In-vivo MR guided High Intensity Focused Ultrasound ablation of pig liver tissues: Preliminary results of a survival study.

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Introduction / objectives

Colorectal cancer remains the third most common cancer as well as the third leading cause of cancer death in males and females in the United States [i]. Development of colorectal metastases in the liver plays a crucial role in poor survival of these patients. Surgical resection of liver metastases is considered the most efficient treatment to improve survival rate today [ii], but is not applicable to a substantial number of patients. Among alternative treatment methods MR guided High Intensity Focused Ultrasound (HIFU) represents a very promising approach. The main objective in this study was to show the relationship between thermal dose deposition in a multiple sonication scheme and achieved tissue damage, verified after one-week survival MRI control followed by histology.

Methods

Male pigs (n=11, 25-40 kg) were anaesthetized, intubated and placed on the HIFU transducer integrated to the bed of a Philips 3T Achieva. Sonication was performed using the Sonalleve HIFU console. MR imaging and sonication were performed during mechanically controlled breath-hold periods. Planning and targeting MR images were acquired using 3ch integrated coil as follows: **A**: SSFP, TR/TE/FA=4.5/2.3ms./120º, 80 slices of 1.5mm thickness, pixel size 1.5×1.5 mm^2, matrix 212×158; **B**: 3D T1w GRE, TR/TE/FA=2.7/1.2ms./7º, 80 slices of 2.5mm (over contiguous), pixel size 1.25×1.5, matrix 220×240, sense factor:1.5; **C**: THRIVE 3D Multi-shot T1w-GRE, TR/TE/FA=6.8/3.4ms./8º, 80 slices of 2.5mm (over contiguous), pixel size 1.10×1.42, matrix 260×260, sense factor: 1.5. Temperature monitoring was performed using Multi slice (4) Fat-suppressed Multi-shot GRE-EPI sequence with 7 mm slice thickness, with a dynamic scan time resolution of 4.2s. Post-sonication MR images were obtained repeating sequence acquisition B and C pre- and post-Gadolinium chelate injection (0.1 mMol/kg Dotarem, Guerbet, France)

HIFU focal point was automatically adjusted electronically to form an ellipsoid "treatment cell" of 8×8×20 or 12×12×30 mm^3, performed individually or in cell clusters. Duration of sonication time was 30 to 48s, at a frequency of 1.2 MHz. and with a power of 120-200 W (Power level was adjusted to avoid cavitation after test sonication control). Multiple sonication periods were used (1-6) to grade the hyperthermia effect. After HIFU the pigs were wakened and moved back to the animal stable. Pigs were anaesthetized again after one week for follow-up. MR Images were acquired using a 6ch cardiac coil and sequences **A**, **B** and **C** as described above, followed by a dynamic 3D T1w-GRE, during Gd bolus passage to evaluate contrast uptake in HIFU ablated regions: TR/TE/FA=3/1.45ms/10º, 140 slices of 3mm thickness, pixel size 1.49×1.5, matrix 252×186, sense fact. 2, 6 dynamic scans with time resolution 6.3s. The pigs were thereafter sacrificed and the liver was extracted. The HIFU lesions were excised with a margin of macroscopically unaffected tissue, sectioned in slices of 3 mm and fixated in formaldehyde 4% solution for one week and then paraffin-embedded. The slices were stained with hematoxilin and eosin and examined for tissue necrosis.

Results

Image subtraction between MRI datasets acquired during different breath-hold periods showed that reliable re-positioning (1-2mm) of the liver was achieved using automatic mechanical respiratory control. Range of ablation size varied from 35×15×14 to 7×7×5 mm^3. Ablation size observed on post-sonication MR images was in good agreement with targeted value, when the temperature curve had a normal appearance. However, a discrepancy was observed when visible vessels were adjacent or included in targeted ablation zone. Follow-up MRI demonstrated no contrast agent uptake in ablated zone. Volume of ablated zone defined by histopathology was less than targeted volume in all cases. Using 3-6 sonication cycles, the ablated volume consisted of fibrous tissues and only 5% necrosis.

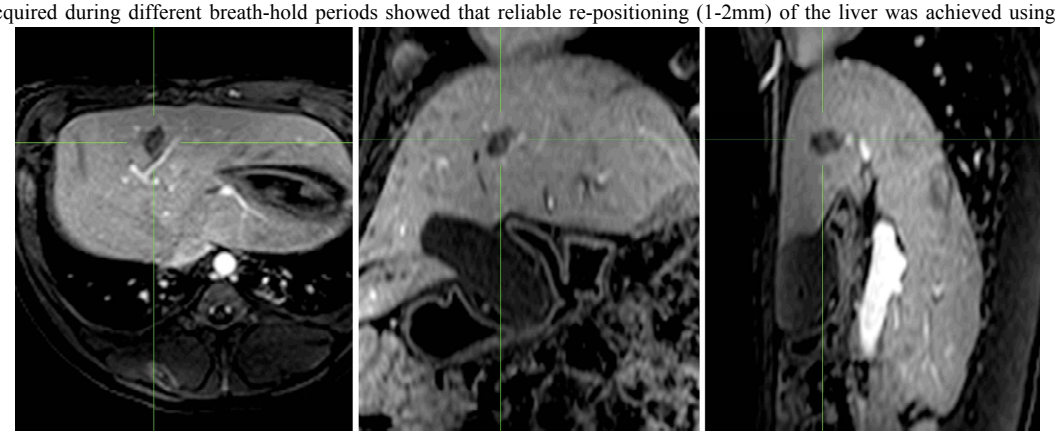

Figure: Transversal, coronal, sagittal views of a treatment cell (8mm) cluster in the vicinity of large veins.

Discussion / conclusion

Minimal localization errors occur between pre-treatment images and applied HIFU ablations when using automatic mechanical breath-holding during MRI acquisition and HIFU sonication. Moreover, mechanical breath-holding limits the occurrence of phase errors, which improve MR thermometry. The presence of large veins produce significant heat-sinks [iii], which may explain the size discrepancy between targeted and confirmed ablation zone. Previous studies have reported coagulation formation at the beginning of sonication [iv]. Local perfusion is then reduced which improves the effect of the following sonication cycles. Increase of the total sonication time is believed to induce complete tissue necrosis in the highly vascularized liver [v]. In our setting, the number of multiple sonication cycles needed to achieve complete tissue necrosis remains to be determined.

References

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