MR ELASTOGRAPHY OF *EX VIVO* PROSTATE CANCER AT MULTIPLE FREQUENCIES AT 7T

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Purpose

Magnetic Resonance Elastography (MRE) is a method to probe the mechanical properties of tissue and has been shown to be capable of diagnosing cancerous tissue [1]. In this work, dynamic 7T MRE was performed on *ex vivo* prostate specimens. Multiple frequency excitation was use to determine whether the frequency dependence of the mechanical properties of tissue can be used to improve the accuracy of cancer detection. The results are compared to whole-mount histopathology. Previously, MRE was performed on prostate cancer specimens using quasi-static methods at 7T [2] and dynamic single tone excitation (350Hz) at 1.5T [3].

Methods

Ethics board approval and informed consent were obtained for four patients (mean age of 64yrs) scheduled for radical prostatectomy. Following surgery, the prostate specimens were immersed in formalin for 72 hours, and imaged with a 7T Bruker MR scanner. After imaging, the specimens were sliced using a custom cutting device [4], in attempt to align the histology slides with the transverse images. The outline of the prostate and the tumours, along with the Gleason score, were marked on the histology slides by an experienced radiologist and pathologist. The 2D segmented contours of the histopathology were then registered to the surface of prostate that was extracted from the segmented T2W volume [5]. The method uses particle filtering to minimize the Euclidean distance between the contours and the surface with respect to in-plane translation and rotation of each histology slice alone, and out-of-plane translation and rotation of all the slices together. For MRE imaging, a conventional motion-sensitized spin-echo pulse sequence was used (G_{max}=200mT/m). The 3D wave field was acquired on 9 slices for a 64x64 matrix with 1 mm^3 isotropic voxels. Echo times from 35 ms to 50 ms and repetition times between 500-1000 ms were used. The mechanical excitation (600, 800 and 1000Hz) was applied externally by a carbon fiber tube connected to a custom electromagnetic driver positioned in the fringe field of the scanner (Fig. 1). The total imaging time was 22 min. The dynamic shear modulus G_d and loss modulus G_l, and complex modulus G_s were calculated by local inversion of the linear viscoelastic 3D wave equation [1]. The frequency dependence of each parameter, modeled by a power law, was assessed using the exponent parameter γ.

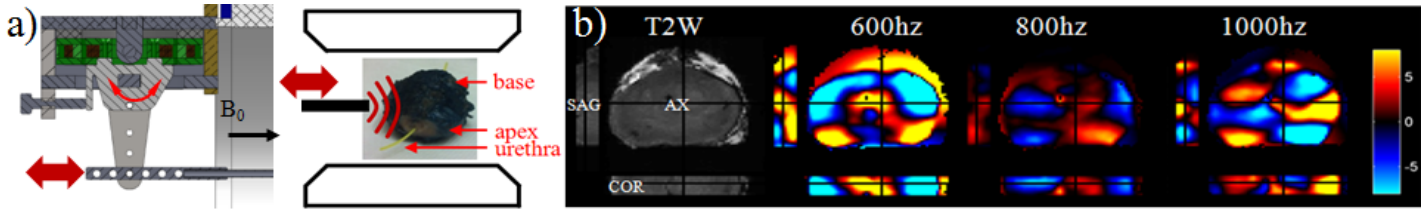

Fig. 1. a) The custom made mechanical driver consists of a rotating current-carrying coil that generates linear vibrations when the driver is placed in the fringe field of the MR scanner. The vibrations are transferred to the specimen using a carbon fiber tube. b) The T2W image of a sample *ex vivo* prostate specimen with its corresponding waves U_x(µm) at 600, 800 and 1000Hz are shown.

