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ORIGINAL ARTICLE

Fluid preinjection for microwave ablation in an *ex vivo* bovine liver model assessed with volumetry in an open MRI system

Federico Collettini, Hendrik Rathke, Bernhard Schnackenburg, Andreas Thomas, Liane Albrecht, Britta Suttmeyer, Martin Jonczyk, Felix Guettler, Ulf Teichgräber, Thomas Kröncke, Bernd Hamm, Maximilian de Bucourt

PURPOSE
We aimed to detect possible differences in microwave ablation (MWA) volumes after different fluid preinjections using magnetic resonance imaging (MRI).

MATERIALS AND METHODS
MWA volumes were created in 50 cuboid *ex vivo* bovine liver specimens (five series: control [no injection], 10 mL water, 10 mL 0.9% NaCl, 10 mL 6% NaCl, and 10 mL 12% NaCl preinjections; n=10 for each series). The operating frequency (915 megahertz), ablation time (7 min), and energy supply (45 watts) were constant. Following MWA, two MR sequences were acquired, and MR volumetry was performed for each sequence.

RESULTS
For both sequences, fluid preinjection did not lead to significant differences in MWA ablation volumes compared to the respective control group (sequence 1: mean MWA volumes ranged from 7.0±1.2 mm [water] to 7.8±1.3 mm [12% NaCl] vs. 7.3±2.1 mm in the control group; sequence 2: mean MWA volumes ranged from 4.9±1.4 mm [12% NaCl] to 5.5±1.9 mm [0.9% NaCl] vs. 4.7±1.6 mm in the control group). The ablation volumes visualized with the two sequences differed significantly in general ($P < 0.001$) and between the respective groups (control, $P \leq 0.001$; water, $P < 0.001$; 0.9% NaCl, $P < 0.001$; 6% NaCl, $P \leq 0.001$; 12% NaCl, $P < 0.001$). The volumes determined with sequence 1 were closer to the expected ablation volume of 8 mL compared to those determined with sequence 2.

CONCLUSION
For the fluid qualities and concentrations assessed, there is no evidence that fluid preinjection results in larger coagulation volumes after MWA. Because ablation volumes determined by MRI vary with the sequence used, interventionalists should gain experience in how to interpret postinterventional imaging findings (with the MR scanner, sequences, and parameters used) to accurately estimate the outcome of the interventions they perform.

From the Department of Radiology (F.C., H.R., A.T., L.A., B.S., M.J., T.K., B.H., M.D.B. ✉ *mdb@charite.de*), Charité University Medicine, Berlin, Germany; Philips Healthcare (B.S.), Hamburg, Germany; Department of Radiology (F.G., U.T.), Jena University, Jena, Germany.

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Thermal ablation techniques are increasingly used in the treatment of various primary and metastatic tumors at different sites, including the liver (1), kidneys (2), and lungs (3). Local ablation is most commonly performed using thermal ablation techniques such as radiofrequency ablation (RFA). Other techniques include laser-induced thermotherapy, cryoablation, high-intensity focused ultrasonography, and microwave ablation (MWA). Local ablation treatment is particularly appealing in combination with image guidance such as ultrasonography, computed tomography, and magnetic resonance imaging (MRI) to allow a minimally invasive approach to therapy (4–8).

Several studies have demonstrated that combining RFA with preinjection of a fluid such as saline (different authors tested a range of concentrations) (9–14) or with diluted hydrochloric acid (15) can yield larger ablation volumes than RFA alone. In addition, both low-field and high-field MRI can be used to monitor the effectiveness of RFA within NaCl-pretreated tissues, and the findings correlate well with pathologic results (9).

Since the advent of MWA, several studies have introduced, tested, and compared this system (16–22), and the legitimate question arose as to whether, with MWA, saline preinjection would also lead to an enlargement of the ablation volume.

