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REVIEW

MR-Guided High-Intensity Focused Ultrasound Ablation of Breast Cancer with a Dedicated Breast Platform

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Abstract Optimizing the treatment of breast cancer remains a major topic of interest. In current clinical practice, breast-conserving therapy is the standard of care for patients with localized breast cancer. Technological developments have fueled interest in less invasive breast cancer treatment. Magnetic resonance-guided high-intensity focused ultrasound (MR-HIFU) is a completely noninvasive ablation technique. Focused beams of ultrasound are used for ablation of the target lesion without disrupting the skin and subcutaneous tissues in the beam path. MRI is an excellent imaging method for tumor targeting, treatment monitoring, and evaluation of treatment results. The combination of HIFU and MR imaging offers an opportunity for image-guided ablation of breast cancer. Previous studies of MR-HIFU in breast cancer patients reported a limited efficacy, which hampered the clinical translation of this technique. These prior studies were performed without an MR-HIFU system specifically developed for breast cancer treatment. In this article, a novel and dedicated MR-HIFU breast platform is presented. This system has been designed for safe and effective MR-HIFU ablation of breast cancer. Furthermore, both clinical and technical challenges are discussed, which have to be solved before MR-HIFU ablation of breast cancer can be implemented in routine clinical practice.

Keywords Breast · Interventional oncology · High-intensity focused ultrasound · Cancer

Introduction

The treatment of breast cancer has radically changed during the past century [1]. Radical mastectomy was standard of care for local control of the primary tumor until the introduction of breast-conserving therapy (BCT), i.e.,

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limited local surgery combined with whole breast irradiation, in the 1950s. Multiple, large, randomized trials reported equal disease-free and overall survival after BCT and mastectomy, establishing BCT as the "gold standard" in patients with localized breast cancer [2–5]. Continuing technological developments have made it possible to ablate tumor tissue with minimally or noninvasive techniques. In the past decade, articles have been published about breast cancer treatment using thermal ablation techniques, such as radiofrequency ablation, cryoablation, microwave ablation, and laser interstitial thermal therapy [6–8]. These are all minimally invasive treatment techniques, in which a probe is inserted through the skin to reach the target lesion for thermal ablation. Minimally invasive treatment techniques have many potential benefits for patients compared with conventional surgery. They are performed as an outpatient procedure, can reduce the risk of complications, such as infections and bleeding, and potentially yield better cosmetic results without scars or deformation of the breast as seen after breast-conserving surgery.

A completely noninvasive technique for thermal ablation is high-intensity focused ultrasound (HIFU). During HIFU, the ultrasound beam is focused into a small target volume to reach high focal power levels, resulting in temperature elevations causing cell death in a small target volume of tissue, while surrounding structures are spared [9]. HIFU can be guided by magnetic resonance imaging (MR-HIFU) or by conventional diagnostic ultrasound (US-HIFU). Worldwide, thousands of patients with uterine fibroids, liver cancer, breast cancer, pancreatic cancer, bone tumors, and renal cancer have been treated by US-HIFU [10]. MRI however is considered to be the most accurate method to guide HIFU treatment. MRI offers excellent soft-tissue contrast and can be used for planning before treatment, for treatment monitoring, including noninvasive temperature assessment during treatment, and evaluation of treatment results after HIFU ablation, because necrotic tissue is visualized as a nonperfused volume after contrast injection [11]. In this article, we only focus on MR-guided HIFU.

In 2004, the first results of MR-HIFU treatment of uterine fibroids were reported. For these benign tumors, MR-HIFU was applied to achieve symptom relief [12, 13]. A second clinical application of MR-HIFU has been proven to be the palliative treatment of patients with painful bone metastases. A significant reduction in pain can be achieved 3 months after treatment [14, 15]. A potential third clinical application is MR-HIFU of liver tumors. Nevertheless, treatment within the liver is difficult because of severe motion of the liver due to breathing and the limited ultrasound window caused by the overlying ribs [16].

In this article, we present a novel, dedicated breast platform for MR-HIFU treatment of breast tumors. Furthermore, the opportunities and future challenges of MR-HIFU in the treatment of breast cancer are discussed.

