

Sonalleve MR-HIFU

Philips MR-guided High Intensity Focused Ultrasound

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Abstract

High Intensity Focused Ultrasound guided by Magnetic Resonance Imaging (also known as MR guided HIFU, MRgHIFU, or MRgFUS) is a non-invasive therapy technique using focused ultrasound waves to heat and coagulate tissue deep inside the body without damaging intervening tissue. MR-guided HIFU will support new treatment alternatives for conditions where current methods come with significant side effects and for patients who may not tolerate an invasive procedure. In this article we discuss the underlying technical principles of volumetric heating with real time feedback implemented in the Sonalleve MR-HIFU system and their implications for the clinical user.

Introduction and background

In medical applications of High Intensity Focused Ultrasound (HIFU), an externally placed transducer is used to focus ultrasound energy into a small focal volume at the specified target location inside the body. During treatment, the beam of focused ultrasound energy penetrates through soft tissue and causes localized high temperatures (55° to 90°C) at a tight focal region as small as 1 mm x 1 mm x 7 mm. This localized hyperthermia, maintained for a few seconds, produces well-defined regions of protein denaturation, irreversible cell damage, and coagulative necrosis. HIFU offers advantages over other methods of inducing hyperthermia as the transducer is located outside the body and focuses the mechanical ultrasound waves toward the targeted region through intact skin. Such local hyperthermia provides the clinician with an elegant approach for selective tissue destruction.

It has been known for over half a century that focusing ultrasound waves into the human body offer the possibility to heat deep-lying tissue noninvasively.¹ However, the lack of suitable means for guidance and

monitoring has prevented it from gaining widespread acceptance for medical use. Applying HIFU power to a patient's lesion needs diligent treatment planning, tools for targeting the US beam, monitoring of the energy delivery and development of heating zones as well as post-treatment assessment and quantification. For many applications and in current products offered, e.g. for prostate HIFU, ultrasound therapy is guided using diagnostic ultrasound. Whereas ultrasound imaging provides some anatomical detail and helps with general procedure planning and targeting, it is severely limited in providing the necessary 3D planning, temperature monitoring during treatment and adequate post-treatment lesion assessment for fast and effective therapy.

MR imaging, with its excellent soft tissue contrast, 3D imaging capabilities, and non-invasive temperature measurement techniques has been suggested as a means of providing the necessary guidance and monitoring. In addition, highly accurate real-time temperature imaging can be used to provide feedback to the HIFU system and control the amount of energy to the focal zone ensuring reproducible results for a wide variety

of tissue types. MR can provide real-time temperature mapping in multiple planes or 3D. Recent advances in MR temperature mapping make it possible to achieve temperature accuracy of 2-3° C in moving tissue such as the liver, and 1° C in stationary tissue.²

The MR-HIFU paradigm

The combination of MR and HIFU provides a complete treatment paradigm:

- Planning: MR imaging for 3D planning
- Tissue Ablation: Focused ultrasound ablates the target non-invasively
- Therapy Monitoring: real-time MR temperature imaging is used to guide and monitor the HIFU treatment
- Therapy Assessment: Post treatment contrast enhanced MR imaging shows the ablated, non-perfused volume

For an MR-HIFU treatment, the HIFU device is positioned inside the MR system for the real time guidance and temperature measurements during the procedure as seen in Figure 1. As a non-invasive alternative to surgery, MR-HIFU has the potential to offer a more patient friendly therapy for many diseases.

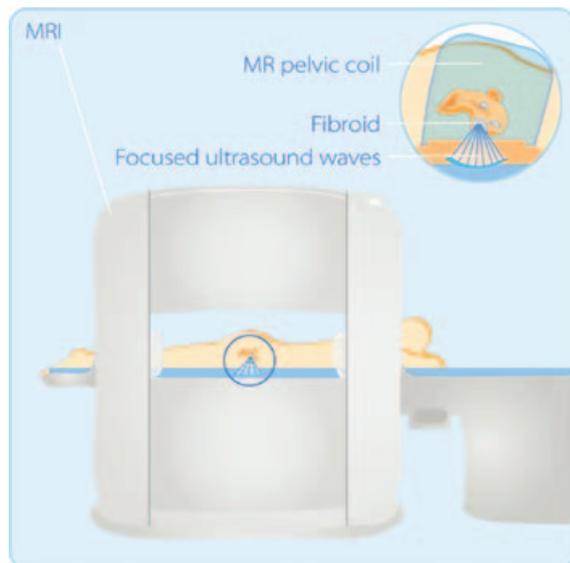


Figure 1: MR-HIFU treatment paradigm – HIFU treatment under real time guidance and monitoring using MR imaging.

The Sonalleve MR-HIFU system

The Sonalleve MR-HIFU system is a clinical HIFU platform and its functionality is based on the seamless interconnection with the Philips MRI systems. Treatment planning images are acquired using the MR Console, while guidance and temperature monitoring during the treatment is controlled via the HIFU Console. The Sonalleve MR-HIFU system is compatible with both Ingenua and Achieva systems, as seen in Figure 2. It consists of the following subsystems which are divided in three separate rooms: the Operator's Room, the Equipment Room and the Magnet Room. See also Figure 3.