Interestingly, to the best of our knowledge, only one study has tested this hypothesis, concluding that preinjected fluids do not enlarge coagulation volumes in MWA (23). That study compared MWA to RFA using default protocols and settings, injecting either 5 mL ethanol, distilled water, 0.9% NaCl solution, or 10% NaCl solution (n=6 each) into *ex vivo* porcine liver (ablations without fluid injection served as the control). Although preinjection of ethanol or 10% NaCl solutions created smaller coagulation volumes, distilled water and 0.9% NaCl solution had no impact.

Hence, initial results indicate that fluid preinjection may not enlarge the ablation volume in MWA, but to the best of our knowledge, it remains unknown whether fluid preinjection in MWA (using different saline concentrations) may affect the appearance of the ablation volume in MRI.

Because a sound understanding of the extent of ablation volumes and ablation margins is imperative for assessing interventional success and successful treatment with MWA, we analyzed whether differences may arise regarding the visualization of MWA volumes with

fluid preinjection using MRI, and in this context, retested whether preinjected fluids enlarge the visualization of coagulation volume in MWA, using our own experimental setup.

Materials and methods

Study design

Our institutional review board approved the present study. MWA ablation volumes were created in 50 cuboid *ex vivo* bovine liver specimens. Five series of 10 repetitions each were conducted as follows: series 1 (n=10, no previous fluid injection as the control group), series 2 (n=10, injection with 10 mL water), series 3 (n=10, injection with 10 mL 0.9% NaCl), series 4 (n=10, injection with 10 mL 6% NaCl), and series 5 (n=10, injection with 10 mL 12% NaCl). After MWA, each specimen was examined with two MRI sequences, and semiautomatic MR volumetry was performed for each sequence (Fig. 1).

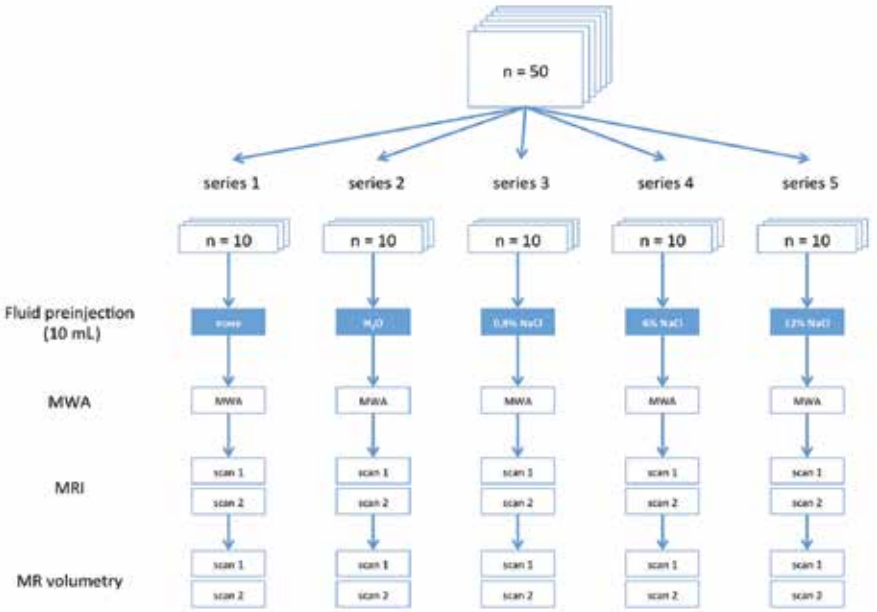

Figure 1. Study design. MRI, magnetic resonance imaging; MWA, microwave ablation.