Patient Selection

Introducing a new technique into clinical practice is difficult. This is particularly true in the field of breast cancer treatment because of the excellent long-term survival of breast cancer patients. A new treatment modality has to compete against conventional clinical practice and prove that it has certain benefits over currently available treatment methods. Therefore, it is important to identify those patients in whom a new treatment technique may be beneficial, before introducing a new technique into clinical practice. The introduction of mammographic screening programs has resulted in an increased reported incidence rate of patients with early breast cancer [17–19]. A high percentage of these tumors are nonpalpable and therefore difficult to localize during surgery. Reexcision rates due to tumor-positive margins after lumpectomy are high, i.e., up to 30 %, in patients with nonpalpable tumors [20]. Ablation techniques often are used in combination with image guidance. Nonpalpable tumors therefore may be easier to localize and treat with image-guided ablation techniques.

In 2001, Faverly identified patients with the optimal tumor profile for BCT as patients with breast carcinoma of limited extent (BCLE) [21]. BCLE was defined as a primary tumor mass in the breast without invasive carcinoma, ductal carcinoma in situ (DCIS), and lymphatic emboli foci beyond 1 cm from the edge of the primary lesion. Faverly's definition was based on mammographic and pathologic criteria. When considering MR-guided ablation of breast cancer, the definition of BCLE has to be extrapolated. It has to be complemented with criteria based on characteristics of the lesion on MRI, which is currently a topic of ongoing research. Patients potentially eligible for MR-guided ablation can be characterized as patients with a well-demarcated, unifocal, small (< 2 cm) lesion in the breast without surrounding DCIS.

MRI for Tumor Targeting, Treatment Monitoring, and the Definition of Margins

MRI can provide anatomical images with excellent soft-tissue contrasts and high spatial and temporal resolution. It is an attractive imaging technique because of its noninvasiveness and the ability to provide three-dimensional image data without exposing patients to ionizing radiation [22]. MRI has a high (>95 %) sensitivity for the detection of invasive breast cancer [23]. Additionally, compared with other imaging techniques, such as mammography and ultrasound, MRI is the most accurate imaging technique to visualize the extent of the invasive component of a tumor in the breast [24–28].

MR imaging can be used before, during, and after treatment with MR-HIFU. Pretreatment MRI is employed to plan the treatment. During MR-HIFU, dedicated MR thermometry techniques allow to map temperature distributions in tissue. Various temperature-sensitive MR parameters can be used to measure the temperature: the water proton resonance frequency shift (PRFS), the diffusion coefficient, the T1 and T2 relaxation times, and the proton density [22, 29, 30]. The most widely used MR thermometry method is based on the temperature dependence of the electron screening of the hydrogen nuclei in water, which leads to a PRFS of the water proton that is proportional to temperature [30]. Using a dedicated MR thermometry technique, it is possible to perform real-time monitoring of the tissue temperature. This is a major advantage of MR-guidance, because the temperature information can be utilized to adapt the treatment plan if needed. Posttreatment MRI is used to evaluate the results of the treatment using several techniques. Contrast enhanced T1-weighted images may show nonperfused volumes after tumor ablation. Furthermore, T2-weighted imaging, diffusion-weighted imaging, and MR elastography are able to detect tissue coagulation [11]. All of these qualities together designate MRI as the best available imaging technique to guide and monitor breast cancer ablation with HIFU.

Finally, MRI is the method of choice for the definition of treatment margins surrounding the primary tumor. In 1985, Holland et al. [31] reported the presence of surrounding tumor foci around the primary index tumor in up to 63 % of patients with invasive cancers. Understanding the spreading of foci around the index tumor is essential to plan treatment margins for MR-HIFU and also to plan radiation therapy after ablation of the index tumor. Schmitz et al. [32] compared lesions visible on MRI with histopathological findings and showed the presence of microscopically visible disease in 52 % of patients eligible for BCT beyond 10 mm of the border of the MRI-visible lesion. The findings of Schmitz et al. imply that a relatively wide ring of tissue around the MRI-visible lesion has to be included in adjuvant external beam radiation therapy after treatment with MR-HIFU.

MR-HIFU

Magnetic resonance-guided high-intensity focused ultrasound (MR-HIFU) is the most promising ablation technique currently available. It combines completely noninvasive thermal ablation with accurate treatment planning, monitoring, and evaluation by MRI. MR-HIFU has been called a “disruptive technology,” because it has the potential to change existing medical disciplines radically and eventually to replace several invasive surgical procedures [33].