Figure 2. The Sonalleve MR-HIFU system with Ingenua MR system

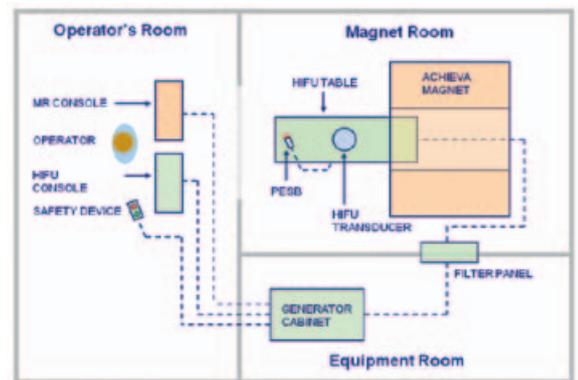


Figure 3: The major components of the Sonalleve MR-HIFU system.

Sonalleve Patient Table

The Sonalleve table is positioned over the lowered MR patient support; the imaging tabletop remains in place. It integrates the transducer and its mechanical positioning system enabling movements in 5 degrees of freedom. Ultrasound waves propagate out of the fluid box, which is filled with a liquid coupling medium, through a thin membrane located on top. To ensure good acoustic coupling with the skin, a gel pad is

positioned between this membrane and the patient's skin. A mixture of degassed water and ultrasound gel is applied on both sides of the gel pad to avoid air bubbles.

The HIFU transducer consists of 256 elements forming a spherical shell with a natural ellipsoidal focus of 1 x 1 x 7 mm at 14 cm distance. Using the elements of the transducer as a phased-array and controlling the phase of the ultrasound field produced by each transducer element individually allows for fast electronic steering of the focal spot.

Also integrated with the table top is the two part dedicated HIFU RF receive coil. The lower part is integrated around the ultrasound window and the other elements are embedded in a freely movable housing that is placed on top of the patient and fixed against the pelvis using straps, preventing excess movement of the patient during the treatment. The HIFU coils are used for both imaging and temperature monitoring.

Sonalleve Console

The Sonalleve console, located in the Operator's Room, is the interface and workhorse used for treatment planning, to calculate real-time temperature maps and control the HIFU energy delivery. The Sonalleve console seamlessly communicates with the MR console, retrieves the planning images and controls the acquisition of temperature sensitive imaging sequences. It also analyses the treatment progress by evaluating the dose size, heating efficiency, recommending power levels and displays warnings about motion, cavitation or risk of excessive heating.

Equipment room components

The HIFU generator cabinet houses the main hardware for generation and delivery of ultrasound power, precise positioning of the transducer plus measurement and communication equipment that are required to conduct the treatment safely and efficiently.

A separate Filter Box is located in a wall opening from the Equipment Room to the Magnet Room. It provides a feed through for the signal and control cables into the examination room without RF interference with the MRI system.

MR thermometry and thermal dose

MR thermometry is based on the proton resonance frequency (PRF) shift of the water proton, which has an almost tissue-independent linear dependency on temperature throughout the temperature range of interest.^{3,4}

This temperature dependency of the PRF is caused by the stretching, bending, and breaking of hydrogen bonds between the water molecules with increasing temperature. This reduces the average time spent by water molecules in a hydrogen bonded state causing a decrease in the local magnetic field and thus also of the PRF of water.

This change in PRF can be deducted from MR phase images,⁵ where the difference of successive phase images multiplied by a scaling factor provides images of the temperature change:

$$\Delta T = \frac{\Delta \Phi}{\alpha \gamma T_E B_0}$$

α = temperature dependent water resonance chemical shift -0.0094 ppm/°C

γ = gyromagnetic ratio - 42.58 MHz/T

B_0 = magnetic field strength

T_E = echo time

It is worth noting that the PRF method measures temperature differences compared to a starting reference point, rather than the absolute temperature. This has practical consequences when monitoring thermal procedures as discussed below.

For the temperature measurement in fatty tissue the PRF method is of limited use. Fat does not contain strong hydrogen bonds and the PRF shift of adipose tissue is almost zero and therefore less dependent on temperature. Consequently, fat suppression is required in most biological tissues to prevent the fat signal contaminating the PRF thermometry measurements.

Given an adequate signal-to-noise ratio (SNR), online analysis of local MR water signal phase variations during HIFU energy deposition provides the clinician with accurate temperature measurements and real-time thermometry to monitor and control the therapeutic

procedure, ensuring that a sufficient amount of thermal energy is deposited at the targeted location and that adjacent healthy tissues remain unaffected. The real-time MR thermometry also works in the presence of HIFU activity and can therefore be used to create either an operator-regulated or automatic feedback control of the treatment in order to improve the efficacy and safety of the HIFU therapy.

For ablation of biological tissue the absolute temperature is not the only important criteria. It is the accumulated temperature over time that is determining cell survival. In their work focused on hyperthermia conducted in the early 1980's, Sapereto and Dewey (1984)⁶ developed the concept of thermal dose (TD). In their studies, Sapereto and Dewey demonstrated that a temperature of 43°C caused a clearly observable tissue necrosis after 240 minutes. Therefore, the TD at which the tissue necroses is defined as 240 equivalent minutes (EMs). TD is calculated by integrating the temperature (T) over time (τ) curve and calibrating this value with heating time at 43°C, which yields the following equation:

$$TD = \int_0^t r^{43-T(\tau)} d\tau, \quad r = 0.25, T < 43^\circ\text{C}, \quad r = 0.5, T > 43^\circ\text{C}$$

As a practical consequence of the definition of TD, a time needed to reach a lethal dose (≥ 240 EM) halves with every degree Centigrade of temperature increase, leading to 4 sec. at 55°C, only one sec. at 57°C and about 1 μsec at 77°C.

