MR imaging–guided breast ablative therapy

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There has been a change in the management of cancer patients with localized disease, from total mastectomy to lumpectomy complemented by adjuvant radiotherapy or chemotherapy, without significant difference in clinical outcome [1–6]. Early detection of smaller breast lesions [7] may further change the attitude toward less invasive and even noninvasive management. Because open surgical excision of breast lesions carries the risks of anesthesia-related complications, hemorrhage, infection, and scarring and disfigurement, minimally invasive percutaneous or noninvasive ablative procedures offer an alternative for tumor control. To achieve wide acceptance, minimally invasive therapies must, in the long-term, achieve equivalent or even greater efficacy as surgical outcomes and, in the short-term, demonstrate total ablation of the dominant lesion with negative margins, while sparing normal tissue beyond the target tissue. Using in situ ablative methods pathologic samples are not obtainable and radiologic assessment must replace histopathology. The lack of pathologic specimen after ablative therapies is a major argument against these minimally invasive approaches. Their practicability has to be justified with greater cosmesis and patient comfort and reduced hospital stays and cost savings.

Minimal requirements for image-guidance

The primary requirements of imaging in minimally invasive ablative therapies are to enable the clinician to localize the tumor and its surrounding anatomic structure, define the targeted tissue volume, optimize the trajectory through which the therapy is introduced, monitor the temperature or the thermal effects during energy deposition in real time, and control the amount of energy deposited and the spatial extent of ablation. Although X-ray mammography and ultrasound (US) are commonly used in tumor localization, MR imaging demonstrates a much higher sensitivity, approaching 100% [8,9], that can be used for target definition. When one takes into consideration the sampling error [10] in tumor margin definition associated with intraoperative histopathologic examination, this sensitivity is appealing even if it is associated with relatively low spatial resolution. The promising evolution of breast MR imaging at higher field strength (ie, 3 T and higher) and refinement of techniques and interpretation of dynamic contrast enhancement may help to reduce rates of false-positives and further improve sensitivity.

The temperature sensitivity of various MR imaging parameters (T1 [11,12], proton resonance frequency shift [13,14], and diffusion [15]) can be exploited for detecting temperature changes. The technique that has emerged as the most practical is water proton resonance frequency shift or phase imaging [16]. This method, however, does not work in the presence of fat. Because the breast contains mostly fatty tissues, infiltrative breast cancer may coexist with normal fatty breast. Temperature-sensitive methods that work in this case are under development [17,18].

Temperature resolutions approaching 1°C are possible and the critical temperature for tissue necrosis, typically around 60°C, can be detected. Critical dose, or time-temperature relationships, can also be used to verify effective treatment [19].

Before any of the available ablative methods supplant conventional surgery and can be offered...
safely to patients, it is essential to demonstrate the procedures are not only safe but efficacious and reliable image guidance can be provided. Most clinical trials of minimally invasive ablative therapies of breast cancer have involved immediate or delayed surgical resection of the treated lesion. The efficacy of the treatment can be histopathologically verified. Several adept reviews of minimally invasive therapy for the breast [20–22], some focusing on MR imaging guidance [23,24], have been published that begin to address these concerns and ask the ethical questions involved with alternative treatments of disease with already favorable prognosis.

**MR imaging–guided lumpectomy**

The goal of open surgical excision or lumpectomy is to achieve negative margins, usually 1 cm, around the tumor. One study correlating MR imaging with histopathology showed MR imaging has a sensitivity of 94% and a specificity of 37% [25]. Frozen section histopathology analysis reveals about half of lumpectomy surgeries exhibit positive margins [26–28]. Many of these patients require a second excision. MR imaging has been used to detect residual tumor following lumpectomy with above 80% agreement with histopathology obtained in a re-excision [29]. In one postsurgical MR imaging study [30], planned surgical management was altered in 69 (26%) of 267 patients; in 49 of those patients (71%) there was pathologic verification of malignancy in the surgical specimen that confirmed the need for wider or separate excision or mastectomy. In another 80-patient study [31], MR imaging changed which procedure was performed next from re-excision lumpectomy to mastectomy (N = 9); biopsy of an additional lesion in the ipsilateral (N = 12) or contralateral (N = 2) breast; or neoadjuvant chemotherapy (N = 1). Bringing this diagnostic ability into the realm of the operating room.