Liver specimens, storage, and preparation

The *ex vivo* trials were performed with fresh bovine liver provided overnight from a local slaughterhouse. Ten fresh livers including the peritoneum were used. Cuboids of about 8×8×8 cm or larger were created to ensure that the entire coagulation necrosis after each MWA would easily be located inside the parenchyma. Before MWA, all liver specimens were kept in a closed cold chain at <4°C from the time of slaughter to prevent premature denaturation and dehydration. Still-sealed <4°C liver specimens were placed in a plastic tub containing 60 L water and equipped with a heating rod (Eheim Jäger, Deizisau, Germany) with a maximum power of 200 watts (W) and a recirculation pump. The temperature of the recirculating water was set to 37°C to simulate physiological body temperature just before MWA. After reaching physiological body temperature, the specimens were transferred into a kidney basin, and the MWA antenna was maneuvered into the center of the specimen (Fig. 2) and securely fixed. Cuboids of the same bovine liver were used for each run (series 1 to 5) to most accurately ensure comparable tissue conditions of the series.

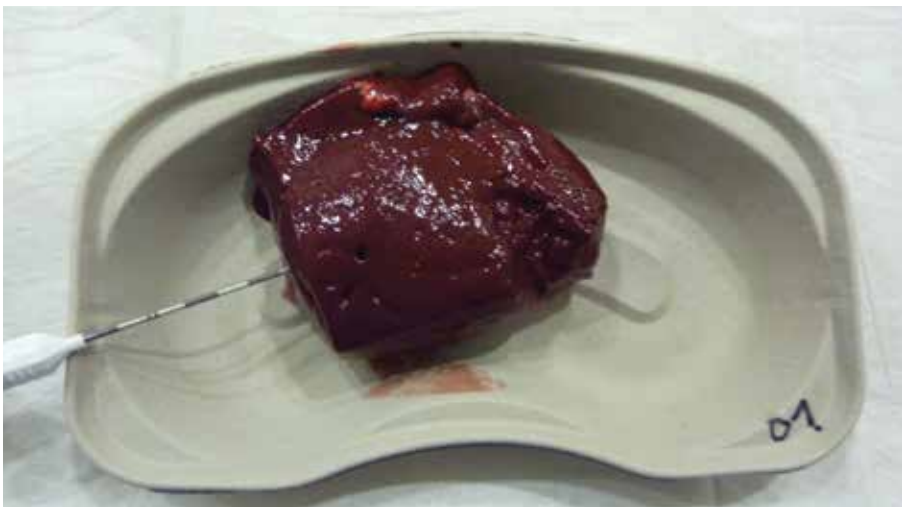

Figure 2. Example of an *ex vivo* bovine liver specimen in a kidney basin with a microwave ablation antenna positioned in the center before microwave ablation.

MWA system, procedure, and semiautomatic volume calculation

The MWA system used consisted of a generator, a pump, and a cart (Evident™ MWA, Covidien, Mansfield, Massachusetts, USA), as well as a percutaneous antenna and pump tubing (Evident™ MWA percutaneous antenna, Covidien). At the operating frequency, the percutaneous antenna delivers electromagnetic waves at 915 megahertz (MHz).

To create ablations, 45 W of power were applied with one antenna for 7 min. All ablations were performed according to the manufacturer's protocol (expected ablation volume with one antenna, 8 mL) and planned with safety margins inside the cuboid liver specimens to ensure that the entire radiating section of

the MWA antenna and the entire consecutive ablation volume would be clearly positioned and measurable inside the cuboid parenchyma. Energy was delivered only when the device was inside the parenchyma. After the preset ablation time was reached, the system shut off automatically.

Immediately after MWA, each liver specimen was scanned in a 1.0 Tesla (T) open MRI system (Panorama HFO, Philips Medical Systems, Best, The Netherlands) with two sequences each (sequence 1: inversion-prepared T1-weighted turbo spin echo [TSE] with inversion prepulse to invert the contrast between the short and long T1 signal, T1-weighted TSE/inversion recovery [IR] [i.e., long T1 appears bright]; sequence 2: pseudo proton-density-weighted TSE; Table 1). Each liver specimen was positioned in a conventional knee coil to obtain a suitable MR signal of the cuboid specimen.