A TD of 30 EM is generally considered as a threshold for any thermal damage and within the transition zone between 30 EM and 240 EM the cells may recover or eventually die. However, these limits show some tissue dependency, e.g. in brain, thermal necrosis has been found to occur at very low thermal dose levels.⁷

For real-time MR thermometry, the Sonalleve MR-HIFU system acquires multiplane temperature images simultaneously. The target region temperature increase is monitored by three adjacent coronal slices and one sagittal slice. The coronal slices are automatically positioned perpendicular to the beam axis, with the

center slice placed at the predefined treatment plane, as shown in Figure 4, Stack A. The sagittal slice, also automatically positioned, is placed including the beam axis of HIFU propagation, Stack B in Figure 4. This imaging plane is used to monitor the temperature rise in the focus and along the beam axis in both the near and far fields. Monitoring potential temperature build up in the near field or far field is accomplished with two additional coronal slices. In the case of uterine fibroid treatment, the near field slice is positioned typically in the muscles layer near the skin, the far field slice in the bowel or close to the spine, Stacks C and D in Figure 4.

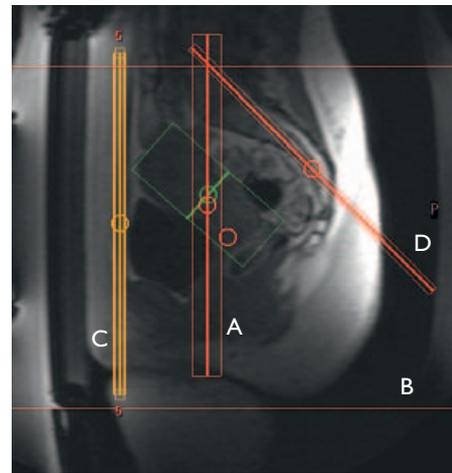


Figure 4: Thermal monitoring slice positioning. Stacks A, B: automatically positioned; stack C: near field in abdominal muscle layer; stack D: far field close to bowel or spine

Temperature sensitive images are acquired using a multishot RF-spoiled FFE-EPI sequence with an in-plane resolution of 2.5 x 2.5 mm and a slice thickness of 7 mm. Identical imaging parameters are used for each slice. The resulting total acquisition time for the 6 slices is 2.9 s.

Real-time two-dimensional (2D) color temperature maps are displayed as an overlay on the MR anatomical images. The composite images show the actual temperature or optional the accumulated thermal dose (2D) information in the treated area, together with the ultrasound therapy parameters such as transmitted output power, frequency, and timing, as shown in Figure 5a. Figure 5b shows an enlarged view of a temperature map with

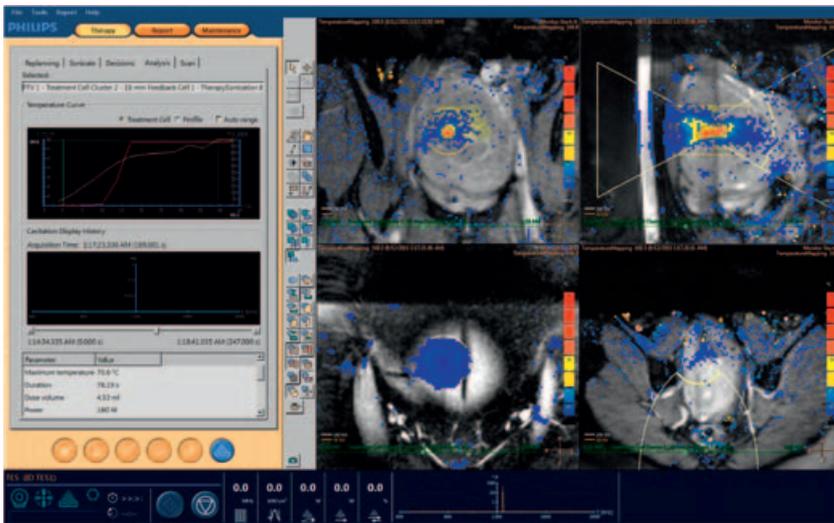


Figure 5a: Real-time temperature imaging as seen by the user during a sonication. Coronal (top left) and sagittal (top right) temperature maps from the treated area superimposed on anatomical images show the progress of sonication at the treated area. The near-field and far-field coronal oblique images (lower left and right) visualize the possible temperature rise at the location of the cone.

