Detection of changes in quadrupolar peaks by FFC-MRI in skeletal muscle

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Introduction and Aim

The concentration of immobilised and soluble protein in skeletal muscle can potentially change during hydration-dehydration, hypertrophy-atrophy or as a result of pathological changes such as oedema or muscle injury and regeneration. The gold standard to measure the concentrations of overall or individual proteins is a muscle biopsy followed by a protein assay or by a Western blot against individual proteins. Muscle biopsy, however, is invasive which limits its applicability. The aim of our study is to develop a non-invasive technique to measure the concentration of immobilised protein using Fast Field-Cycling MRI (FFC MRI).
Fast Field Cycling (FFC) is a technique that emerged some decades ago [1] as a means to measure changes in relaxation rates at different magnetic fields. This proved useful for many applications, from characterisation of polymers to liquid crystals. However, it is still rarely applied to MRI because of technical challenges.
The experiment here uses one of the FFC MRI scanners that have been developed in our laboratory [2]. This FFC MRI scanner has the capability to change its magnetic field between 0 and 120 mT, allowing us to perform image acquisition with T_1-dispersion contrast.
One of the numerous uses of field cycling is to detect and measure the coupling between the water protons and the quadrupolar moment of immobilised ^{14}N [3]. This is of special interest in living tissues since proteins are rich in nitrogen and water. Moreover, since it has been shown that the quadrupolar signal recorded by FFC MRI is proportional to the concentration of immobile proteins [4], this technique allows the possibility of measuring the quantity of quadrupole-interacting protein in a tissue, thus making it a good candidate for the detection of protein changes in response to physical training.

Methods and Materials

In a pilot study we manipulated the concentration of immobilised protein in the gastrocnemius and soleus muscles by changing fluid content via venous occlusion or by eccentric exercise (which induces oedema).
We used FFC-MRI to detect the quadrupolar relaxation from immobilised proteins in the region of interest before and after swelling. The data was acquired using a gradient-echo scout image to select the region of interest, and then by applying a sequence similar to PRESS but with adaptations made for field-cycling MRI, therefore called FC-PRESS [5].
The data obtained was processed by Matlab 2009a (Mathworks) in order to obtain the amplitude of the quadrupolar signal. The results were compared by T-tests to provide the probability of rejection of the null hypothesis.

Results

Preliminary experiments showed quadrupolar dips clearly visible from the dispersion curve (see Figure 1) with a signal-to-noise ratio of 26.4. The amplitude estimation from these data were measured by curve fitting using an adapted model [6] and shows a difference between the untreated and the swelled tissues with a significance level of $p < 0.01$.

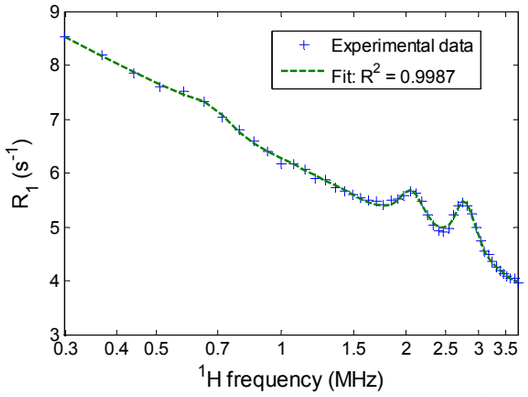

Figure 1: Dispersion curve obtained from muscle tissues. Two large quadrupolar peaks can be seen at 2.8 and 2.0 MHz and a smaller one appears at 0.6 MHz

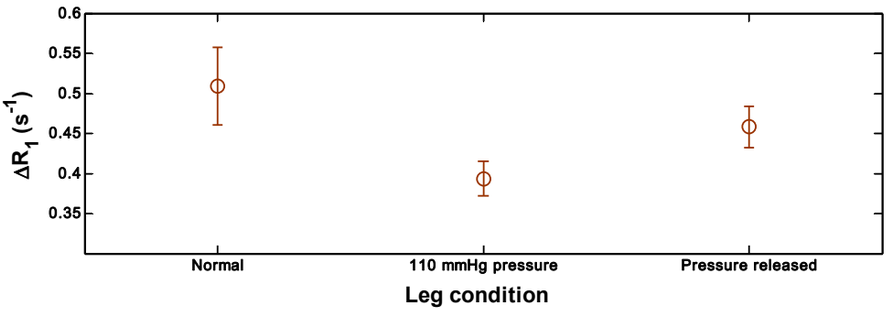

Figure 2: Average amplitude of the quadrupolar signal for (left) muscle at rest, (middle) increased blood pressure and (right) after application of the pressure. A difference can be observed with a significance of $p < 0.01$.

Conclusion

We have shown that current, state of the art field-cycled MRI is sensitive enough to visualise changes in the FFC-MRI signal that are consistent with the expected changes in the concentration of immobilised protein due to venous occlusion and muscle damage or injury. The method is likely to be usable for the detection of other types of tissue and protein gels and agglomerates. This opens the way for using the method to detect physiologically or pathologically meaningful changes in the concentration of protein. Challenges are the reliable validation, quantification and interpretation of these changes.

References

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