It's Freezing to Death

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Percutaneous treatment of breast cancer was born out of the desire for immediate minimally invasive therapy along with the availability of a variety of emerging ablative tools. Several investigators have published the results of percutaneous ablation using cryoablation, radiofrequency ablation (RFA), laser, high intensity-focused ultrasound (HIFU), and microwave for benign tumors as well as breast cancer followed by confirmatory excision and pathology (reviewed in Ref. 1). Others have attempted percutaneous ablation with careful follow-up and periodic peritumoral bed fine-needle or core biopsy (reviewed in Ref. 1).

The study by Simmons et al. represents one of the first small multicenter phase I trials of an ablative instrument by a cooperative group, Alliance.² One of the advantages of using cryoablation is the ability to continuously monitor by handheld ultrasound the development and extent of the ablation zone. It can also be done potentially in an outpatient office setting. Despite this and like most of the percutaneous cryoablation studies, the results show a significant lack of complete ablation within the present parameters. The authors also studied the ability of magnetic resonance imaging (MRI) to determine complete ablation and reported a relatively poor negative predictive value. MRI in our own ablation studies with RFA only seems best suited for ruling out multicentric disease. MRI both overestimates and underestimates residual tumor.¹ However, the extent to which this is true is difficult to tell from the study of Simmons et al. as details of the scans as well as the pathology results are limited.

Credit goes to the principal investigator and coauthors for overcoming the multiple hurdles necessary to complete

this trial in the cooperative group setting. This is monumental in paving the way for other similar advanced technology surgical trials. However, it would seem that percutaneous cryoablation for breast cancer is on its way but is not quite ready for prime time. On subset analysis, the authors state that cryoablation would be best for lesions that are small, less than 1 cm, that do not contain ductal carcinoma in situ (DCIS), that are located deep to the skin and unicentric, and are discretely localized on MRI. Patients with DCIS are not candidates for such a procedure as an invasive component would need to be ruled out by complete sampling of tumor. Likewise patients with invasive lobular carcinoma are not considered candidates for percutaneous ablation. Having said this, relatively few patients would be candidates for such a procedure via cryoablation and that would require yet another phase I trial.

The other problem that the authors touch upon is the expertise needed for this procedure. The surgeon must place the needlelike probe in the 3-dimensional center of the tumor. The cryoablation is continually monitored until the ice ball covers the previously known tumor location with an additional margin. The authors attribute several of their failures to operator error in placing the needle, as well as underestimation of tumor size and multifocality.

We suggest a better path going forward would be to percutaneously excise the tumor with a vacuum-assisted or other percutaneous device followed by the ablation as we have done in a single-institution phase I trial with RFA.¹ This may or may not be possible with cryoablation with presently available needle probes. However, in this way, most if not all the tumor is retrieved for pathological examination, DCIS could be treated as well, and tumor tissue would be available for molecular analysis and research. The ablation would be to create a margin around the tumor bed. Removal of the tumor may allow the cryoablation to proceed more smoothly when considering

ablation of tumor versus fibroglandular tissue, the mechanics of which may be substantially different.

An alternative approach, which would be more readily applicable and require much less expertise, would be open excision of breast tumors followed by pericavitary ablation. We have demonstrated the feasibility of this concept in both a single-institution trial as well as a multicentric phase II trial using RFA without radiation.^{3,4} In this way, less expertise is needed, more patients can qualify for the procedure (same as partial breast), and the devices are used for their FDA-approved purpose—soft tissue ablation—and as such are billable. More importantly, in small favorable tumors, if I had to withhold surgery versus radiation, I would much rather obviate the need for radiation. The fact is that in the National Surgical Adjuvant Breast and Bowel Project (NSABP) B-21 trial where patients with favorable tumor with a size of 1 cm or less were randomized to tamoxifen, radiation, or both, more than 85 % of the patients did not benefit from the addition of radiation.⁵ The problem has always been in telling who will benefit or will not. In an era when we know for such tumors brachytherapy is an acceptable alternative, intraoperative pericavitary ablation may be an oncological equivalent, cosmetically more acceptable, and less

expensive alternative to breast irradiation in the patient with a small favorable tumor.

Many do not appreciate what it takes to get a trial like this initiated. Gratitude to Dr. Rache Simmons and her coinvestigators for persisting and paving the way for new technologies within the cooperative group mechanism.

REFERENCES

1. Klimberg VS, Boneti C, Adkins LL, et al. Feasibility of percutaneous excision followed by ablation for local control in breast cancer. *Ann Surg Oncol*. 2011;18:3079–87.
2. Simmons R, Ballman K, Cox C, Ballman K, Cox C, Carp N et al: A phase II trial exploring the success of cryoablation therapy in the treatment of invasive breast carcinoma: Results from ACOSOG (Alliance) Z1072. *Ann Surg Oncol*. 2016. doi:[10.1245/s10434-016-5275-3](https://doi.org/10.1245/s10434-016-5275-3).
3. Klimberg VS, Ochoa D, Henry-Tillman R, et al Long-term results of phase II ablation after breast lumpectomy added to extend intraoperative margins (ABLATE 1) trial. *J Am Coll Surg*. 2014;218:741–9.
4. <https://clinicaltrials.gov/ct2/results?term=Klimberg+and+RFA&Search=Search>. Accessed March 5, 16.
5. Fisher ER, Costantino JP, Leon ME, Bandos H, Palekar AS, Fisher B et al. Pathobiology of small invasive breast cancers without metastases (T1a/b, N0, M0): National Surgical Adjuvant Breast and Bowel Project (NSABP) protocol B-21. *Cancer*. 2007;110:1929–36.