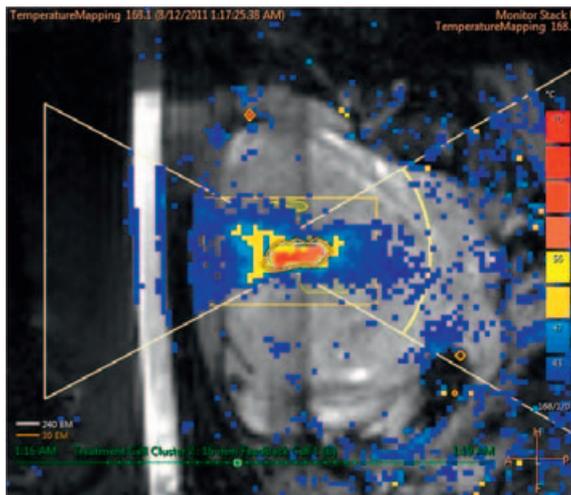


Figure 5b: Enlarged view of a temperature map with the thermal dose contours, TD 240 EM iso-dose in white, TD 30 EM iso-dose in orange.

the thermal dose contours, TD 240 EM iso-dose in white, TD 30 EM iso-dose in orange. The operator can also select specific areas on the 2D anatomical images to obtain temperature values at those locations. The temperature maps are updated every three seconds. After each sonication the user can visualize and replay the temperature maps superimposed on the planning images (typically T2- or T1-weighted) and can get a full analysis of the event.

Volumetric heating with real-time feedback

A single exposure of focused ultrasound energy is referred to as a “sonication.” Multiple sonications are necessary to ablate an arbitrarily shaped target lesion. Traditionally, HIFU ablation has been performed by iteratively sonicating a single focal point at a time until the desired volume is ablated, with each sonication followed by a cooling period. During this time the tissues cool down to average body temperature and provides the starting reference point for the next temperature mapping sequence. It serves as a safety measure to avoid successive heat build up and reduces the risk of unintended heat lesions, e.g. skin burns. The efficiency of this point-by-point method of ablation remains limited since a relatively large part of the energy deposited is lost via heat diffusion out of the small targeted region without being utilized for ablation.

Based on a substantial body of work by C. Moonen and coworkers in 2009,^{8,9,10,11} Köhler et al.¹² presented an alternative volumetric sonication approach that efficiently utilizes the inherent heat diffusion by electronically switching the focal point between a number of predetermined locations, which forms the basis for the implementation in the Sonalleve MR-HIFU system.

Volumetric ablation is achieved by electronically steering a single focus along trajectories, which consist of multiple outward-moving concentric circles positioned in the plane perpendicular to the direction of HIFU propagation and centered on the axis of propagation. Each circle consists of several predetermined focal points that are regularly positioned on the circumference of the circle. Each location is sonicated for a short period of time with immediate switching to the next position.

The sonication order of these locations is designed to maximize the distance between successive points, ensuring an even temperature rise over the entire sonicated circle. The rapid and repetitive switching of the locations further improves the homogeneity of the temperature distribution at each circle by limiting the instantaneous peak temperature. The size of the trajectories, and thus the volumetric ablation performed, is adjusted by adding or removing outside circles.

These circles have a diameter of either 4 mm, 8 mm, 12 mm, or 16 mm. Any given trajectory include all circles with a diameter equal to or smaller than the trajectory diameter, as shown in Figure 6. The central point of a trajectory is never directly sonicated because inward heat diffusion from the surrounding 4 mm circle is sufficient to reach the thermal dose required for necrosis.

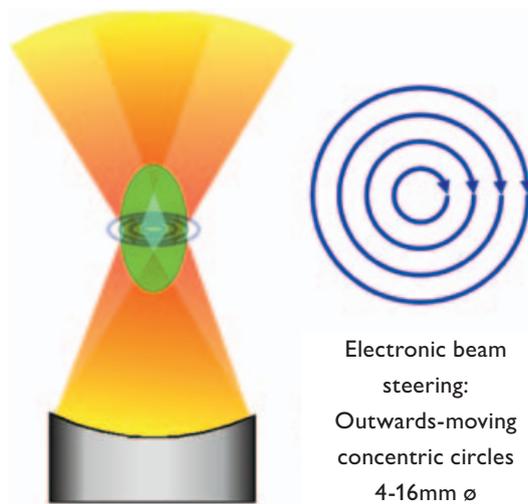


Figure 6. Volumetric heating: Beam steering profiles of successive outwards moving circles.

The resulting ablated volumes are referred to as treatment cells. The average dimensions and volumes of treatment cells with respect to their nominal diameter are given in Table 1, with a length of typically 2.5 times the diameter.

Diameter (mm)	Length (mm)	Volume (ml)
4	10	0.1
8	20	0.6
12	30	2.3
16	40	5.4

Table 1: Volumetric heating: Average dimensions and volumes of treatment cells per nominal cell diameter

Clinical work with MR-HIFU has also been shown to suffer from great variability in the treatment outcome with varying temperatures leading to both over- and under-treatment of the target tissue. One reason is that the temperature increase depends on several typically unknown tissue specific parameters, such as attenuation, perfusion and absorption. It is therefore difficult to achieve the desired ablation result without a priori knowledge of these tissue parameters. To overcome this problem, the Sonalleve MR-HIFU system uses a feedback algorithm developed by Enholm et al.,¹³ using the online thermometry data to modify the sonication parameters and generate a spatially controlled temperature profile at the treatment location.

