

Thermal ablative lesions in sheep's renal cortex using respiratory gated MRgHIFU: spatial accuracy and complications

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Introduction and purpose. High Intensity Focused Ultrasound (HIFU) is a therapeutic approach coupling flexibility and minimally-invasive features. MR guidance of HIFU offers excellent tissue contrast for both targeting and online thermometry for per-operative control of the thermal dose delivery. A significant challenge lies in obtaining thermal lesions of oncologic quality in moving organs, despite the respiratory motion, while preserving the surrounding healthy tissue. The current *in vivo* study was performed on healthy sheep kidney and aimed to demonstrate the capability of producing sharply delineated thermal lesions in the renal cortex using MRgHIFU.

Materials and Methods. The MR compatible HIFU platform consists of a phased array transducer (256 elements, F=1MHz, Imasonic, France) driven by a programmable 256-channel generator and positioned by a 2D mechanical system in the XZ plane (both from Image Guided Therapy, Pessac, France). MR thermometry (TE/TR/BW/voxel size = 8.4, 107, 584, 1x1x5) was performed on a 3T whole body MRI scanner (Magnetom Trio a Tim system, Siemens AG, Germany) using the PRFS method in 3 orthogonal planes. The tests were performed in the right kidney of 7 healthy sheep under general anesthesia (approved protocol by the Veterinary Cantonal Authority of Geneva). The animals were positioned in a dedicated holder and elementary sonications were generated at predefined locations in the renal cortex. Respiratory gating was achieved using an in-house built optical sensor for analogical encoding of thorax expansion and a Smart Star CPU/ADC/DAC (Rabbit Semiconductor Inc, California) interface to the HIFU generator, with embedded in-house written real-time software. The sonication window was generated during 10 respiratory cycles (60 sec, forced breathing) with a duty-cycle of 40-45%. The same external signal was used for gating the HIFU sonication and the MR acquisition. Semi-chronic MRI follow-up was performed at day 7 post-treatment with Gd-DTPA bolus contrast agent using a Turbo-Flash sequence with non-rigid registration (5 coronal slices, 5 min scanning time) following which the animal was euthanized. Visual inspection of the perirenal regions was performed by an anatomopathologist expert while the kidney was being removed, in order to detect eventual collateral damages or suspicious changes. After fine slicing (0.6 mm thick) of the post-mortem formalin fixated organ, a 3D reconstruction of the anatomical pieces was performed using Osirix (OsiriX Foundation, Geneva). The regions of thermal coagulation were sent for microscopic histology inspection.

Results. MRI visualization of the target (T1w VIBE) was excellent in all cases, moreover, the MR thermometry sequence (GRE-EPI) itself permitted to clearly identify online during HIFU sonications the anatomy of the kidney and the surrounding tissues. The results obtained for the elementary sonications systematically showed sharply delineated regions of thermal ablation of typical size 3x3x5 mm³ (see an example of the temperature maps Fig 1, 3 orthogonal planes, at the end of the HIFU sonication). The circular ablation spot (Fig 2c) on the macroscopic section orthogonal to the HIFU beam is a "gold standard" proof for the accurate management of the motion during HIFU sonication. The perfusion study enabled the detection of the non-perfused regions and also enabled the signal kinetics curves to be obtained after administration of the contrast agent (see Fig 2a,b). The homogenous necrosis visualized on Gd T1w MR images was confirmed by the histological analysis (Fig 2d). Significant heat deposition and semi-chronic complications were observed (Fig 3) in 5 cases out of the 7, occurring either at the interface of the spinal process adjacent to the kidney capsule (even laterally from the main beam axis) or at the air-filled bowel interface.

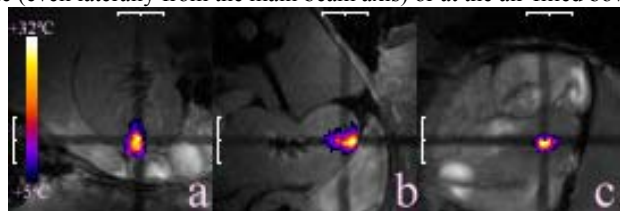


Figure 1. Three orthogonal temperature maps (shown FOV = 90 mm square) overlaid on magnitude EPI-GRE images, for single point sonication in sheep renal cortex. Anatomic structures are clearly identified (ureter-1, pelvis-2, calyx-3, renal capsule-4).

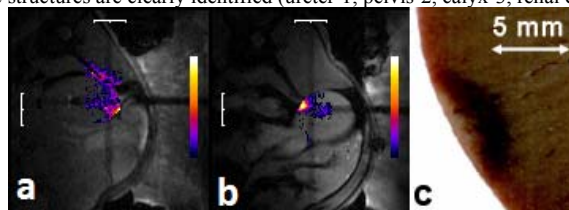


Figure 3. Thermometry maps for 2 different animals showing the reflections of the HIFU beam on vertebra transversal process and perineal membrane (a,b) and post-mortem image of the kidney showing the superficial unwanted lesion (c).

Discussion. The current study demonstrated that sharply delineated and homogenous thermal ablations in the renal cortex can be obtained using the same trigger signal for gating the HIFU sonication as for the PRFS MR thermometry, despite the respiratory motion. The induced lesion was clearly visualized day7 post-treatment and was further confirmed by post-mortem histology. High quality MR thermometry data (both magnitude and phase) in 3 interleaved orthogonal planes are required to enable online detection of undesired hot spots before irreversible collateral lesions are caused.

Conclusion. Sharply delineated and accurately targeted thermal lesions in the renal cortex using MRgHIFU were demonstrated, but side-effects remain a major safety problem to be addressed when performing HIFU ablations in the abdomen. A careful on-line monitoring of temperature in three orthogonal planes and semi-chronic follow-up (e.g. 7 to 10 days) is mandatory for preclinical validation and assessment of the HIFU therapy.

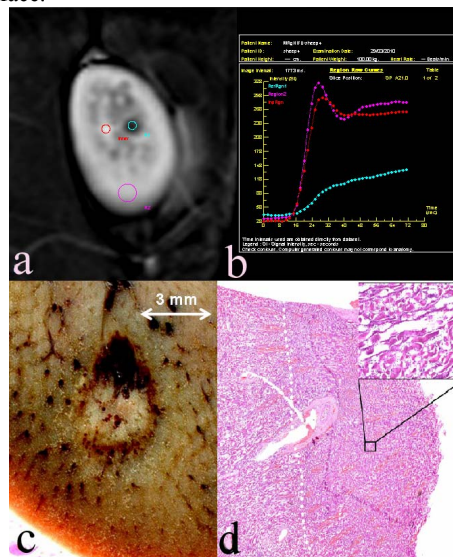


Figure 2. a) Perfusion MR image of the kidney showing 3 different regions: the ablated region (light blue circle), a medium size artery (red) and normally perfused cortex (pink circle); b) signal kinetics curves from regions described before; c) macroscopic picture of the kidney showing the circular and homogenous ablation spot; d) microscopic image of the ablated tissue delineated by the dotted white line.