![Fig. 1. (Top) Precontrast and postcontrast images acquired intraoperatively before resection. The arrow indicates the target tumor. (Bottom) Precontrast and postcontrast images acquired after the surgeon completed resection to her satisfaction. Imaging revealed residual tumor (arrow), which was confirmed by histopathology. (From Hirose M, Kacher DF, Smith DN, Kaelin CM, Jolesz FA. Feasibility of MR imaging–guided breast lumpectomy for malignant tumors in a 0.5-T open-configuration MR imaging system. Acad Radiol 2002;9:933–41; with permission.)](image)
may influence the surgical decision process and improve completeness of resection.

Two lumpectomy studies have been performed with mid-field MR imaging guidance (0.5 T Signa SP, General Electric Medical Systems, Milwaukee, Wisconsin). Gould et al [32] reported close agreement between maximum dimensions of MR imaging localization of benign breast lesions (N = 10) and histopathologic examination (P > .17). All post-procedure scans demonstrated complete resection. Hirose et al [33] reported MR imaging–guided lumpectomy for patients with an invasive breast cancer diagnosed by core needle biopsy. All tumors (N = 20) were localized with MR imaging. Postresection contrast-enhanced MR imaging enabled intraoperative evaluation of the surgical bed to assess for residual tumor (Fig. 1). MR images were compared with gross and permanent histopathology margin assessment (Table 1). These preliminary results are promising; however, definitely more sensitivity is necessary, which can be achieved with both improved coil design and higher field strength.

### Laser interstitial thermal therapy

Laser interstitial thermal therapy is a minimally invasive technique for local tumor ablation that can be monitored by MR imaging [34]. LITT has been used successfully for the treatment of benign fibroadenoma [35,36] and is being studied as treatment for breast cancer in a number of institutions [24,37–39]. During LITT, light energy is delivered by percutaneous optical fiber directly to tissue and creates a zone of thermal ablation. Optical fibers are inherently MR imaging–compatible and can be extended such that the laser device can be situated outside the scanner room. The light energy does not affect and is not affected by MR imaging. A single fiber or multiple fibers with a beam splitter can be used. Diffusing tips enable treatment of greater volumes, compared with bare fibers, at the expense of increasing effective fiber diameter [40,41]. An important additional advantage of the diffuser is that a larger region can be treated over its entire length in one session, whereas the bare fiber needs to be pulled back several times or used in conjunction with multiple fibers.

Laser interstitial thermal therapy can be the direct extension of a breast biopsy, because the fiber is commonly placed through the outer cannula of a needle. The targeting needle should be pulled back far enough over the optical fiber as not to obscure the region of interest with susceptibility artifact. A brief test delivery of optical energy during temperature-sensitive imaging can confirm the location of the fiber tip. Use of imaging systems at field strengths as low as 0.2 T has been reported for breast LITT (Fig. 2) [42]. During LITT a region of T1-hypointense signal appears around the optical fiber tip, first appearing at around 30 seconds after the start of treatment and reaching a plateau at its maximum size at about 270 to 400 seconds [43]. Phase imaging may also be used for temperature and dose monitoring.

Macroscopically, an LITT-induced lesion in the breast consists of a central charred cavity surrounded by a broad area of pale tissue and a peripheral hemorrhagic rim beyond which is viable tumor [44]. Microscopically, the pale zone of tissue shows in situ heat fixation characterized by cells that are morphologically normal but have hyperchromatic, smeared nuclei and hypereosinophilic cytoplasm consistent with the presence of coagulated proteins. The extent of in situ fixation is variable, depending on the site of laser fiber in the tumor and its relationship to normal breast tissue and fat. The hemorrhagic rim contains cells that are less damaged whose nuclei are only slightly hyperchromatic and retain their chromatin.

### Table 1

Margin comparison of the postresection MR image with intraoperative gross pathology and permanent pathology

<table>
<thead>
<tr>
<th>Postresection MR image</th>
<th>Intraoperative gross pathology evaluation</th>
</tr>
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<tbody>
<tr>
<td>True-positive</td>
<td>True-positive</td>
</tr>
<tr>
<td>True-negative</td>
<td>4(a)</td>
</tr>
<tr>
<td>False-positive</td>
<td>1(d)</td>
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<tr>
<td>False-negative</td>
<td>5</td>
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\(a\) Concordance among all three evaluation modalities.