This binary feedback algorithm regulates the treatment by controlling the duration of the sonication at each sub-trajectory, instead of using predetermined durations. For each dynamic image set, the feedback algorithm uses the temperature and/or thermal dose information at the target volume to determine whether to continue sonicating at the current sub-trajectory or switch to the next. The algorithm calculates the mean temperature in the currently sonicated target voxels (see Figure 7) and compares the value to a certain predefined target temperature. When the target temperature is reached the feedback algorithm switches the sonication to the next sub-trajectory. The target temperature limits were defined with simulations and optimizations in order to reach a lethal thermal dose of 240 EM within the entire volume enclosed by the trajectory in a minimum amount of time. By using a constant and high acoustic power the heat diffusion out of the region of interest is minimized leading to a minimum amount of total deposited energy. The sonication is stopped when the outermost sub-trajectory has reached its target temperature or alternatively when all voxels in the entire intended ablation volume have reached a thermal dose of 240 EM.

The performance of the volumetric heating method with real-time feedback had been validated in a porcine in-vivo model. The first observation is an increased efficiency in the use of applied acoustic energy with increasing cell sizes, as can be seen in Figure 8. The 12 and the 16 mm diameter trajectories had shown to be 8 and 17 times more efficient than the 4 mm diameter trajectory, respectively. This improvement in energy efficiency with cell size is primarily related to

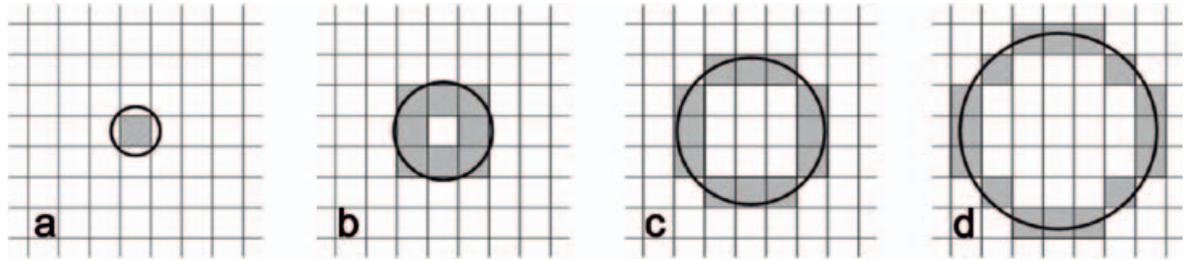


Figure 7: The 4 mm (a), 8 mm (b), 12 mm (c) and 16 mm (d) diameter sub-trajectory circles of a feedback trajectory with the corresponding voxels used for calculating the mean temperature.

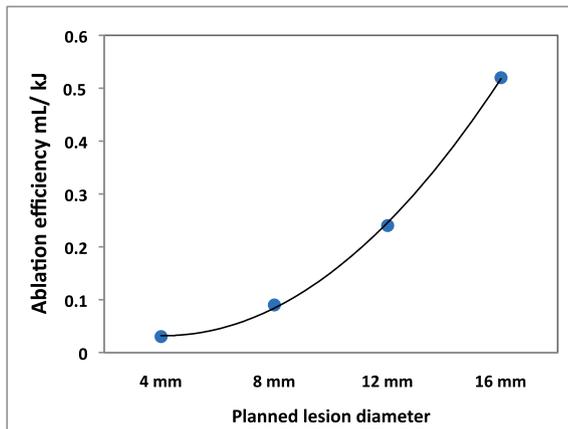


Figure 8: Ablation efficiency of volumetric heating, i.e. ablated volume (ml) per unit of input energy (kJ) as a function of the planned lesion diameter or cell size. The 12 and the 16 mm cells are 8 and 17 times more efficient than the 4 mm diameter trajectory, respectively.

the trajectory design of concentric outward moving circles. Heat applied at the inner circles does not so much diffuse out of the cell volume, instead it is used to preheat outer circles not yet sonicated and thereby reducing the required thermal energy deposition at these outer circles.

The effect of the feedback algorithm becomes very visible when looking at the maximum temperature in each ablation volume, Figure 9a, and the duration of each sonication. Using a constant power and sonication time without feedback, the variable tissue properties like perfusion, diffusion and absorption result in a wide spread of temperatures in the ablation volumes. Applying the feedback algorithm transforms this variability in temperature into a variability in sonication time, e.g. between 38.7 s to 70.6 s for a 12 mm cell.

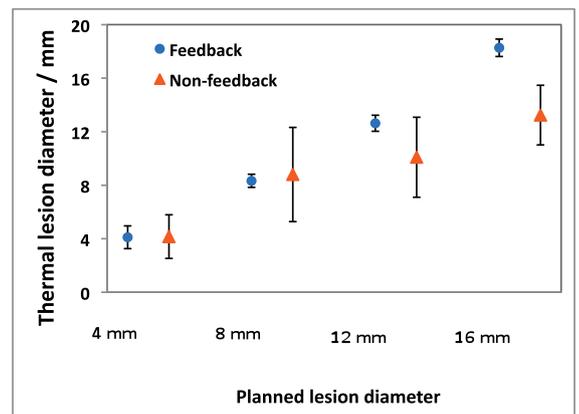
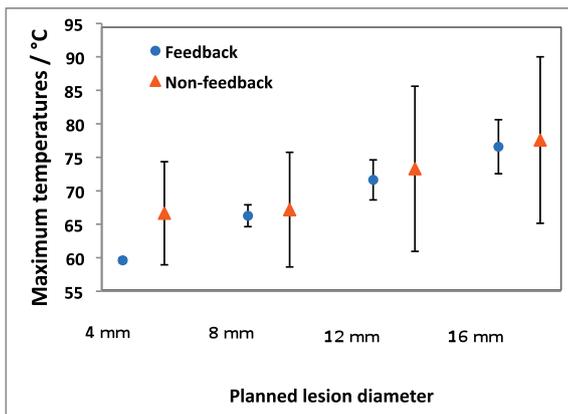


Figure 9a/b: Maximum temperatures (a) and thermal lesion diameter (b) for the four different cell sizes applying feedback and without feedback. Sonications applying feedback result in a reduced spread in both maximum temperature and realized thermal lesion size, respectively.