The idea to use focused ultrasound for noninvasive thermal ablation of tumors inside the body originates from 1942 [34]. Diagnostic ultrasound uses frequencies in the range of 1–20 MHz, whereas frequencies for therapeutic HIFU applications lie between 0.8 and 3.5 MHz [9]. Focused ultrasound is generated when a beam of ultrasound waves is concentrated into a focal point. Ultrasound waves can be focused by lenses, reflectors, or a spherically curved transducer. Additionally, if the transducer consists of an array of small transducer elements, electrical focusing may be used to create a focal point. All transducer elements are driven separately by alternating signals of a predefined phase and amplitude to be in phase at the focal point [35]. The ablation volume of one single HIFU exposure or sonication is small and varies according to the characteristics of a transducer and the use of mechanical and/or electronic steering of the focus position. Typically, the focus volume resembles the shape of a cigar and has a transverse diameter of 1–3 mm and an axial length of 8–15 mm [9]. Many single focal points can be successively ablated in a grid to ablate a larger volume. With this “point-by-point” method; however, a large part of energy is lost by heat diffusion due to the cooling time between sonications. To increase the efficacy of HIFU and to reduce treatment time, volumetric ablation methods have been proposed. In the latter case, the deposited energy is more efficiently used and it is possible to ablate larger volumes in shorter time. Salomir et al. [36] described a spiral trajectory of the focal point and proved that a uniform temperature distribution can be reached in a larger target volume. In 2009, a new method of volumetric ablation was introduced in which the ultrasound energy is applied in a continuous manner over a number of concentric circular trajectories of increasing size [37, 38].

Despite its complete noninvasiveness and other attractive properties, HIFU has not been widely used in clinical practice. Until a few years ago, no high-quality imaging technique was available for target delineation and monitoring of tissue changes or treatment response during HIFU. In 1993, Hynynen et al. demonstrated the feasibility of combining MRI and HIFU. It was shown that it is possible to perform sonications inside the magnet of an MRI scanner [39]. Also, the potential of MRI to detect tissue damage immediately after the sonications was proven. Based on these findings, the first system for MR imaging-guided tumor ablation with HIFU was developed. The transducer positioner was computer-controlled and integrated into the patient table of an MR-system.

A workstation outside the MRI scanner was programmed to plan, control, and monitor the treatment [40]. The combination of MRI and HIFU caused a major breakthrough in the field of HIFU. It has led to many technological advances in the development of dedicated HIFU systems and also to the development, optimization, and validation of pulse sequences dedicated for MR temperature mapping [41].

Two major applications of MR-HIFU are first the creation of mild hyperthermia and second thermal ablation at higher temperatures [42]. In this article, we will only discuss thermal ablation, because we think this is the first clinical application of MR-HIFU for the treatment of breast cancer. A high tissue temperature (50–100 °C) for a short period of time is necessary to thermally ablate tissue [43]. When the threshold for protein denaturation (57–60 °C) is passed, only a few seconds of heating is required to reach coagulation necrosis [33].

MR-HIFU Therapy of Breast Tumors

In 2001, the first work concerning MR-HIFU ablation in the breast was reported. Hynynen et al. [44] treated nine patients with fibroadenomas and showed that these benign breast tumors can safely and noninvasively be ablated. In the same year, Huber et al. [45] performed MR-HIFU in a single patient with breast cancer who underwent breast-conserving surgery 5 days after MR-HIFU treatment. Histopathological analysis showed lethal and sublethal tumor damage, but no exact percentage of tumor necrosis was reported. Table 1 shows an overview of studies on MR-HIFU ablation of breast tumors. Gianfelice was the first who reported a phase I trial in 12 breast cancer patients who were treated with MR-HIFU according to a treat-and-resect protocol [46]. To remove all cancerous tissue and to achieve equal results as those after conventional tumor resection following breast-conserving surgery, it is believed that complete necrosis has to be achieved with MR-HIFU ablation. Gianfelice reported the presence of residual cancer cells mainly at the periphery of the tumor mass, indicating that a larger margin around the tumor as seen on MR images has to be targeted to reach complete eradication of all tumor cells. Between 2003 and 2007, several clinical trials reported treatment of breast cancer patients using MR-HIFU [46–52]. Most of these studies were performed according to a treat-and-resect protocol. Zippel et al. [52] reported complete necrosis in 20 % of patients, whereas Khiat showed a lack of residual cancer cells in 27 % of treated lesions [51]. Furusawa demonstrated the best results to date with complete necrosis in 54 % of treated patients [47]. Two studies were performed without surgical resection after MR-HIFU ablation. The first study by Gianfelice et al. used MR-HIFU as an adjunct to chemotherapy for treatment of high-risk surgical patients [50]. Success of MR-HIFU treatment was assessed with follow-up MRI and biopsies. After one or two treatment sessions, 79 % of patients had negative biopsy results. Furusawa performed local treatment of 21 patients with MR-HIFU only [48]. Patients underwent one or two treatment sessions, and after a median follow-up of 14 months with breast ultrasound imaging and MRI, one local recurrence was detected.

