## Controlled Apnea for Focused Ultrasound Ablation of Liver Tissue - Animal Model

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<u>Background:</u> The aim of this study was to evaluate the safety and accuracy of the non-invasive technology of MR guided Focused Ultrasound Surgery (MRgFUS) in focal ablation of liver tissue. However, to allow safe and effective treatment one has to overcome the problem of liver motion during the respiratory cycle. This motion causes defocusing of the energy, difficulty in achieving a continuous treatment region, and prevents quality MR thermal imaging.

<u>Material and methods</u>: Two pigs were treated, under general anesthesia, with an MRgFUS system (ExAblate 2000, InSightec, Israel). Several tissue regions in different segments of the pig's liver were chosen as targets for complete ablation. Each lesion was created by 30 to 40 adjacent treatment foci, called 'sonications'. Each sonication was monitored in real-time by the MR, for anatomical accuracy and thermal efficiency. Each sonication was performed during 22 to 30 sec. of apnea. Between sonications the pig was kept under controlled, positive pressure, mechanical ventilation, using an OR portable ventilator (Ivent 201 v. 1.4, Versamed, Israel). The intermittent apnea periods were always started at the end of inspirium. Range of controlled mechanical ventilation (CMV) periods was 60 to 150 sec. At the end of the ablative procedure an MR scan with i.v. contrast was performed to evaluate the location, shape, and volume of the ablated, non-perfused areas. The pigs were sacrificed 4 days after the procedure and their livers were examined.

<u>Results:</u> The range of temperatures achieved in the ablated foci of each sonication was 60 to 80 °C, which created a continuous lesion as seen in post treatment contrast enhanced MR imaging (Fig 1A). There was no inter or post procedural morbidity. The macroscopic appearance of the treated liver showed a distinct lesion per each sonication in full accordance with the planed map of treatment (Fig. 1B). The range of microscopically measured distances between sonication spots, in comparison with the planned locations, was 0 to 0.6 mm. Histo-pathological examination showed, within the areas of necrosis, identifiable liver cell outlines, but no cellular detail – typical of coagulation necrosis. An interim zone, 0.4 mm of coagulative necrosis with some viable vascular elements is a typical finding at the borders of the treated areas (Fig. 1C, 1D).

<u>Conclusions:</u> Mechanical ventilation with intermittent apnea periods overcomes the problems associated with liver movements during the respiratory cycle. Consecutive sonications can be delivered to a continuous tissue volume in a very accurate manner (less than 1mm away from planned location). MRgFUS creates distinct lesions of complete tissue destruction (Fig 1). Our experiment indicates that MRgFUS under general anesthesia could become a safe and accurate, non-invasive technology for the ablation of liver tissue.



Fig 1. A: Post treatment contrast image showing a consecutive ablated region.

B: Gross pathology of the thermal lesion.

C: The areas of macroscopic damage show a clear 'zonal' pattern, or 'geographic' pattern of necrosis (picture x 12,5 – arrow on border between preserved and necrotic).

D: The border between the preserved and necrotic liver parenchyma is vascularized and shows an isolated residual viable hepatocytes (picture x100).