The spread in maximum temperature and the control thereof, respectively, directly translates into the realized thermal lesion diameter, Figure 9b. Applying feedback substantially reduces the standard deviation of the thermal lesion diameter for each cell size and makes the necrosis volume predictable. The spread in realized lesion diameter in case of non-feedback cells directly correlates with the spread in maximum temperature as discussed above. A low perfused volume may experience a substantial overheating and hence due to heat diffusion a larger thermal lesion than a highly perfused volume, where the same amount of energy may not be able to heat the tissue to target temperature.

The even temperature elevation leads to well-defined thermal lesions with homogeneously necrosed tissue within the trajectory and sharp thermal dose borders. Histology has confirmed that the transition zone from the thermal lesion to the surrounding healthy tissue is very narrow, and it is independent of the trajectory size.

Thus constraining the maximum temperature results in a predictable necrosis volume and yet efficient treatment with neither excessive nor insufficient temperature increase. The simplicity of the algorithm design makes it insensitive to changes in tissue parameters, also allowing for changes in perfusion without compromising the treatment results.

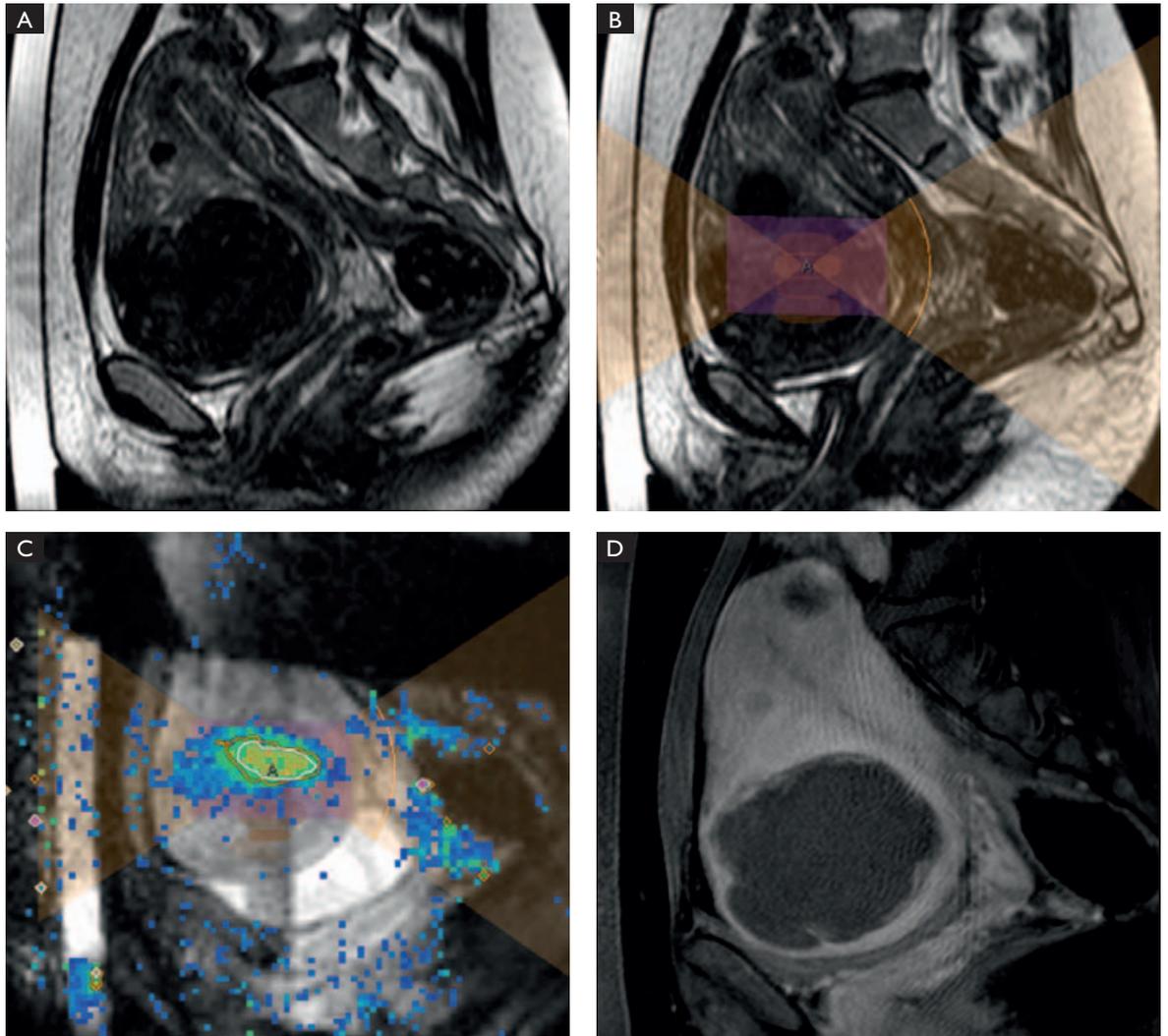


Figure 10a/b/c/d: For explanation see text

Application in ablation of uterine fibroids

Uterine fibroids are non-malignant growths, which are affecting women primarily between the ages of 30 years and the onset of menopause. A study in the USA showed a cumulative incidence of fibroids by age 50 is more than 80 percent for black women and nearly 70 percent for white women.¹⁴ They are more common in African-American women than in Caucasian women, and in women with a high body mass index. There is a similar incidence rate of these growths in European women and a higher incidence in Africa and some parts of Asia.