Most studies performed MR-HIFU treatment with the ExAblate 2000 (InSightec, Haifa, Israel) [46, 47]. This system consists of a spherically shaped transducer embedded in a water bath, built-in into an MR table top. Ultrasound beams target the breast from anterior using the "point-by-point" method. In 2006, a dedicated breast MR-HIFU system was presented in which the breast is targeted with a lateral ultrasound beam with the phased array transducer moving around the breast [53]. Another laterally mounted phased array transducer in a dedicated design has been presented recently by Payne et al. [54]. As far as we know, only one patient with breast cancer has been treated with a laterally shooting transducer in a first feasibility study [45]. Furthermore, no treatments have ever been performed with a dedicated system specifically developed for breast tumor ablation.

Dedicated MR-HIFU Breast Platform

Recently, a dedicated MR-HIFU breast platform has been developed for ablation of breast tumors (Sonalleve, Philips Healthcare, Vantaa, Finland). The breast platform was designed to dock on top of a standard 1.5 Teslan MRI scanner (Achieva, Philips Healthcare, Best, The Netherlands) and is presented in Fig. 1. The platform consists of a water-filled table top with a breast cup positioned in the middle of the table. During MR-HIFU treatment, patients are positioned prone on the table with the targeted breast inside the cup. The space in the breast cup surrounding the breast is filled with water to enable ultrasound waves to target the breast. Eight separate focused ultrasound modules with 32 transducer elements of 6.6-mm diameter each form a circular structure of 270° surrounding the breast cup (Fig. 2). The frequency for ablation is 1.45 MHz, and the focal length of the transducers is 13 cm. The circular structure of the breast platform uses a mainly horizontal beam path orientation. Ultrasound beams target the breast from the lateral sides, hereby increasing the effective distance from focal point to rib cage, heart, and lungs. The larger distance reduces the heating of critical structures, because the far field, i.e., the area after the focal point, is mainly located inside the breast (Fig. 3) [55]. More

