Detection of fibrin by Fast Field-Cycling magnetic resonance techniques

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Aggregated proteins are central to several diseases such as thrombosis, Huntington's disease, Alzheimer's disease or Parkinson's disease. An early detection of protein aggregate formation in the human body could therefore be of great interest for the diagnosis of such diseases. The aim of our research is to investigate the possibility of detecting protein aggregation by using fast field-cycling (FFC) nuclear magnetic resonance relaxometry and FFC-MRI.

Here we examine the feasibility of detecting one particular type of protein aggregation: the fibrin clot, which is the protein network that stabilises a thrombus. This choice was motivated by the wide literature available about fibrin that provides much detail about the model system of the formation of fibrin clots [1]. Fibrin clot formation is a key process in haemostasis, which restricts blood loss from wounds, and of thrombosis, which results from increased fibrin stability in the circulation, leading to a blockage of blood vessels. Fibrin, like proteins in general, is rich in ^{14}N and its mobility is reduced due to the web-like structure of a clot so it is a potential source of ^{14}N quadrupole dips in a ^{1}H T_1 dispersion plot [2]; a sample that presents quadrupole dispersion plot therefore indicates the formation of fibrin clots.

Samples of clotted fibrinogen were prepared through the cleavage of fibrinogen by an enzyme, thrombin, and were analysed by NMR relaxometry using a STELAR SMARtracer FFC relaxometer. This provided a measure of the T_1 dispersion curve between 1.5 and 3.5 MHz, which included the region of the two main quadrupole dips of ^{14}N (at 49 mT and 65 mT – i.e. 2.1 MHz and 2.8 MHz), using an inversion recovery pulse sequence. The determination of the relationship between fibrin concentration and dip amplitude was investigated by preparing samples with differing concentrations of fibrinogen (between 0.4 mg/ml and 20 mg/ml) and monitoring the corresponding quadrupole dip amplitude.

Preliminary results suggest that FFC relaxometry should be able to provide useful information concerning thrombus production. This may lead to novel diagnostic imaging techniques using FFC magnetic resonance imaging.

References:

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[2] Winter F. and Kimmich R, 1982, NMR field-cycling relaxation spectroscopy of bovine serum albumin, muscle tissue, micrococcus luteus and yeast. $^{14}N^{1}H$-quadrupole dips, *Biochim. Biophys. Acta* **719**, 292-298.