\(b\) Concordance between postresection MR image and gross histopathology, with both discordant with permanent histopathology.

\(c\) Re-excision prompted by a true-positive postresection MR image, sparing these four patients a second surgery.

\(d\) Unnecessary re-excision was prompted by a false-positive postresection MR image.
pattern and nucleoli. These cells become surrounded by proliferating fibroblasts, blood vessels, and extravasated red blood cells.

The maximum measurement of this region of signal loss corresponds to the extent of thermal damage mapped histopathologically [45]. Delayed follow-up of treatment effect may be made using contrast-enhanced MR imaging [44]. The extent of laser damage is seen as areas of nonenhancement and these correspond with areas of necrosis seen histopathologically.

Mumatz et al [44] correlated preprocedural and postprocedural MR imaging with histopathology in a 20-patient study of women with proved breast cancer. The correlation coefficients of delayed gadolinium-enhanced images for the laser-burn diameter and residual tumor were 0.80 and 0.86, respectively. Akimov et al [46] report on 35 patients with primary breast cancer who underwent LITT with no image guidance. Twenty-eight of these patients underwent radical resection. Of seven patients treated without surgery, local tumor control was achieved in five. Harms et al [36] reported on a series of 25 women diagnosed with fibroadenoma treated with LITT guided by images acquired with a conventional diagnostic closed-bore 1.5-scanner. Although there was no histopathology correlation available, tumor sizes were reduced at 5 months (mean >75% reduction in tumor size) as assessed on US or MR imaging follow-up imaging. Dowlatshahi et al [38] found complete necrosis in 66% of malignant neoplasms treated in 35 patients using X-ray mammography guidance. Total tumor ablation with negative margins was observed whenever 2500 J/mL of tumor was delivered or when the temperature sensor adjacent to the laser fiber recorded 60°C.

Radiofrequency ablation therapy

Radiofrequency ablation (RFA) refers to the destruction of tissue by the application of electro-
magnetic fields, created by interstitial electrode delivery of high-frequency waves (0.4–8 MHz). Current density is induced in the tissue, causing resistive heating. Current is returned through a gel pad electrode placed on the thigh or back. Radiofrequency power deposition is a function of tissue conductivity and is difficult to predict and control. The formation of the lesion may be inhomogeneous, especially in regions of tissue boundaries. Various developments in probe geometry, and cooling of probe shafts to prevent charring, enable creation of large regions of necrosis in comparison with LITT fibers and cryoablation probes. In the breast where larger lesions are not germane for thermal ablation radiofrequency has no specific advantages over laser or cryoablation. Susceptibility artifacts around the probe during MR imaging prevented accurate temperature monitoring. Recently, however, MR imaging–compatible probes approved by the Food and Drug Administration have become available from several vendors. No commercial solution is available to remedy the problem of electromagnetic interference emitting from the radio-frequency generator manifesting itself as noise in the MR images. Several research sites have implemented gating [47] or filtering solutions. A growing concern is patient burns as the use of high-field imaging and fast pulse sequences increases. The greater specific absorption rate may be a concern for heating at the site of the return electrode pad, beyond the nominal heating caused by the treatment.

Although MR imaging–guided RFA [48] for various indications and RFA of breast are independently growing in popularity, there have yet to be any published reports of MR imaging–guided RFA of the breast. Animal studies, treatments with no guidance, X-ray mammography guidance, US guidance, and pre- and post-MR imaging studies, however, have been performed before surgical excision and pathology.

Boehm et al [49] compared vacuum-assisted biopsy only (N = 10) with vacuum-assisted biopsy followed by US-guided RFA (N = 10) in implanted tumors in a rabbit model. Local recurrences occurred in 8 of 10 cases (80%) after vacuum excision alone, whereas recurrence after combined excision and RFA occurred only in 2 of 10 cases (20%; P < .05). In an extension of this study [50], local relapses occurred in 51.8% of tumors. In 42% of cases, they were already detected sonographically. In two cases, “islands” of vital tumor were detected only during histopathologic assessment. The authors conclude B-mode US is not suitable for guiding RFA ablation of tumors embedded in fat. McGahan et al [51] used domestic swine (N = 3) to study US-guided RFA of 18 sites in normal mammary tissue. Histopathologic examination was performed immediately after (acute animal), 2 weeks after (subacute animal), and 4 weeks after (chronic animal) treatment. In the acute animal, lesions were firm nodules on palpation and had a distinct line of demarcation between necrotic and viable mammary tissue. In the subacute animal, there was diffuse coagulation necrosis with neutrophilic infiltrates at the periphery. In the chronic animal, lesions were still palpable with firm fibrotic tissue that blended with the surrounding tissue. Secondary bacterial infection was noted in two treatment areas.