Table 1 Overview of MR-HIFU ablation in the breast

Study	N	Tumor characteristics	Tumor size	Surgery	Outcome assessment by	Success of ablation procedure
Hynynen et al. [44]	11	Fibroadenomas ($n = 11$)	1.9 cm^3 (mean)	No	DCE-MRI	73 % (8/11): successfully treated (partial or total) 27 % (3/11): treatment failure
Huber et al. [45]	1	Invasive ductal carcinoma ($n = 1$)	2.2 × 2 × 1.4 cm^3	Yes (breast-conserving surgery)	Histopathology	No exact percentage of tumor necrosis provided
Gianfelice et al. [46]	12	Invasive ductal carcinoma ($n = 11$) Adenocarcinoma ($n = 1$)	0.11–8.8 cm^3 (range)	Yes (segmental tumor resection)	Histopathology	Mark 1* 43.3 % tumor necrosis (mean) Mark 2 88.3 % tumor necrosis (mean) 16.7 % (2/12): complete necrosis
Gianfelice et al. [49]	17	Invasive ductal carcinoma ($n = 14$) Adenocarcinoma ($n = 2$) Invasive lobular carcinoma ($n = 1$)	0.11–8.8 cm^3 (range)	Yes (segmental tumor resection)	Histopathology	24 % (4/17): complete necrosis 53 % (9/17): <10 % residual cancer 24 % (4/17): 30–75 % residual mass
Zippel et al. [52]	10	Infiltrating breast carcinoma ($n = 10$)	2.2 cm (mean)	Yes (standard lumpectomy)	Histopathology	20 % (2/10): complete necrosis 20 % (2/10): microscopic foci of residual carcinoma 30 % (3/10): 10 % residual tumor 30 % (3/10): 10–30 % residual tumor
Khiat et al. [51]	26	Invasive ductal carcinoma ($n = 25$) Lobular carcinoma ($n = 1$)	0.11–11.2 cm^3 (range)	Yes (segmental tumor resection)	Histopathology	27 % (7/27): complete necrosis 40.7 % (11/27): <10 % residual cancer 27 % (7/27): 20–90 % residual cancer 3.7 % (1/27): missing
Furusawa et al. [47]	30	DCIS ($n = 4$) Invasive adenocarcinoma ($n = 1$) Invasive ductal carcinoma ($n = 25$)	0.5–2.5 cm (range)	Yes (breast-conserving surgery or mastectomy)	Histopathology	96.9 % tumor necrosis (mean) 54 % (15/28): complete necrosis 43 % (12/28): 95–100 % necrosis 11 % (3/28): <95 % necrosis
Gianfelice et al. [50]	24	Nonmetastatic breast neoplasm ($n = 24$)	0.6–2.5 cm (range)	No	Biopsy	After first treatment: 58 % (14/24): no residual tumor on biopsy specimens After second treatment: 79 % (19/24): successfully treated 21 % (5/24): treatment failure
Furusawa et al. [48]	21	Invasive and noninvasive ductal carcinoma ($n = 21$)	1.5 cm (median)	No	Clinical follow-up with MRI and ultrasound	One recurrence during an observation period of 14 months (median)

* Patients in this study were treated with two different ultrasound systems (Mark 1 and Mark 2), for which results separately were reported

Fig. 1 MR-HIFU breast platform consists of a water-filled table top with breast cup, integrated in a 1.5 T clinical MRI scanner

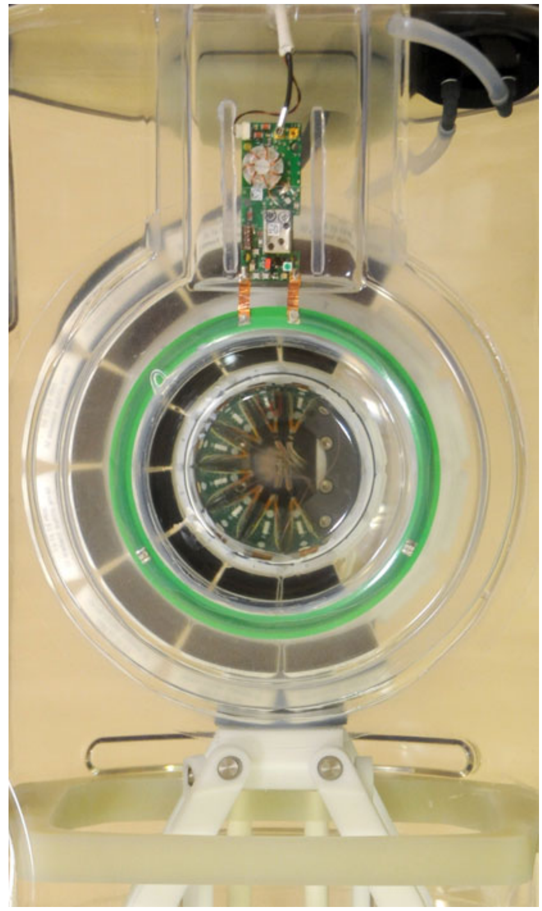

Fig. 2 Eight separate focused ultrasound modules with 32 transducers elements each are surrounding the breast cup for 270°