Approximately 10% to 20% of women with fibroids have symptoms severe enough to require treatment. The primary symptoms are pain and hemorrhage. Each year, in the US, almost 300,000 of these growths cause sufficient complications for hysterectomy procedures to be performed. With similar numbers in Europe, uterine fibroids cause a major cost burden for health care systems. MR-HIFU may offer a cost effective alternative to traditional treatment strategies.¹⁵

MR-HIFU offers a non-invasive, out-patient treatment alternative to surgery. Sonalleve MR-HIFU had been validated in clinical trials and is approved for clinical treatment of uterine fibroids in Europe (2009), Korea (2010) and Canada (2011). The early experience from these clinical trials with volumetric feedback MR-HIFU ablation of uterine fibroids have been published by Voogt et al¹⁶. They demonstrate the safety and technical feasibility of this concept.

The example in Figure 10 illustrates the sequence of events. Figure 10a shows the T2 weighted TSE planning image with a large uterine fibroid clearly visible. In Figure 10b, the ultrasound beam cone and the planned treatment cells are overlaid onto the planning image, both in orange. Figure 10c shows a thermal map in the sagittal plane of an ablated Ø12 mm cell in the cool down phase after the sonication was finished. The 240 EM dose contour of the ablated volume is shown as a white line and in this case is 28 mm long. The 30 EM dose contour is indicated in orange. Figure 10d shows the final result as an almost completely non-perfused fibroid in a contrast enhanced T1 weighted TFE image in the sagittal plane. The treatment time for this patient was 130 minutes.

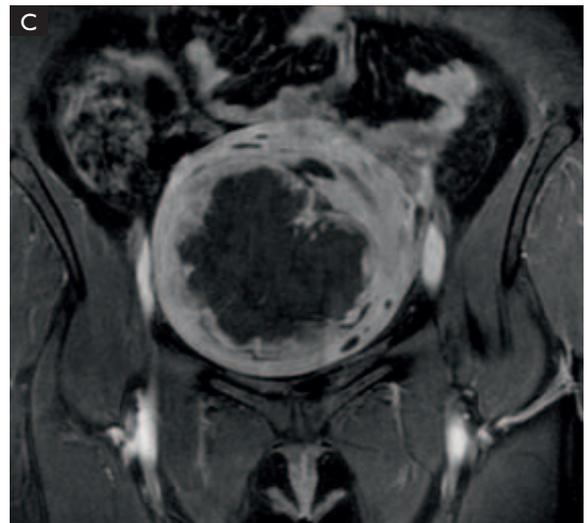
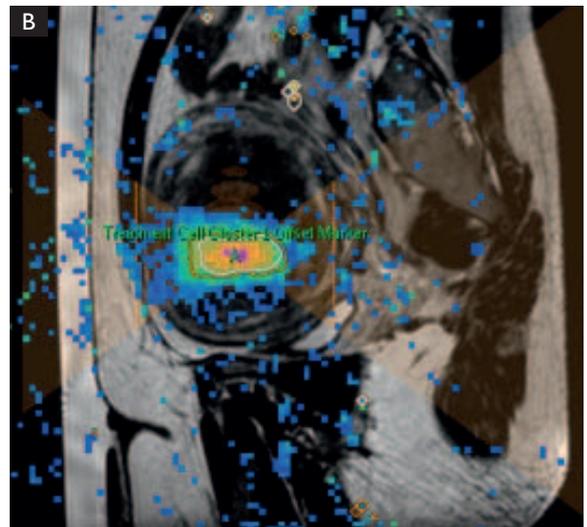
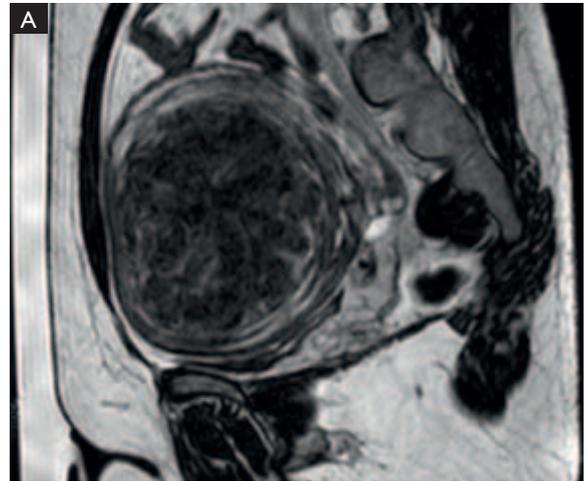


Figure 11a/b/c: For explanation see text

The second example in Figure 11 shows an even larger fibroid in the T2 weighted TSE image (Figure 11a) and the thermal map of a 16 mm cell (Figure 11b). The contrast enhanced T1 weighted image after the procedure demonstrate a successful treatment showing an almost completely non-perfused fibroid (Figure 11c). To achieve this result, a total of 48 Cells were treated (4*16mm + 21*12mm + 23*8mm) in a total treatment time of 142 minutes.