Results

Eight tumors were analyzed with an equivalent diameter between 2mm and 9.4mm (mean=9.4mm) and Gleason score more than 3+3. The acquired images were free of artifact from the electromagnetic driver. The waves are clearly present at multiple frequencies as shown in Fig1b (only x-component of wave is shown), and the total wave amplitude was 57µm (600hz), 18µm (800hz), 19µm (1000hz). The reconstructed images of viscoelastic parameters as registered to histology are shown for two cases in Fig2a. In terms of registration performance, the area overlap between the segmented histology and registered segmented MR slices was 94.8±3.5%, and the error between landmarks on histology and the corresponding registered MR was 1.8±1.1mm. The mean values for G_d (G_l) for cancerous tumors were 67±24(138±49), 86±38(139±63), 150±52(199±47)kPa; and for healthy tissue 67±42(118±56), 69±29(107±43), 117±44(157±70)kPa for excitation frequencies of 600hz, 800hz and 1000hz, respectively. The mean value for G_s for cancerous versus healthy tissue is shown in Fig2b, where the separation power (*p*-value) was 0.51, 0.1 and 0.09 at the three frequencies. The receiver operating characteristic of G_s is shown is Fig2c where the area under the curve was 0.65, 0.69 and 0.72 for excitation frequency of 600hz, 800hz and 1000hz, respectively. This resulted in a sensitivity of 63%,75%, 75% and specificity 72%, 83%, 67% at a threshold of G_s=154, 149, 245kPa, for the three frequencies, respectively. The differentiation was not significant (*p*-value=0.37) for the power law exponent γ from G_d (G_l) and were 1.56±1.47 (0.68±0.73) for cancerous tumor and 1.12±0.79 (0.55±0.45) for healthy tissue.

Discussion and Conclusion

The chemical fixation of the prostate dramatically increased the stiffness of the prostate as was also observed by others [2]. Thus, the excitation frequencies and resulting elasticity values are significantly higher compared to other experiments in this field. There are therefore limitations on how these results can be translated for *in vivo* applications. Cancer was distinguished from healthy tissue with modest separation power but with many false positives, although only eight tumors were analyzed. Stiffer structures within the prostate may be mistaken for tumors, and also the effect of other confounders such as Benign prostatic hyperplasia (BPH) on the mechanical parameters is not known. The narrow frequency span limits the applicability of power law which may be widened for future experiments and is typically several orders of magnitude in materials sciences. We noted that the images acquired are very sensitive to image filtering parameters and the methods used. This warrants further work in the use of inversion methods, and in the repeatability and sensitivity of the resulting mechanical parameters.

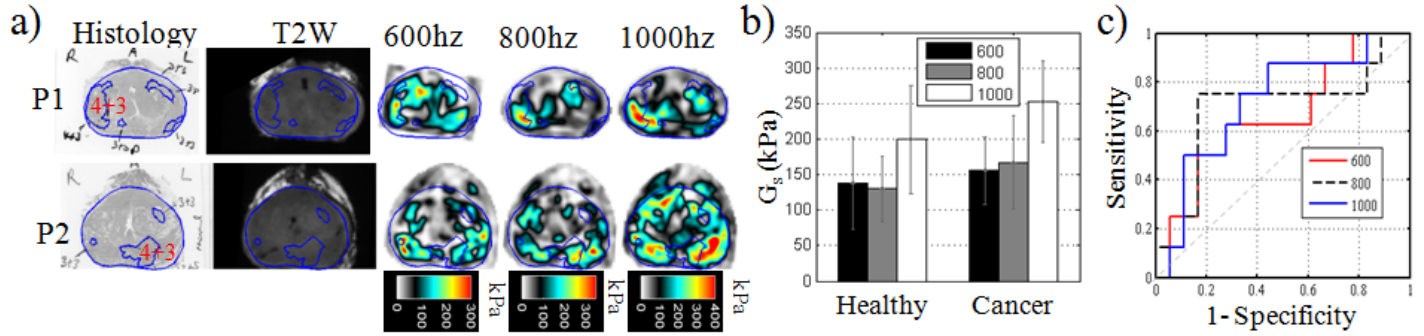

Fig. 2. a) The histology slides marked for Gleason score for two cases is shown. The registered T2W image, dynamic shear modulus G_d and loss modulus G_l are also shown at three excitation frequencies (600, 800 and 100Hz). b) Cancer detection (Gleason score > 3+3) with G_s improves with excitation frequency *p*=0.51 at 600Hz, *p*=0.1 at 800Hz and *p*=0.09 at 1000Hz. c) The area under the curve was 0.62 at 600hz, 0.65 at 800hz and 0.72 at 1000hz.

References

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