importantly, the large aperture design of this system lowers the local energy density on the skin, consequently reducing the risk of skin burns. The drawback of this wide aperture transducer design is that the focus is more vulnerable to distortion due to large differences in the acoustic path of the individual elements. These focus aberrations will be larger if the tissue is heterogeneous. Because breast tissue consists of a mix of fibroglandular and adipose tissue, the quality of the ablation focus in the breast will require attention. If the amount of adipose and glandular tissue within the beam paths of the individual elements vary greatly, it might be difficult to create a homogeneous ultrasound focus. Mougenot et al. [56] proposed a method to apply a phase correction based MRI method to improve the focal point quality. These phase aberrations might cause an offset of the ablated region from the intended sonication location to which tissue parameter heterogeneities might contribute further. This mandates test sonications to be performed and the results to be carefully evaluated and compensated before allowing any therapeutic ablation. Another advantage of the breast platform is that it uses a volumetric ablation method, which allows larger and more homogeneous ablation volumes compared with single-point ablation methods [37]. The shape of a single ablation with the breast platform will be approximately that of an oblate ellipsoid. The diameter of the available treatment cells (i.e., the planned ablation size per sonication) vary between 3 and 12 mm and the corresponding length between 3 and 8 mm. However, the resulting diameter and length of the ablated region will differ based on tissue perfusion, attenuation, and diffusion as well as the chosen acoustic power and the extent of the phase aberrations induced by the variance in the beam paths. Figure 4 shows the MR images of a healthy volunteer and the schematic display of the ultrasound transducers around the breast cup on the HIFU console.

Technical and Clinical Challenges

An invasive tumor in the breast is best visualized using contrast-enhanced MRI. However, concerns about administration of gadolinium-based MR-contrast agents just before or during MR-HIFU treatment have been raised. Gadolinium-based MR-contrast agents consist of a complex of gadolinium with a carrier molecule like DTPA (diethylenetriaminepentaacetate). The effects of heating of

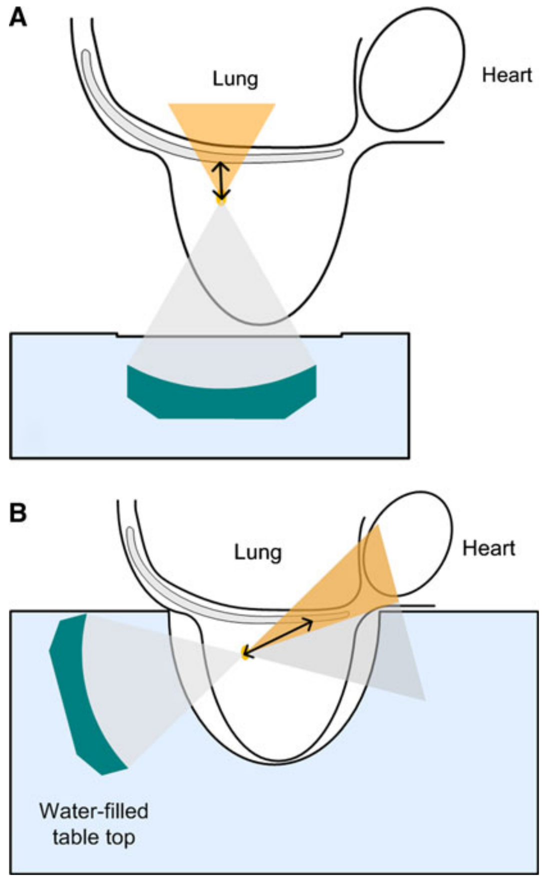

Fig. 3 **A** Schematic view of an ultrasound transducer targeting the breast from anterior. It shows the small distance between focal point and ribs. The main part of the far field is located in rib cage and lungs. **B** Schematic view of the lateral sonication method of the dedicated MR-HIFU breast platform. The distance from focal point to rib cage is increased. Due to the lateral sonication method, the far field is mainly located inside the breast

this complex in human patients are currently unknown. A potential hazard is decomposition of the Gd-chelate leading to free Gd^{3+} or entrapment of the chelated compound inside the ablated tissue. Furusawa reported in 2006 about the use of contrast-enhanced imaging before MR-HIFU. In this article, no related complications were mentioned [47]. The planning of a target volume for treatment with MR-HIFU will be more difficult when only noncontrast-enhanced MR images are available. Diagnostic contrast-enhanced MRI before treatment would need to be compared with unenhanced images during treatment.