Izzo et al [52] performed RFA on 26 patients with invasive breast carcinoma, with no image-guidance, followed by immediate resection. Treatment was planned to ablate the tumor and a 5-mm margin of surrounding breast tissue. Complete necrosis was achieved in 96%. A full skin thickness burn was noted over the ablation site in one patient. Elliot et al [53] report a case study of a nonpalpable breast tumor X-ray mammographically guided RFA. There was no definite viable residual tumor and the margins were clear.

Multiple centers have reported on US-guided RFA of breast tumors. Fornage et al [54] report 21 malignant lesions in 20 patients were ablated immediately before lumpectomy or mastectomy. In all 21 cases, complete ablation of the target lesion was visualized with US; one patient had residual invasive cancer not seen on US or mammography. Jeffrey et al [55] report intentional partial RFA in five patients followed by immediate resection. Complete necrosis was achieved in two patients, whereas histopathology revealed heterogeneous pattern of necrotic and normal-appearing cells within the ablated tissue (Fig. 3). Hayashi et al [56] noted central ablation zone surrounded by hyperemia in the 19 patients of their study. Coagulative necrosis was complete in 86% of patients. Disease at the ablation zone margin was found in three patients, and five patients had disease distant to the ablation zone consisting of multifocal tumors (N = 2), in-transit metastasis (N = 1), and extensive ductal carcinoma in situ with microinvasive carcinoma (N = 2).

Burak et al [57] report US-guided RFA in 10 patients followed by MR imaging and resection. A pre-RFA MR imaging scan showed enhancing tumors in 9 (90%) of 10 patients. A post-RFA MR imaging scan revealed no residual lesion enhancement in eight of these nine patients (89%), and the zone of ablation was demonstrated in all patients. One patient had residual enhancement anteriorly consistent with residual tumor, which was confirmed histopathologically. Evaluation of the remaining
Ablated lesions revealed a spectrum of changes ranging from no residual tumor to coagulation necrosis with recognizable malignant cells. Immunostains for cytokeratin 8/18 were negative in these recognizable malignant cells. A 5-year outcome study is planned by Singletary et al[58,59] with US-guided breast RFA as the sole treatment.

**Microwave ablation therapy**

Both superficial focused phased array and percutaneous microwave have used hyperthermia and tissue ablation, respectively. Energy is typically on the order of 1 GHz. The focused phased array microwave procedure entails compressing the breast between two waveguide applicators. Skin cooling is typically necessary. The energy preferentially heats the high-water-content breast carcinomas, compared with surrounding adipose and glandular tissues. Percutaneous temperatures probes can also serve as an antenna to guide the microwave energy. The approach for percutaneous treatment is similar to RFA, except treatment areas are typically smaller. Multiple tracks must be used to treat large tumors.

The focused phased array device developed by Fenn et al[60] has been tested in animal models and underwent trials for breast cancer treatment at several...
institutions. A series of 10 patients \[61\] resulted in a size reduction in 60% of cases as seen on US and necrosis in 80% of cases as assessed by histopathology. Another series of 25 patients \[62\] achieved pathologic necrosis in 68% of patients and complete necrosis of the invasive component was achieved in two patients. An earlier device was used to treat chest wall recurrences from breast cancer \[63\]. Eight patients in 42 cases were treated with hyperthermia or in conjunction with chemotherapy. No complete response was observed in either set of patients. Like RFA, experience with MR imaging–guided microwave ablation has yet to be published. Other indications for percutaneous microwave ablation have been shown to be technically feasible, however, at 2-T MR imaging units \[64\]. The safety and efficacy of the procedure was shown in a series of 34 treatments of liver tumors (Fig. 4) \[65,66\]. This practice easily could be extended to percutaneous breast ablation.

