Measurements of T_1-relaxation in *ex vivo* prostate tissue at 132 μT

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Overview

Current technologies for imaging prostate cancer such as T_2-weighted MRI and MRSI have limited clinical utility and are most useful for detecting metastasis and post-therapy recurrences. We are investigating potential medical applications of ultralow-field MRI. NMR relaxometry data for different kinds of tumors and healthy tissue suggest an enhanced contrast in the T_1 at very low magnetic fields compared to that of clinical MRI [1]. We have imaged prostate specimens *ex vivo* with our ultralow-field MRI system to determine the T_1 contrast between different types of prostate tissue. Our preliminary results consistently show good differentiation between prostate cancer and healthy prostate tissue.

Apparatus

Our MRI system shown in Fig. 1 operates at 132 μT (proton Larmor frequency 5.6 kHz). At such low fields, the very small nuclear polarization and the frequency dependence of conventional Faraday detection would lead to extremely weak signals. To overcome this problem we use a combination of prepolarization at fields up to 150 mT and frequency-independent detection with an untuned superconducting gradiometer coupled to a Superconducting Quantum Interference Device (SQUID) [2] which has a magnetic field noise below 1 fT/Hz$^{1/2}$. We have acquired images of phantoms with a resolution of 0.7 x 0.7 mm^2 and demonstrated the applicability to *in vivo* imaging by acquiring three-dimensional MR images of human arms [3]. Adding a relaxation period in an arbitrary magnetic field between prepolarization and detection enables us to measure T_1 and to acquire T_1-weighted contrast images over a wide range of fields, from 1.4 μT to 0.15 T. In a model system of water and different concentrations of agarose gel we have shown that the T_1-weighted contrast can be greatly enhanced in microtesla fields [4].

Figure 1: Photograph of the SQUID-MRI system configured for *in vivo* imaging of the forearm.

Experiment

To investigate the use of this enhancement for tumor imaging we measured the T_1 relaxation times of healthy and cancerous prostate tissue specimens shortly after their surgical removal. To slow changes of the relaxation times due to degradation we maintained the sample temperature at 4°C. We determine the T_1 relaxation time from an exponential fit of the signal amplitudes at six different delay times between the prepolarization pulse and measurement. For NMR measurements, each sample consisted of two tissue specimens, approximately 5 x 5 x 1 mm^3, one predominantly healthy and the other predominantly malignant. We measured normal and cancerous tissues simultaneously—separating their NMR signals by applying a magnetic field gradient—so that the elapsed time between surgery and measurement was the same for both specimens. We also imaged several samples, ranging in size up to 40 x 50 x 5 mm^3, and acquired six 2D images with 4 x 4 mm^2 resolution to provide a pixel-by-pixel T_1-map. After completing the measurements the specimens were formalin-fixed, processed, and histology sections were reviewed in order to determine the tissue type.

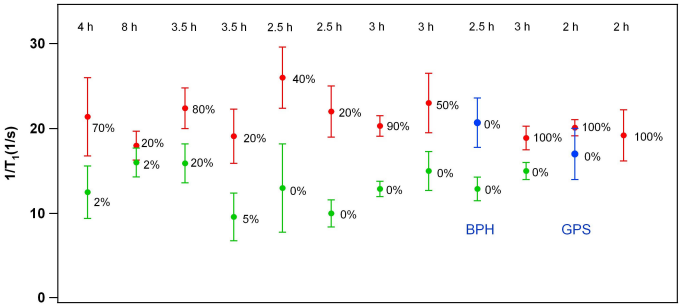

Figure 2. T_1-relaxation rates measured at 132 μT for twelve pairs of prostate tissue specimens; the percentage values next to each data point give the amount of tumor in this particular specimen. The time delay between surgery and experiment is shown above each specimen. Red–tumor; green–healthy tissue; BPH–benign prostate hyperplasia; GPS–gland poor stroma.

Results and Discussion

The results from twelve pairs of specimens are summarized in Fig. 2. The graph shows relaxation rates and the percentage of tumor for each specimen. For each pair the specimen containing more tumor tissue has a higher relaxation rate $1/T_1$ (shorter relaxation time T_1) than the specimen containing predominantly normal tissue. Additionally, results from benign prostate hyperplasia (BPH) and gland poor stroma (GPS) are shown. Figure 3 shows a T_1-map and histological overlay of the largest specimen we received. At the field we have chosen, however, some benign tissues (such as atrophy and BPH in Fig. 3) have similar relaxation properties to tumors. Combining the data from both T_1 measurements and images, we found the average T_1 of tumor to be 47±5 ms and the average T_1 of healthy tissue to be 76±2 ms. Using these T_1 values we project that in a system similar to ours reconfigured for *in vivo* imaging, we can image the prostate with 2 x 2 x 2 mm^3 resolution in 10 minutes with a contrast-to-noise ratio of 5 between healthy and cancerous tissue.

We have measured the T_1 degradation of the samples over a period of several hours. As indicated by point #2 in Fig. 2, there is virtually no difference in T_1 between healthy and cancer 8 hours after surgery, and minimal difference after 6 hours. Because our preliminary results look very promising and to avoid the effects of degradation, we intend to construct a system suitable for imaging the prostate *in vivo* to explore the (possibly even higher) contrast at different magnetic fields.

References

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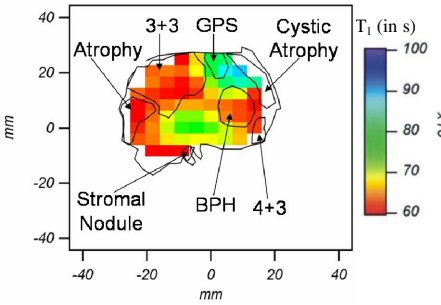

Figure 3. T_1 map of *ex vivo* prostate tissue with histological overlay. Areas not labeled are healthy tissue. Numbers are the Gleason score of tumors.

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