

Harnessing ultrasound-guided cryoablation for breast cancer

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For more than 20 years, cryotherapy has been used to treat locally advanced prostate cancer, liver metastases and some renal cell carcinomas. More recently, there have been pilot studies to remove small cancers of the breast utilizing this technique.^{1,2}

Advantages of the technique include low-cost equipment, excellent patient comfort and safety, and fast recovery time. Several clinical trials have been performed, mostly with small lesions measuring 1.5 cm or smaller. However, cryoablation has also been successfully used in elderly patients with non-resectable breast cancer, or patients refusing surgery, with no recurrence in these individuals reported at 18 months.^{2,3,4} Cryoablation is already approved by the U.S. Food and Drug Administration for excision of small benign fibroadenomas.

In some reports, a proposed argument against cryoablation for tumors is that residual tumor could be left behind after treatment. However, very small tumors seem to be less affected. A report from a multi-institutional trial comprising 29 ultrasound-guided cryoablations of primary invasive breast cancers measuring 2 cm or smaller showed that complete ablation was achieved for tumors 1 cm and smaller. For tumors larger than 1 cm but smaller than 1.5 cm, complete ablation was achieved only in patients with pure invasive ductal carcinoma, with no DCIS component.

Cryoablation was not reliable for tumors measuring 1.5 cm and larger.⁵

For eligible small cancers based upon evidence-based criteria, this method could potentially eradicate both the tumor and margins. In the future, surgical lumpectomy for small lesions could be avoided in some instances. With the near future holding promise for fine-tuning immunotherapy for breast cancer, this trinity of ultrasound-guided cryoablation, freezing of any residual tumor and the tumor bed in situ, and focused immunotherapy could hold promise as an effective, three-part solution for patients with early small cancers. The extra benefit of avoiding the risks of surgical anesthesia and radiation therapy would be a worthwhile consideration.

Yet another benefit of cryoablation would include platelet aggregation and vascular stasis.⁶ In fact, cryotherapy has been recently described as a useful method of hemostatic therapy in patients with advanced prostate cancer and hematuria.⁷ The key to success, of course, would be in having clear tumor-free margins which, at this juncture, may be difficult to prove. Further studies would be warranted to confirm that no residual positive tumor margins would be left in the patient.

The potential side benefit of creating a cryo-immune response to tumors may hold promise. Indeed, triggering an immune response to fight



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The potential of cryoablation in breast cancer

- Cryoablation of very small breast cancers may hold promise, studies show.
- Augmented immune response against tumor-specific antigens is a secondary benefit; potential irradiation of systemic micrometastases and reduced tumor recurrence rate compared with results of surgical excision has been demonstrated in animal studies.
- Hemostasis as a secondary benefit has already been proven to be useful in prostate cancer studies.
- Studies suggest that cryoablation may be more cost effective and efficient than lumpectomy and radiation therapy. However, a potential challenge is confirming clear, tumor-free margins. Cancer size, type and extent must be considered.

tumor cells is one of the most exciting features of cryoablation. Alternative techniques such as radiofrequency ablation and laser irradiation result in complete coagulation necrosis and total protein denaturation in tumors. Therefore, the tumor-associated antigen would not be well-preserved with those methods. In comparison, cryoablation does not denature proteins, specifically tumor-associated antigens. This allows the patient's own immune system to fight tumor-associated antigens, by improving both the cytotoxicity of lymphocytes and the activation of natural killer cells.

This tumor-specific immune response stimulated by damaged cells may contribute to controlling metastases distant from the primary breast tumor. In fact, animal studies have demonstrated that high-freeze-rate cryoablation of breast cancer in mice generated a tumor-specific immune response that eradicated systemic micrometastases and reduced the tumor-recurrence rate compared with results of surgical excision.^{8,9} Another great feature of ultrasound-guided cryoablation is the easy visualization of the lesion in real time, and excellent tolerance by patients. The cold effect of cryoablation serves as an analgesic; the patient typically only requires limited local anesthesia without any sedation.

Treating small cancers with percutaneous ultrasound-guided cryoablation holds much promise. Not only does it represent an alternative to surgical intervention, but it also creates a

tumor-specific immune response stimulated by damaged cells. This cryoimmunologic response may contribute to controlling metastases far from the primary breast tumor.

Beyond breast cancer treatment, I believe cryotherapy holds much promise for other tumors, including prostate cancers. This would be particularly appealing to older patients with concerns about surgery, hormone-treatment side effects and radiation therapy risks.

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