinoma. Am Fam Physician 2012;86:161-8.
110. Tchanque-Fossuo CN, Eisen DB. A systematic review on the use of cryotherapy versus other treatments for basal cell carcinoma. Dermatol Online J 2018;24:13030/qt49k1c38t.
111. Garner KL, Rodney WM. Basal and squamous cell carcinoma. Prim Care 2000;27:447-58.
112. Kash N, Silapunt S. Cryotherapy and electrodesiccation& curettage for basal cell carcinoma. In: Basal Cell Carcinoma: Advances in Treatment and Research. United States: Nova Science Publishers, Incorporated; 2020. p. 101-20.
113. Thai JN, Sevrukov AB, Ward RC, Monticciolo DL. Cryoablation

therapy for early-stage breast cancer: Evidence and rationale. J Breast Imaging 2023;5:646-57.

114. Fine RE, Gilmore RC, Dietz JR, Boolbol SK, Berry MP, Han LK, *et al.* Cryoablation without excision for low-risk early-stage breast cancer: 3-year interim analysis of ipsilateral breast tumor recurrence in the ICE3 trial. Ann Surg Oncol 2021;28:5525-34.
115. Sabel MS, Kaufman CS, Whitworth P, Chang H, Stocks LH, Simmons R, *et al.* Cryoablation of early-stage breast cancer: Work-in-progress report of a multi-institutional trial. Ann Surg Oncol 2004;11:542-9.
116. Xiong T, Turner RM, Wei Y, Neal DE, Lyratzopoulos G, Higgins JP. Comparative efficacy and safety of treatments for localised prostate cancer: An application of network meta-analysis. BMJ Open 2014;4:e004285.
117. Nathan A, Ng A, Mitra A, Sooriakumaran P, Davda R, Patel S, *et al.* Comparative effectiveness analyses of salvage prostatectomy and salvage radiotherapy outcomes following focal or whole-gland ablative therapy (high-intensity focused ultrasound, cryotherapy or electroporation) for localised prostate cancer. Clin Oncol (R Coll Radiol) 2022;34:e69-78.
118. Takemura LS, Costa PH, Claros OR, Tourinho-Barbosa RR, Teles SB, Sanchez-Salas R, *et al.* Salvage local treatment for recurrent prostate cancer after focal therapy: A systematic review and meta-analysis. In: Urologic Oncology: Seminars and Original Investigations. Netherlands: Elsevier; 2024.
119. Mpourazanis G, Mpourazanis P, Stogiannidis G, Ntritsos G. The effectiveness of photodynamic therapy and cryotherapy on patients with basal cell carcinoma: A systematic review and meta-analysis. Dermatol Ther 2020;33:e13881.
120. Lv R, Sun Q. A network meta-analysis of non-melanoma skin cancer (NMSC) Treatments: Efficacy and safety assessment. J Cell Biochem 2017;118:3686-95.
121. Morton C, Horn M, Leman J, Tack B, Bedane C, Tjioe M, *et al.* Comparison of topical methyl aminolevulinate photodynamic therapy with cryotherapy or fluorouracil for treatment of squamous cell carcinoma *in situ*: Results of a multicenter randomized trial. Arch Dermatol 2006;142:729-35.
122. Woodrum DA, Kawashima A, Gorny KR, Mynderse LA. Targeted prostate biopsy and MR-guided therapy for prostate cancer. Abdom Radiol (NY) 2016;41:877-88.
123. De Marini P, Cazzato RL, Garnon J, Shaygi B, Koch G, Auloge P, *et al.* Percutaneous MR-guided prostate cancer cryoablation technical updates and literature review. BJR Open 2019;1:20180043.
124. Woodrum DA, Kawashima A, Gorny KR, Mynderse LA. Prostate cancer: State of the art imaging and focal treatment. Clin Radiol 2017;72:665-79.
125. Wimper Y, Fütterer JJ, Bomers JG. MR imaging in real time guiding of therapies in prostate cancer. Life (Basel) 2022;12:302.