A second technical challenge is the improvement of MR thermometry (MRT) in breast tissue. The success of MR-guided thermal therapy depends for a major part on the accuracy of the estimation of temperatures [22]. MRT has to visualize and quantify the deposition of heat energy in the treated tumor and surrounding tissue with adequate spatial and temporal resolution. As previously mentioned, PRFS-based MRT is the most widely used method during MR-guided thermal therapies. Unfortunately, this technique does not work for protons in fat molecules. Fat-suppression techniques therefore have been employed during PRFS-based MR thermometry in fat-containing tissues. However, during breast tumor ablation, preferably both the temperature of the tumor and surrounding adipose tissue should be measured. Monitoring of temperatures in fat tissue is important to reduce the risk of skin burns and also when treating a margin around the tumor. Furthermore, a second problem related to the use of PRFS-based MRT for breast thermometry has been recently raised. This problem is the occurrence of temperature-induced susceptibility changes of fat, which can introduce significant errors in PRFS-based MR thermometry and may cause inaccurate temperature measurements in the fibroglandular breast tissue during MR-HIFU ablation [57, 58]. An additional problem is caused by respiration. The fact that the air volume inside the lungs changes over the respiratory cycle gives rise to time-varying changes in the magnetic field inside the breasts that can cause considerable temperature errors in PRFS-based MR thermometry [59]. It has been shown that these errors can be corrected using a multi-baseline correction method, either with or without a model for the magnetic field disturbances [60]. Regarding these difficulties of monitoring temperature in fat tissue, the selection of patients could be restricted to patients with well-defined lesions, i.e., with regular margins and without fatstranding to achieve better temperature monitoring.

Furthermore, the following clinical issues need attention before successful translation of MR-HIFU. First, no excision specimen will be available after MR-HIFU ablation. The ablated tumor remains in the breast, and therefore, no histopathological analysis can be performed on the excised tumor tissue. Currently, the indication for additional chemotherapy is based partially on prognostic factors derived from histopathology of the excision specimen (e.g., the grading and receptor status of a tumor). If no excised tumor tissue is available, a different method has to be found to predict the clinical outcome of breast cancer patients. This may done from core biopsies, although discordance between prognostic factors derived from biopsy and excision specimens have been reported [61, 62]. Furthermore, tumor-positive margins cannot be determined. An imaging method has to be found to validate complete necrosis of all tumor cells after MR-HIFU ablation.

Second, a sentinel node procedure is currently indicated in patients with early breast cancer to assess one of the most important prognostic factors of breast cancer: the lymph node status. The effect of MR-HIFU on the drainage pattern of the sentinel node is currently unknown. Besides, a noninvasive therapy like MR-HIFU preferably should be combined with a noninvasive procedure to stage the lymph node status. In the future, new techniques, such as diffusion-weighted MRI, Sonovue contrast-enhanced ultrasound