One hundred semiautomatic volumetries were performed (for all 50 MWA ablations and for both MRI sequences) using a semiautomatic volumetric software tool (MR Systems Panorama HFO, Release 2.6.5.0 2009-09-30, Philips Medical Systems).

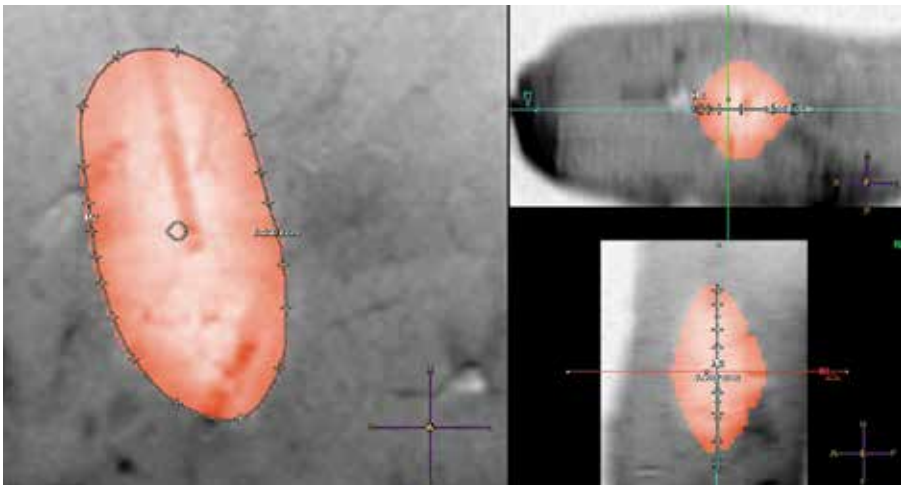

Figure 3. Example of an MR volumetry in coronal, sagittal, and axial views performed for sequence 1 (T1-weighted TSE/IR) with preinjection of 10 mL 6% NaCl. Software tool is MR Systems Panorama HFO (Release 2.6.5.0 2009-09-30, Philips Medical Systems, Best, The Netherlands). Note the filiform signal loss (left) inside the volume, indicating the previous antenna position.

Table 1. MR sequence parameters applied

		Sequence 1 T1-weighted TSE/IR[a]	Sequence 2 PDW TSE[b]
Echo time (ms)		12	30
Repetition time (ms)		800	1800
Inversion time (ms)		50	-
Voxel size (mm)	Foot-head	0.5	0.6
	Right-left	0.6	0.8
Slice thickness (mm)		4	3

[a]Inversion-prepared T1-weighted turbo spin echo sequence with inversion prepulse to invert the contrast between the short and long T1 signal.
[b]Pseudo proton-density-weighted turbo spin echo sequence.

Statistical analysis

Statistical analysis was performed with paired t tests (with and without Bonferroni adjustment), comparing all MR ablation volumes of sequence 1 with the respective MR ablation volume in sequence 2, individually comparing the respective groups (control, 10 mL water, 10 mL 0.9% NaCl, 10 mL 6% NaCl, and 10 mL 12% NaCl) of the two sequences as well as comparing the respective preinjection groups (10 mL water, 10 mL 0.9% NaCl, 10 mL 6% NaCl, and 10 mL 12% NaCl) in each sequence with its respective control group. For group comparison the dataset was in advance ratified to comply with normality distribution using Kolmogorov-Smirnov test. Statistical analysis was executed using a commercially available software (Statistical Package for Social Sciences for IBM, version 19, release 19.0.0.1, SPSS Inc., Armonk, New York, USA).

Results

All MW ablations were performed successfully according to the manufacturer's protocol with sufficient safety margins inside the cuboid liver specimens, and all MW ablations were included in the semiautomatic volumetry for both MR scans.