**Focused ultrasound surgery**

Focused US surgery (FUS) is a completely non-invasive, trackless ablation method \[67\]. Focal heating of target tissue is achieved by deposition of acoustic energy (1 – 2 MHz) generated by a spherical piezoelectric transducer array. The transducer is acoustically coupled with a water bath to the breast of prone patients. A temperature elevation to 55°C to 90°C is produced during a 10- to 20-second sonication. With a first-generation single-transducer system (General Electric Medical Systems, Milwaukee, Wisconsin) \[68\], a thermal lesion with a size of approximately 4 × 4 × 7 mm\(^3\) was produced \[69\]. With a second-generation system (ExAblate 2000, InSightec, Haifa, Israel) that uses a phased array transducer consisting of hundreds of transducer elements, however, the lesion size can be increased substantially. The transducer is then moved or refocused to treat a prescribed area with software control outside the scanner room and actuators in the patient table \[68,70\]. The goal is to achieve a well-defined area of irreversible cell damage, protein denaturation, and coagulation necrosis, while sparing overlying and surrounding tissues. With the first-generation system, the treatment time was long; for a 2-cm lesion the treatment time was approximately 2 hours and for a 1-cm lesion, approximately 45 minutes. The treatment time with the second-generation system can be reduced substantially to the larger lesion size that can be created with each sonication. MR imaging guidance has proved invaluable to visualize the lesion, target with the FUS focal spot position, and monitor and control beam dosimetry \[71–73\].

The feasibility of guiding FUS treatments with MR imaging has been reported with biopsy-proved fibroadenoma \[74\] and breast cancer \[75,76\]. These studies were performed with a 1.5-T closed-bore MR imaging scanner (GE Medical Systems, Milwau-
Chung et al [77] and Mulkern et al [78] reported on nine women with 11 lesions (mean volume 1.9 cm$^3$) who underwent partial ablation of their lesions. Partial or total success was reported in 73% of treatments. Problems included motion and undertreatment because of conservatively low power settings in early cases or beam reflection caused by formation of gas bubbles (cavitation) or injection of local anesthetic. General anesthesia, which prevents problems with motion, is not used because of the need for feedback from the patient regarding pain or discomfort. Additional challenges include difficulty in monitoring temperature and dose in perilesional fat using phase difference techniques and tumor margin treatment cannot be verified intraprocedurally.

The target volume is outlined on T2-weighted images, in the plane perpendicular to the US beam (Fig. 5). Phase-difference images for monitoring the temperature during therapy are shown in Fig. 6 and demonstrate the temperature increase in the focus during sonication, the slight temperature spreading, and the temperature decrease in the focus after the 10-second sonication. Treatment was assessed with contrast-enhanced long-term follow-up images, as shown in Fig. 7. The fibroadenoma in the upper portion of the left breast was treated in a 1-hour and 15-minute session. After therapy, there was no evidence of contrast material enhancement up to 3 years after FUS. Surrounding edema was visible up to 2 days after therapy. After 3 years, the lesion is visible as only a small hypointense area of reduced signal intensity on nonenhanced T1-weighted images.

Gianfelice et al [75] reported on 12 patients with invasive breast carcinomas who underwent FUS. Correlation between histopathologic analysis of resected tumor sections and MR imaging revealed 95.6% of the tumor was within the targeted zone and a mean of 88.3% of the cancer tissue was necrosed in their later series. Residual tumor was identified predominantly at the periphery of the tumor mass. The group concluded the treatment area should be increased. In more recent work [79], the group showed good correlation between residual tumor and dynamic contrast-enhanced MR imaging. Huber et al [76] reported on a FUS treatment in a single core biopsy-proved invasive breast cancer patient. Immunohistochemistry of the resected specimen demonstrated that FUS homogeneously induced lethal and sublethal tumor damage with consecutive

Fig. 5. Fat-suppressed T2-weighted fast spin echo MR images (2500/100) obtained for planning on the day of treatment of a fibroadenoma. The patient is lying in a prone position, with the breast positioned on the water pillow. The transducer is outlined at the bottom. Transverse sections (A, C) and the corresponding coronal sections (B, D) of the planning target volume outlined in two sequential planes are shown. The positions of the treatment foci are demonstrated in B and D. (From Hynynen K, Pomeroy O, Smith DN, Huber PE, McDannold NJ, Kettenbach J, et al. MR imaging–guided focused ultrasound surgery of fibroadenomas in the breast: a feasibility study. Radiology 2001;219:176–85; with permission.)
up-regulation of p53 and loss of proliferative activity. With the exception of minor skin burns, no complications occurred in these studies.