In 2009, Enholm et al. presented preliminary results of MR guided volumetric HIFU ablation of uterine fibroids with binary feedback control based on the first 13 patients treated in Bordeaux, France¹⁷. Analysis of 132 individual sonications and cell sizes showed a similar dependency of maximum temperature, lesion diameter and energy efficiency with respect to feedback vs. non-feedback cell and planned lesion diameter as discussed above for the in-vivo experiments. Cells which applied feedback showed a much higher reproducibility and predictability in size measured as non-perfused volume in contrast enhanced T1 weighted MR images. Additionally, the ablation speed as ablated ml per minute significantly increased with the planned cell diameter, with the 4 mm cells ablating only at a rate of <0.5 ml/min and the larger 12 mm and 16 mm cells at 6 ml/min and 12 ml/min, respectively (Figure 12). In a similar manner Kim et al. analyzed the improvement in energy efficiency using volumetric ablation¹⁸. Looking at the ablated volume (ml) per unit unit of energy (kilo Joule, kJ), the efficiency showed an improvement by a factor of 15 when comparing 4 mm (0.06 ml/kJ) to 16 mm (0.91 ml/kJ) treatment cells. These improvements in ablation speed and energy efficiency do not yet include the cool-down periods after each sonication, which will lead to a somewhat slower treatment speed. However, these results give a clear indication for an effective strategy to minimize treatment time by applying as many large cells as safely possible, continuing with the next smaller and smaller cell sizes to fill remaining volume of the fibroid.

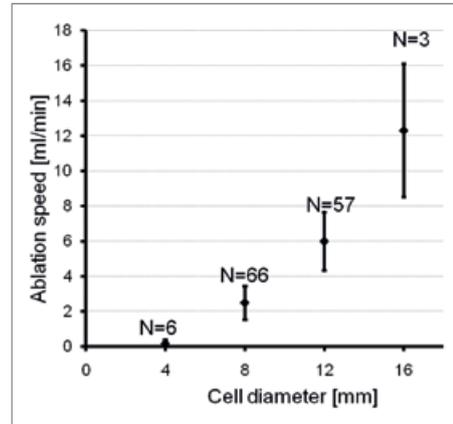


Figure 12 Clinical data demonstrate a more than 10 fold improvement in ablation speed when using 16 mm cells

The success of this treatment strategy has been demonstrated by YS Kim et al¹⁹. They report treating a 12.3-cm subserosal uterine fibroid (volume, 599.5 ml) using 49 treatment cells (16 mm, n=22; 12 mm, n=26; 8 mm, n=1) within 163 minutes from the first to last sonication. Immediate follow-up contrast-enhanced MRI showed 431.4 ml of nonperfused volume (NPV), representing 72% of the fibroid volume resulting in a treatment speed (NPV divided by treatment time) of 158.8 ml/h. In another patient, a 13-cm subserosal fibroid (643.5 ml) was treated using 52 treatment cells (16 mm, n=27; 12 mm, n=23; 8 mm, n=2) in a treatment times of 191 minutes. resulting in a posttreatment NPV of 569.8 ml (88.5% of the fibroid volume) and a treatment speed of 179 ml/h.

Conclusion

The Sonalleve MR-HIFU system represents a new approach to MRI-guided HIFU ablation. It combines volumetric sonication with rapid multislice temperature monitoring enabling a real-time binary feedback loop resulting in well controlled maximum lesion temperatures, predictable lesion volumes and a very energy efficient and fast ablation for larger treatment cells.

A major advantage of the volumetric sonication design is the uniform temperature distribution within the entire trajectory above the minimum temperatures required for necrosis. The trajectories are designed to raise the temperature evenly in all circles of the trajectories to a temperature that is sufficient to create necrosis within the volume enclosed by that circle, thereby reducing the risk of leaving tissue untreated while still presenting with sharply defined borders.

The volumetric sonication of large treatment cells comes with the price of an increase in near-field temperatures, making a careful monitoring of the temperature rise in critical areas outside the target region necessary. The multiplane thermometry provides a good visibility of temperature elevations in critical structures and as such reduces the risk of unintended lesions.

The 30 and 240 EM thermal dose thresholds have been shown to give a simple and robust estimate of thermal damage onset and necrosis size, both parallel and perpendicular to the beam path. Thermal dose maps deducted from multiplane thermometry can thereby provide the clinician with rapid and accurate online control of the temperature evolution and a clinical end point to this noninvasive therapy.

Last but not least, the volumetric heating with feedback has shown to substantially increase energy efficiency and speed of clinical MR-HIFU procedures, increasing the chances of making it also an economical viable procedure in today's cost constrained healthcare systems.

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Philips Healthcare wishes to express its appreciation to Hôpital Saint André, Bordeaux, France, Samsung Medical Center, Seoul, Korea and the University Medical Center, Utrecht, The Netherlands for the valuable contribution these hospitals made to the development of the Sonalleve MR-HIFU fibroid therapy system.

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Printed in The Netherlands
4522 962 81351 * DEC 2011