Fig. 3 depicts an example of an MR volumetry performed for sequence 1 (T1-weighted TSE/IR) with preinjection of 10 mL 6% NaCl. Within sequence 1, the fluid preinjection yielded no significant difference in the visualization of the MW ablation volumes compared to the control group without fluid preinjection (Tables 2 and 3). The mean MWA volumes ranged from 7.0±1.2 mm (water) to 7.8±1.3 mm (12% NaCl) vs. 7.3±2.1 mm in the control group.

In addition, within sequence 2, fluid preinjection demonstrated no significant difference in the visualization of the MW ablation volumes compared to the control group (Tables 2 and 3). The mean MWA volumes ranged from 4.9±1.4 mm (12% NaCl) to 5.5±1.9 mm (0.9% NaCl) vs. 4.7±1.6 mm in the control group.

There was, however, a significant difference in ablation volume visualization between the two sequences in general ($P < 0.001$), as well as between corresponding groups between the two sequences (Table 4;

control, $P \leq 0.001$; 10 mL water, $P < 0.001$; 10 mL 0.9% NaCl, $P < 0.001$; 10 mL 6% NaCl, $P \leq 0.001$; 10 mL 12% NaCl, $P < 0.001$). The volumes determined with sequence 1 approximated the expected ablation volume of 8 mL (at 45 W, 7 min, and one antenna, according to manufacturer's protocol) closer than sequence 2.

After Bonferroni adjustment, all significant multiple comparisons remained statistically significant.

Discussion

Comparisons of two MRI sequences revealed no significant differences in the visualization of MWA volumes with fluid preinjection compared to the respective control group without preinjection. Hence, for the tested fluid qualities and concentrations assessed by an open MRI system at 1.0 T, our experiments provide no evidence for enlargement of coagulation volumes in MWA with fluid preinjection, and thus confirm those by Ji et al. (23) in that preinjected fluids do not seem to enlarge coagulation volumes created by MWA.

The two MRI sequences and parameters were initially chosen because they had been found before MR volumetry was performed, to clearly delineate the MWA volume from the surrounding tissue in the open 1.0 T MR scanner we used. However, comparison of the semiautomatic MR volumetry results obtained with the two pulse sequences in the present study revealed that sequence 1 approximated the expected ablation volume of 8 mL significantly better than sequence 2. As different MR sequences may visualize the extent of the same ablation volume differently, the difference may be even greater when imaging is performed on different MR scanners. Hence, it may always be helpful for interventionalists to gain experience regarding how to interpret postinterventional imaging results (with the individual MR scanner, sequences, and parameters used) to accurately estimate the outcome of the interventions they perform.

Table 2. MR volumetry of microwave ablation volumes in the different fluid preinjection groups vs. the control group for sequences 1 and 2

Fluid	None (control)	H_20	0.9% NaCl	6% NaCl	12% NaCl
Preinjection volume (mL)	0	10	10	10	10
Microwave ablation volume (ccm)					
Sequence 1	7.3±2.1	7.0±1.2	7.7±1.8	7.4±1.9	7.8±1.3
Sequence 2	4.7±1.6	5.3±1.4	5.5±1.9	5.2±1.3	4.9±1.4

Data are presented as mean±standard deviation.

Table 3. Paired-samples test of MR volumetry of microwave ablation volumes in the different fluid preinjection groups vs. the control group for sequences 1 and 2

