

Image-guided Percutaneous Ablation of Small Breast Cancer: Which Technique is Leading the Pack?

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In the past few decades, the surgical treatment of early breast cancer has evolved from radical mastectomy to breast conservation surgery and the current practice of segmental mastectomy and radiotherapy. As these less invasive techniques have gained acceptance with excellent long-term rates of local-regional control, there has been a growing interest in the surgical community in techniques to ablate the primary tumor percutaneously with the ultimate goal of omitting the need for surgical excision of the primary tumor.

There are two basic categories of techniques that are used to physically destroy the breast tumor in situ: 1) those that heat up the tumor to a sufficient temperature during a prescribed time sequence to achieve the denaturation of proteins and result in coagulation necrosis that will encompass the entire tumor (thermal therapy) and 2) those that freeze the tumor long enough to achieve cell death (cryotherapy). Recently, however, irreversible electroporation, which uses a different physical approach and can be compared to the “electrocution” of the tumor, has been introduced in the arena of percutaneous ablation techniques. Irreversible electroporation is still early in its development for the treatment of breast lesions and will not be discussed in detail here.

Ablation of small breast cancers is different from all other applications of percutaneous ablation, which were designed for palliation and improvement of quality of life in patients with a poor prognosis or in whom there are no other treatment options (*e.g.*, radiofrequency ablation (RFA) or cryotherapy of liver metastases, RFA of bone metastases, and cryotherapy of prostate cancer). In early stage breast cancer, the challenge for choosing to use such minimally invasive treatment is that the prognosis is excellent with standard surgical approaches, and if the “new” treatment fails, the patient may have a delay in curative therapy. Another major limitation to the development of percutaneous ablation for breast cancer is the inability to verify the completeness of ablation and the margins of the ablated tumor histologically if the tumor is not excised.

With the exception of a few studies done under stereotactic guidance, the vast majority of percutaneous ablation techniques have been performed using ultrasound (US) or magnetic resonance imaging (MRI) guidance. US guidance is preferred for the techniques that require the insertion of a needle or probe because of the unique advantage of real-time imaging with US. A prerequisite for success of any US-guided ablation technique is the very accurate placement of a probe in the geometric center of the small tumor. Ultrasound imaging is best performed by an

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experienced operator familiar with all possible artifacts and pitfalls associated with US. MRI guidance is preferred over US for high-intensity focused ultrasound (HIFU), also known as focused ultrasound (FUS), the only technique that is performed without the insertion of a device inside the tumor.

Thermal ablation techniques “heat” the tumor with the use of radiofrequency currents (RFA), laser irradiation, microwave irradiation, or HIFU. Of all the thermal therapy techniques, the one that has been tested the most is RFA, probably because of its many applications to other organ sites and its previous relative successes in the palliative ablation of liver and bone metastases.

Numerous “feasibility” studies of RFA ablation of breast cancer have been published since the first report by Jeffrey *et al.* in 1999 (1). These studies generally targeted T1 tumors and were small series of less than 30 patients. In most studies, the US-guided procedures were performed by surgeons (1-6). The completeness of ablation when pathological examination of the surgical specimen was performed rarely reached 100% in the targeted lesion. At MD Anderson Cancer Center, we achieved excellent results due in part to the careful selection of patients and target-lesions by the team approach of a radiologist experienced in US-guided breast interventions and a breast surgeon (7). After completing our study, it became clear that RFA was associated with two specific drawbacks that would be difficult to overcome. First, it was difficult to monitor the procedure in real-time as the region surrounding the small tumor became rapidly and diffusely echogenic from the very beginning of the procedure, thereby obscuring the tumor and preventing assessment and adjustments to the amount of damage inflicted to the tissues. Second, heating tissues at 95 degrees Celsius during 15 minutes results in significant patient discomfort as confirmed by reports of attempts to perform the procedure under local anesthesia by some clinicians. Therefore specific techniques for pain control such as heavy sedation or paravertebral blocks would be necessary. We have not pursued RFA for breast tumor ablation at our center.

Few thermal ablation studies have been performed using laser irradiation with US or MRI guidance. The effectiveness of ablation with laser has been lower than that reported with RFA (8, 9). A recent study of US-guided ablation using microwave irradiation under general anesthesia demonstrated 95% effectiveness in complete ablation with a few complications including thermal injuries to the skin and pectoralis major muscle (10).

Significant interest was generated when the technique of HIFU or FUS, which is derived from the successful lithotripsy, was developed and began to be used under US guidance in China and MR-guidance in Canada and Israel (11, 12).

The concept of treating from outside of the breast without a probe inserted through the tumor and using sophisticated MRI guidance is certainly attractive (13). However, as the treatment duration is long and the risk of the target lesion moving during the procedure is high, interest has waned. In addition, the procedure is painful, results have not been up to the expectations (12), and the cost of MR-guided or even US-guided FUS machines remains prohibitive.

At the same time that thermal ablation techniques were tested, investigators also started to examine cryotherapy as a method to ablate breast tumors. The interest initially focused on fibroadenomas, with initial results being touted as excellent but soon some inconsistencies surfaced (14). In parallel, however, studies showed that cryotherapy of small breast cancers could be as effective as RFA if performed by operators experienced in US imaging and after proper selection of cases, with the technique achieving the best results on smaller lesions (15-18). Most importantly, two limitations of thermal therapy, the pain and the inability to monitor the changes in the tissues with US are not limitations of cryotherapy. During cryoablation, there is formation of an iceball which is neatly visualized and controlled with real-time US and the procedure is virtually painless as the cold temperatures are anesthetic. At MD Anderson, we perform the procedure with local anesthesia (for the insertion of the cryoprobe) and no sedation with patients reporting no pain during or after the procedure. The procedure has been well accepted and tolerated by patients and is truly a minimally invasive “patient-friendly” procedure.

There is another theoretical advantage to the use of cryotherapy as it has been suggested that the cryoablation not only causes cell death but also induces an immunologic response, which might reduce the risk of recurrent and metastatic disease (19). This is still being investigated as part of the ongoing clinical trial Z1072, by the American College of Surgeons Oncology Group (ClinicalTrials.gov identifier: NCT00723294), which aims to evaluate the efficacy of cryoablation of small breast cancers and the utility of MRI to predict complete ablation of the tumor.

At this time, cryoablation—especially with recent development of argon-based machines employing very thin cryoprobes—emerges as the technique that does the job with a high cost-effectiveness ratio and is the easiest for the interventionist and the patients. However, the use of all the various image-guided ablation techniques for breast cancer has raised numerous questions that will need to be addressed before one (or more) technique(s) can be used as a replacement to the standard surgical resection of early breast cancers, ranging from the issue of selecting patients to the difficulties of providing an adequate assessment of the completeness of ablation with imaging and/or biopsies (7).

Conflict of Interest

None of the authors has a conflict of interest.

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