Cryoablation

Cryoablation is a method used to ablate tumor tissue using freezing temperatures. Early application of cryoablation for treatment of breast lesions has evolved and today delivery systems with liquid nitrogen cooled [80] or nozzled gas (Joule-Thompson effect) cooled probes [81] make a percutaneous approach possible. MR imaging guidance is well suited as a guidance and monitoring modality. As the probe cools the surrounding tissue, the tissue water crystallizes. In most MR imaging sequences, the solid ice crystals give no measurable MR imaging signal and the edges of the iceball are well delineated even without postprocessing techniques. Because of T2* shortening in frozen tissue, the expanding iceball appears as an increased area of signal void in MR images. Alternatively, with ultrashort echo times, a temperature map within the iceball may be derived [82]. The suitability of MR imaging guidance is bolstered by the fact that the freezing interface moves slowly enough to image the therapy in real-time [83].

Several mechanisms work in synergy to cause necrosis from cryoablation. Extracellular ice forms, rejecting solutes from the growing crystal. The lipid bilayer of the cell membrane transitions into a gel phase and becomes more permeable, allowing ions to enter the cell. High ion concentration disrupts functioning of the cell when it is returned to normal temperature [84]. A second mechanism is simple mechanical damage [85]. Low temperature weakens the bonds between the membrane proteins and the cell scaffold. Stress placed on the membrane by formation of ice crystals promotes this damage [86]. A third mechanism is the direct effect of protein denaturation because of the low temperatures and high intracellular ionic content. Rapid cooling favors the freezing of intracellular water and prevents equilibration (ie, water leaving the cell), and is more

Fig. 6. Temperature-sensitive fast spoiled gradient echo phase-subtraction MR images (27.3/13.5) of a single 10-second therapeutic sonication in the tumor. MR image on the top shows the temperature elevation at the end of a sonication during therapy in the tumor in Fig. 2A, with proton resonance frequency imaging. The temperature focus appears as a small hyperintense spot in the breast. MR images on the bottom show the temperature time-course of the same sonication in the region of interest. The indicated temperature increase is above body temperature. (From Hynynen K, Pomeroy O, Smith DN, Huber PE, McDannold NJ, Kettlenbach J, et al. MR imaging–guided focused ultrasound surgery of fibroadenomas in the breast: a feasibility study. Radiology 2001;219:176–85; with permission.)
likely to cause cell death. During thawing, ice has a tendency to recrystallize, disrupting the macroscopic structure of the tissue. As the extracellular ice melts, the extracellular solution becomes hypotonic, causing water to enter the cell, possibly rupturing the weakened membrane. Slow thawing favors cell death. Secondary cell death, over the course of days, is believed to be caused by ischemia because of disruption of microvasculature [87].

Ex-vivo [88], animal model [89,90], and clinical trials for breast cancer [88,90–98] and fibroadenoma [99] studies involving cryoablation of the breast have been reported. An US-guided percutaneous study concluded that the invasive components of small tumors can be successfully treated using cryoaulation; however, remnant ductal carcinoma in situ components seen in postmastectomy histopathology, which may not be detected preprocedurally,
represent a challenging problem for complete ablation [100].

An ongoing study by Morin et al [101] aims to demonstrate that MR imaging–guided percutaneous cryoablation is feasible, safe, and efficacious in the treatment of invasive breast carcinoma. Twenty-five patients diagnosed with invasive breast carcinoma having indications for a lumpectomy or a total mastectomy underwent cryoablation and Tc99m-sestamibi scintimammography before surgery. The cryoablation procedure was monitored under the near-real-time imaging mode of a 0.5-T open-configuration MR imaging system (Signa SP, General Electric Medical Systems, Milwaukee, Wisconsin). Patients were positioned supine with no compression device; however, the breast was transfixed with an 18-gauge puncture needle through the long axis of the tumor (Fig. 8). The tumor was first targeted with introducers using a free-hand technique. Two 3-mm diameter MR imaging–compatible cryoablation probes (Cryo-Hit, Oncura, Plymouth Meeting, Pennsylvania) were then positioned in a head-on configuration at the center of the lesion. Images were acquired with a standard transmit-receive linear surface square coil placed directly onto the treated breast (Fig. 9). The protocol involves encompassing the targeted lesion and a 1-cm margin in the ice ball, as it appears on the MR image, with several cycles of freezing (10-minute freeze, 2-minute thaw, 10-minute freeze). Internal probe temperatures were targeted to $-180^\circ$C.