		Paired differences					
				Standard error of the mean	95% Confidence interval of the difference		
		Mean	Standard deviation		Lower	Upper	*P*
Sequence 1							
Pair 1	Control vs. H_20	0.29990	2.48257	0.78506	-1.47602	2.07582	0.711
Pair 2	Control vs. 0.9% NaCl	-0.37320	1.90357	0.60196	-1.73493	0.98853	0.551
Pair 3	Control vs. 6% NaCl	-0.07950	3.23802	1.02395	-2.39584	2.23684	0.940
Pair 4	Control vs. 12% NaCl	-0.49450	2.12461	0.67186	-2.01435	1.02535	0.480
Sequence 2							
Pair 1	Control vs. H_20	-0.60440	2.37339	0.75053	-2.30222	1.09342	0.441
Pair 2	Control vs. 0.9% NaCl	-0.74460	1.64281	0.51950	-1.91980	0.43060	0.186
Pair 3	Control vs. 6% NaCl	-0.51880	2.28404	0.72228	-2.15271	1.11511	0.491
Pair 4	Control vs. 12% NaCl	-0.17000	2.06753	0.65381	-1.64902	1.30902	0.801

Table 4. Paired-samples test of pairwise comparison of corresponding groups in the two sequences

		Paired differences					
				Standard error of the mean	95% Confidence interval of the difference		
Sequence 1 vs. Sequence 2		Mean	Standard deviation		Lower	Upper	*P*
Pair 1	Control	2.57780	1.62100	0.51261	1.41820	3.73740	0.001
Pair 2	H_20	1.67350	0.61390	0.19413	1.23434	2.11266	< 0.001
Pair 3	0.9% NaCl	2.20640	1.26936	0.40141	1.29836	3.11444	< 0.001
Pair 4	6% NaCl	2.13850	1.45174	0.45908	1.09999	3.17701	0.001
Pair 5	12% NaCl	2.90230	1.42156	0.44954	1.88538	3.91922	< 0.001

Another interesting aspect worth discussing is why the fluids (10 mL water, 10 mL 0.9% NaCl, 10 mL 6% NaCl, and 10 mL 12% NaCl) injected before MWA consistently did not significantly enlarge the ablation volume in our *ex vivo* experiment. Hence, fluid preinjection appears to enhance the effectiveness of RFA but not MWA. This difference may be attributable to different effects of RFA and the microwave technique—with RFA, the amount of heat generated in the target tissue is determined by the amount of current that passes from the electrode through the tissue. Current is defined as the electric charge per unit time (I=Q/t, where I is current in amperes, Q is charge in coulombs, and t is time in seconds)

and heats the tissue via impedance (resistance). Fluids such as saline can lower tissue impedance. The lower the impedance, the more efficiently a generator can deliver the desired current, resulting in more heat per unit time delivered. In addition, saline can effectively increase the size of the electrode, reducing current density at the electrode-tissue interface and the likelihood of high impedance buildup around the electrode. Sustained and higher-power delivery to the tissue results in larger ablation volumes.

Because MWA systems do not rely on electrical impedance to produce heat, saline injection cannot influence energy delivery via that physical mechanism. In other words, saline preinjection should result in about the same heat per unit time as no saline preinjection, or maybe even less (with the possibility of creating a smaller ablation volume): some of the applied MWA heat may be absorbed by saline, reducing the energy reaching the tissue. Furthermore, saline may actually reduce the amount of energy delivered by the antenna due to conductivity: MW energy may reflect a conductive boundary, and saline present at the target site may to some extent block the energy from leaving the probe. Conversely, however, one recent publication has provided initial evidence that extension of microwave coagulation may still be possible using a special perfusion microwave electrode (24).

Our study has several limitations. This was an *ex vivo* study with a small number of MWA treatments performed in the individual fluid preinjection groups and the control group. Although the *ex vivo* setup simulated some physiological conditions (e.g., warming up the fresh bovine liver cuboids to physiological temperature of 37°C just before MWA), other *in vivo* conditions such as vascular perfusion (to account for possible heat-sink effects) were not modeled. In addition, as discussed above, MR visualization of ablation volumes varies with the pulse sequence used and may also differ among MR scanners, manufacturers, and field strengths.

In conclusion, interventionalists must consider the characteristics of ablation volumes when using MWA instead of RFA and when using MRI for visualization and validation of the ablation volumes created.

Acknowledgements

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Conflict of interest disclosure

The authors declared no conflicts of interest.

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