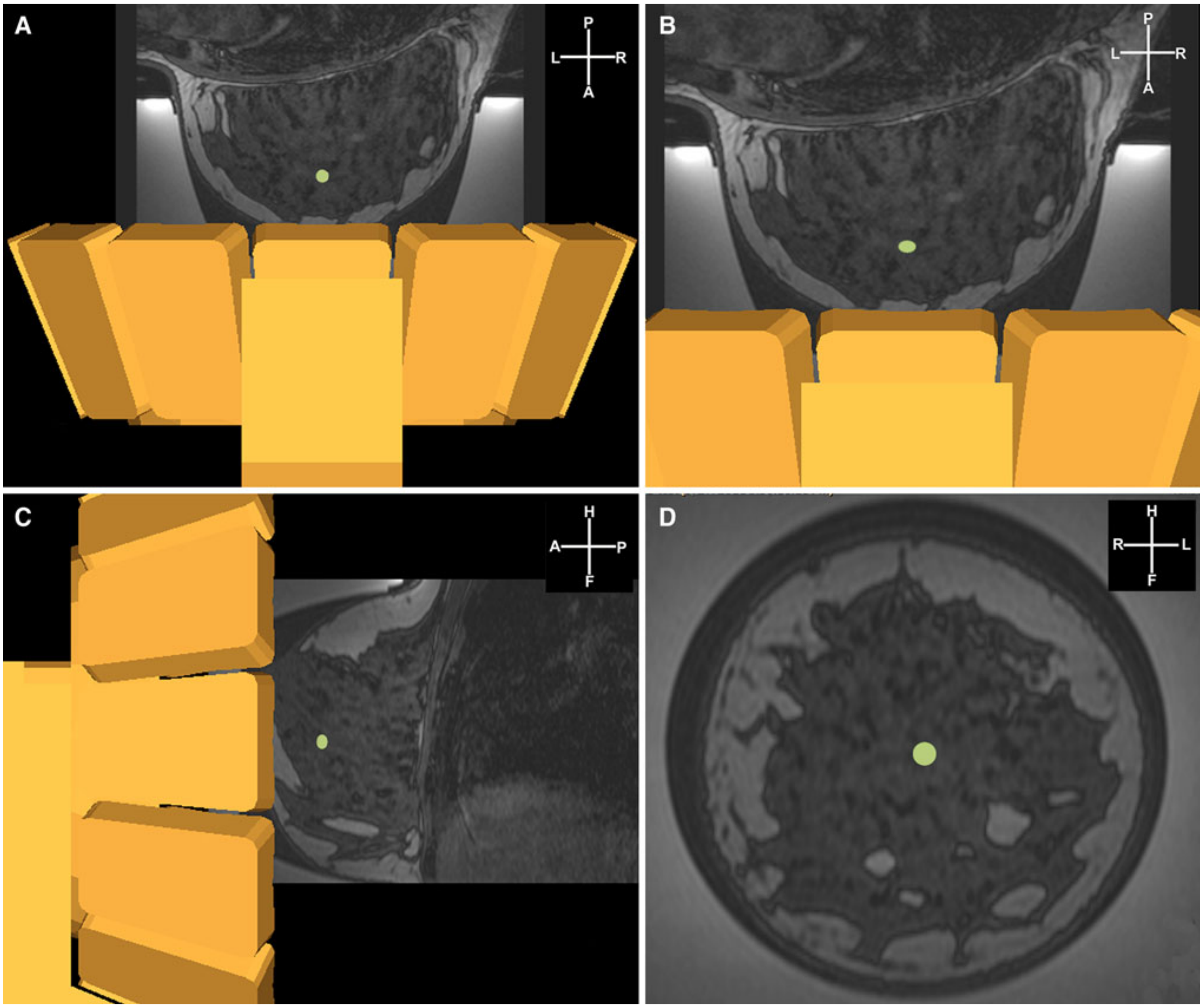

Fig. 4 T1-weighted 3D gradient echo images without fat suppression of a healthy volunteer with a schematic display of the ultrasound transducers around the breast cup (**A** transversal, **B** transversal close-up, **C** sagittal, **D** coronal). The *green spot* shows a sonication cell in the middle of the breast

localization, or FDG-PET may be used to assess the lymph node status of breast cancer patients.

Third, radiotherapy will remain an essential part of breast cancer treatment after MR-HIFU ablation of the index tumor. Additional radiotherapy after breast-conserving surgery has proven its value by showing a 3.3 % (pN0) and 8.5 % (pN1) absolute reduction in 15-year breast cancer death [63]. At this moment, delineation of radiotherapeutic target volumes after breast-conserving surgery is difficult because of a number of reasons. Delineation is mostly done based on CT scans, which provides no optimal soft tissue contrasts. Large differences in target volume delineation therefore are observed [64–67]. The total radiotherapeutic dose and the irradiated volume should both be kept as minimal as possible to gain the best cosmetic results [68]. Nonetheless, a recent study by den Hartogh et al. [69] showed no correlation between excised specimen volume and irradiated volume in early breast cancer patients treated with BCT. After MR-HIFU ablation, the breast will not be distorted in the same way as after surgery, and MR-HIFU will leave a well visible region to serve as a target for radiotherapy. Hence, the precision of conventional CT-guided radiotherapy could improve after treatment with MR-HIFU. The combination of MR-guided radiotherapy after MR-HIFU also potentially allows a more accurate delineation of the target volume. Research in this area is ongoing [70, 71].

Conclusions

Magnetic resonance-guided high-intensity focused ultrasound is a promising technique for completely noninvasive treatment of breast cancer. Previous studies of MR-HIFU in breast cancer patients reported a limited efficacy, which hampers the clinical translation of this technique. These prior studies were performed without an MR-HIFU system specifically developed for breast cancer treatment. In this article, a novel and dedicated MR-HIFU breast platform is presented. Technical and clinical challenges are discussed, which may help to improve clinical translation in future studies.

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Conflict of interest This research was performed in collaboration with Philips Healthcare. Max O. Köhler is currently employed in this company. The other authors declare that they have no conflict of interest.

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