126. Mathew MS, Oto A. MRI-guided focal therapy of prostate cancer. Future Oncol 2017;13:537-49.
127. Liao Y, Chen Y, Liu S, Wang W, Fu S, Wu J. Low-dose total body irradiation enhances systemic anti-tumor immunity induced by local cryotherapy. J Cancer Res Clin Oncol 2023;149:10053-63.
128. Machlenkin A, Goldberger O, Tirosh B, Paz A, Volovitz I, Bar-Haim E, *et al.* Combined dendritic cell cryotherapy of tumor induces systemic antimetastatic immunity. Clin Cancer Res 2005;11:4955-61.
129. Morrison PR, Silverman SG, Tuncali K, Tatli S. MRI-guided cryotherapy. J Magn Reson Imaging 2008;27:410-20.
130. Xu K, Li R. Imaging technology in cryosurgery. In: Modern Cryosurgery for Cancer. Singapore: World Scientific; 2012. p. 249-66.
131. Littrup PJ, Lee FT Jr., Rajan D, Meetze K, Weaver D. Hepatic cryotherapy state-of the-art techniques and future developments. Ultrasound Q 1998;14:171-88.
132. Bala MM, Riemsma RP, Wolff R, Pedziwiatr M, Mitus JW, Storman D, *et al.* Cryotherapy for liver metastases. Cochrane Database Syst Rev 2019;7:CD009058.
133. Ravikumar TS, Kane R, Cady B, Jenkins R, Clouse M, Steele G Jr. A 5-year study of cryosurgery in the treatment of liver tumors. Arch Surg 1991;126:1520-3.
134. Mascarenhas BA, Ravikumar TS. Experimental basis for hepatic cryotherapy. Semin Surg Oncol 1998;14:110-5.
135. Akay BN, Aydemir AT. Combining immunotherapy and targeted therapies with cryotherapy in patients with cutaneous metastatic melanoma. Dermatol Surg 2024;50:770-2.
136. Costello JT, McInerney CD, Bleakley CM, Selfe J, Donnelly AE. The use of thermal imaging in assessing skin temperature following cryotherapy: A review. J Therm Biol 2012;37:103-10.
137. Swenson C, Swärd L, Karlsson J. Cryotherapy in sports medicine. Scand J Med Sci Sports 1996;6:193-200.
138. Gao L, Yang L, Qian S, Tang Z, Qin F, Wei Q, *et al.* Cryosurgery would be an effective option for clinically localized prostate cancer: A meta-analysis and systematic review. Sci Rep 2016;6:27490.
139. Gage AA. Cryotherapy for oral cancer. JAMA 1968;204:565-9.
140. Wentzensen N, Chirenje ZM, Prendiville W. Treatment approaches for women with positive cervical screening results in low-and middle-income countries. Prev Med 2021;144:106439.
141. Cubie HA, Campbell C. Cervical cancer screening - The challenges of complete pathways of care in low-income countries: Focus on Malawi. Womens Health (Lond) 2020;16:1745506520914804.
142. Meneghel J, Kilbride P, Morris GJ. Cryopreservation as a key element in the successful delivery of cell-based therapies-a review. Front Med (Lausanne) 2020;7:592242.
143. Robinson D, Yassin M, Nevo Z. Cryotherapy of musculoskeletal tumors-from basic science to clinical results. Technol Cancer Res Treat 2004;3:371-5.
144. Aarts BM, Klompenhouwer EG, Rice SL, Imani F, Baetens T, Bex A, *et al.* Cryoablation and immunotherapy: An overview of evidence on its synergy. Insights Imaging 2019;10:53.
145. Yakkala C, Chiang CL, Kandalaft L, Denys A, Duran R. Cryoablation and immunotherapy: An enthralling synergy to confront the tumors. Front Immunol 2019;10:2283.
146. Pediconi F, Marzocca F, Cavallo Marincola B, Napoli A. MRI-guided treatment in the breast. J Magn Reson Imaging 2018;48:1479-88.
147. Cho S, Kang SH. Current status of cryotherapy for prostate and kidney cancer. Korean J Urol 2014;55:780-8.