In vivo evaluation of MRgHIFU volumetric sonication using interleaved electronic-and-mechanical displacement of focus

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Introduction : High Intensity Focused Ultrasound (HIFU) is a therapeutic approach coupling flexibility and non-invasive features. A successful therapy can be reached under MR guidance that offers excellent soft tissue contrast and online thermometry enabling thermal dose delivery control. Phased array technology significantly reduces the latency time for repositioning the focus whereas mechanical displacement of the focus does not generate steering lobes. In order to evaluate the lesion formation and the potential interest of dual-modality (electronic-and-mechanical) interleaved displacement of the focus for volumetric sonication paradigms, we performed *in vivo* experiments on rabbit thigh using a prostate-dedicated endorectal phased array and a translation-rotation mechanical actuator.

Methods : The study was performed on a clinical 1.5T Philips (Achieva) scanner on the thigh of 4 healthy rabbits (F, race New Zeeland, 3 to 3.5 kg, hair removed on thigh), under general anesthesia following an IEB-proofed *in vivo*. The method combined a phased-array HIFU transducer and a MR-compatible 3D positioning system. The HIFU device (Imasonic, France) consisted of 16 concentric circular rings placed on a truncated spherical cap (f=3 MHz, natural focus: 60mm), see Fig. 1a, designed for endorectal use. Degassed water was circulated inside a tip cooling balloon around the HIFU transducer. Electronic change of the focal depth was available in the range of 32mm to 69mm from the pole of the spherical cap and enabled rapid radial line-scan sonications. The LR and HF translations and the rotation around the B_0 axis were implemented using a mechanical system. The stepper motors operated in the magnet fringe field, and were driven by an ESP300 Controller. The latter one operated outside the scanner room. A multi-channel RF generator (Image Guided Therapy, France, 16W/channel) provided an independent control of the signal amplitude and phase for each element. The HIFU beam direction was top-bottom. A water bag relying on the rabbit skin through ultrasonography gel enabled both mechanical decoupling of the transducer displacement from the skin, i.e. no induced tissue motion, and acoustic coupling for HIFU. Two orthogonal planes (axial and sagittal) were simultaneously monitored using fast MR-thermometry (PRFS method) and the temperature and thermal dose maps were displayed in real time. The spatial resolution for the thermometry images was $1x1x5mm^3$ with a temporal resolution of 2.5s. Short test sonications and MR thermometry were used to verify the focusing ability and the centering of the two acquisitions plans on the prescribed treatment zone. The rabbit thigh was sonicated using complex patterns of foci positions (1 or 2s / focus position, no waiting delay between shots excepting for the system latency), describing slices (Fig 1.b) or volumes (a stack of 7 parallel axial slices). The shape of the thermal lesions was examined 5 days later using MRI T2w sequence and Gd-T1w-TFE. Post-mortem histological analysis was performed on sonicated tissue.

Results : The average standard deviation in MR thermometry was 1.8ºC as determined from baseline acquisitions. Temperature maps (Fig. 2), thermal dose maps and MRI assessment of the lesion at D+5 (Fig. 3) indicated that dual-modality displacement of the focal point can induce homogenous lesions in a pre-defined zone. Post-operatory examination of the rabbit thighs indicated no thermal lesion of the skin in any experiment. The T2w and Gd-T1w-TFE sequences indicated a distance between the edge of the lesion and the surface of approx. 4 mm for the case presented in Fig. 2b and Fig. 3. Histological analysis showed a distance of approx. 0.9 mm but here we need to include also the skin thickness (approximately 2 mm) so the near field safety distance as required from rectal wall in prostate treatment was respected.

Discussion : Electronic displacement of the focus (along the ultrasound propagation axis) interleaved with mechanical XZ translations and rotation around B_0 is suggested to be a suitable modality to treat patient-specific size and shape of pathologic tissue. The phased-array electronic displacement of focus (0.1s latency) is faster than the mechanical motion of the HIFU device (1s latency). While electronic focusing (radial line scan) is necessary to speed up the procedure, one should consider as drawback the non-negligible risk for generating secondary lobes with full-steering in 3D. No artifacts were found to corrupt the MR acquisition during the mechanical trajectory, while mechanical displacement induces strictly no secondary lobes. Therefore the dual-modality volumetric sonication paradigm represents an interesting method to induce the desired shape of the lesion in prostate through the limited endorectal space, in a reasonable period of time and without side effects.

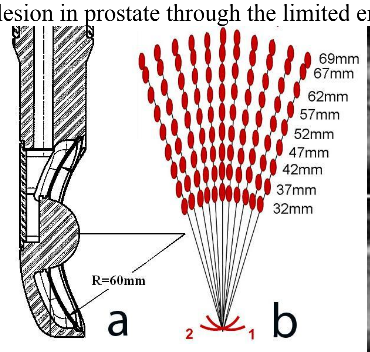

Figure 1. a). Phased array HIFU transducer with natural focus at 60 mm, **b).** example of slice sweeping paradigm; 9 foci/line were chained electronically, and 11 line-scans were successively performed with 2.7º mechanical rotation increment.

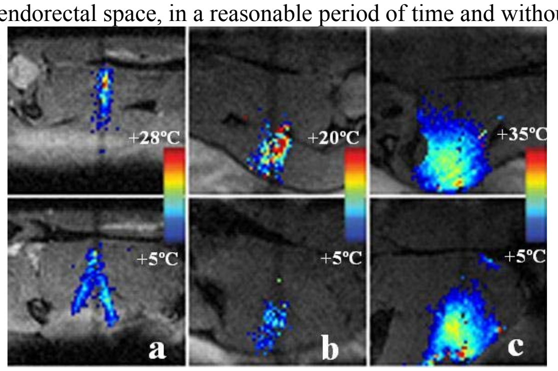

Figure 2. Axial (up) and sagittal (down) temperature maps at the end of: **a).** elementary sonication (F=69mm, P=36W_{ac} during 13.5s), **b).** slice sweeping and **c).** volume sonication. For b) and c) focal depth range /time per focus /power range /total sonication time were respectively 32-47mm /2s /17.4-39.1Wac /65s and 32-47mm /1s /15.5-34.8Wac /408s. Shown images (64 mm FOV) are flipped top-bottom.

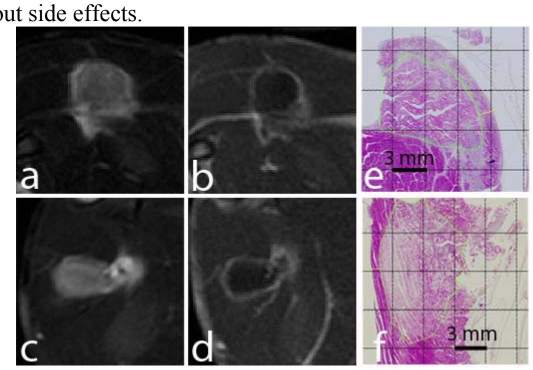

Figure 3. Lesions obtained with slice sweeping sonication (see Fig 1,b) shown in axial (**a,b**) and sagittal (**c,d**) plane. T2w (**a.c**) and Gd-T1w (**b,d**) contrast. Shown FOV: 35.7x35.7mm; **e).** and **f).** histological images of the same lesion. Lesion size in histology was 9.5x6.3mm for image e) and 16.5x6.2mm for image f).

References: 1. F.A. Jolesz et al, Magn. Reson Imaging Clin. N. Am. 2005; **13**, 545–560, 2. A Blana et al. Eur Urol 2008; 53:1194-201, 3. L Petrusca et al, ISMRM proc., Honolulu 2009, ISBN 1545-4428.