No viable tumor cells were found in any of the histopathologic region covered by the ice ball.

![Fig. 9. Typical cryosurgical MR images: (left) the viable tumor before procedure, (middle) iceball, (right) cryonecrosis 1 month later (with traumatic lesion to the pectoral muscle behind). The extent of the ice ball is well delineated as a signal void in the periablation image. (From Morin J, Traoré A, Dionne G, Dumont M, Fouquette B, Dufour M, et al. MR-guided percutaneous cryosurgery of breast carcinoma: technique and early clinical results. Can J Surg, in press; with permission.)](image1)

![Fig. 10. Tc99m-sestamibi scintimammography examinations performed 1 week before (left) and 1 month after (middle) the cryosurgery. The corresponding mastectomy sample at pathology analysis is also shown (right). The results show a significant drop in Tc99m uptake characterized by a cold area at the location of the treated lesion surrounded by an inflammatory halo. Postmastectomy histology and pathology results further support that this cold spot corresponded to a total necrosis of the tumor. (From Morin J, Traoré A, Dionne G, Dumont M, Fouquette B, Dufour M, et al. MR-guided percutaneous cryosurgery of breast carcinoma: technique and early clinical results. Can J Surg, in press; with permission.)](image2)
Technically, a total pathologic tumor ablation was obtained in 52% of the tumors treated. Two failures were caused by underestimate of treatment. The remaining 10 were related to limitations of availability of appropriate probes in the earlier cases or a challenge because of the teardrop shapes ice ball created by the probes. This latter problem can be compensated for with placement of additional probes.

Te99m-sestamibi scintimammography (Fig. 10) had only one false-negative and no false-positives. Despite the extent of the ice balls generated, postablation complications from weekly follow-ups were found to be limited to minimal skin necrosis at the probes’ entry points. The study concludes total necrosis in lesions of 2 cm can be achieved with placement of two cryogenic probes head-on at the center of the lesion. Furthermore, any tissue inside the MR imaging–visualized ice ball was necrosed.

Summary

Image-guided thermal ablations can combine exact targeting with controlled energy deposition. The integration of imaging and thermal therapy can provide a minimally invasive or even noninvasive alternative to surgery. This is a well-justified goal for breast-conserving debulking of breast cancer, which in combination with adjuvant chemotherapy or radiation therapy may result in complete cure. The current deficiencies of the ablative procedures encompass the limitations of the energy delivery modality and the imaging modality. MR imaging is the best modality for both target definition and energy deposition control. Because tumors are typically biopsy proved, the lack of specificity of MR imaging is not a concern, and its exquisite contrast for tissue characterization and temperature sensitivity for measuring the deposited thermal dose are considerable assets. In contrast to other energy-delivery modalities, MR imaging–guided FUS offers the most control over energy delivery, with sculpted treatment areas, and most closely approximates the ideal for image-guided thermal therapy.

The stage is set to expand the numerous pilot studies for minimally invasive breast ablation therapy into large-scale clinical trials, with study of long-term patient outcome. Technologic development and increased understanding of the energy-delivery devices are arising from treatment of other organs. More physicians and vendors see the advantage of MR imaging–guidance, and as a consequence, MR imaging–compatible devices for ablation have become available. Dedicated coils, fixation, and targeting devices are now widely available because of the need for MR imaging guidance to biopsy mammogram and US occult lesions. The unique ability of MR imaging to enable tumor visualization, targeting, monitoring, and control of the extent of ablation makes it the ideal modality for guiding thermal ablations. Challenges are being met for selecting patients eligible for therapy by development of better screening methods [102] to rule out ductal carcinoma in situ and invasive carcinoma that are not candidates for targeted thermal therapy. It is clear the elements are available and the benefits are desirable to usher in the adaptation of MR imaging–guided minimally invasive breast ablation therapies.

References


