Towards the Direct *in vivo* Detection of Proteins, Macromolecules, and Drug Delivery Systems by 13C-edited 1H MRI and MRIS

R. Alvares (Univ. Toronto); G.A. Walter (FSU); H. Zeng (FSU); Prosser, R. S. (University of Toronto)

Introduction

Modern pharmacological applications increasingly make use of therapeutic proteins in tackling a wide range of diseases and improving specificity, while ameliorating challenges associated with toxicity. Polymeric drug delivery systems are also gaining traction for similar reasons. Both therapeutics and drug delivery systems are typically modified by covalent attachment of polyethylene glycol (PEG) groups. PEGylation retards immune response to foreign proteins, resulting in significantly improved retention times for therapeutics. We have devised a way of efficiently making functionalized ^{13}C-enriched PEG, in a PEG-PLA polymeric drug delivery micelle or append to a protein such as albumin. By filtering ^{1}H signal through the directly coupled ^{13}C nucleus (Fig. 1), one can acquire the ^{1}H signal of the ^{13}C-PEGylated protein or drug delivery system, while filtering out the background water and (unlabeled) ^{1}H signal.

Results and Discussion

The ability to image labelled PEG was tested by appending the HMQC filtering element to a standard gradient echo imaging sequence. PEG images were readily obtained at concentrations of 10 mM (Fig 2, top row). Much of the several days spent on the scanner was used to develop imaging sequences, with the intention of returning to future in vivo animal experiments.

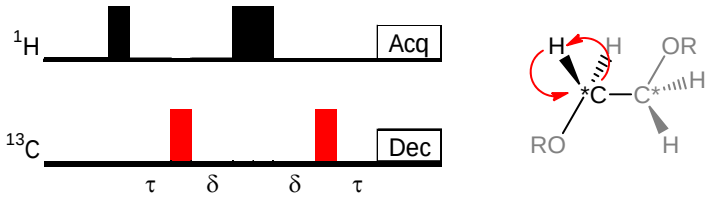

Figure 1. HMQC pulse sequence used to filter out ^{1}H magnetization. This transfer is shown schematically for poly(ethylene glycol) (PEG) (right). The filter can be appended to the beginning of any MRI pulse sequence to select for the PEG signal.

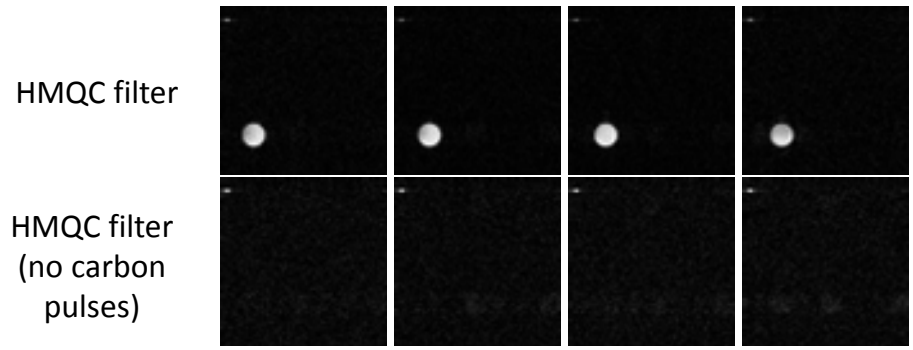

Figure 2. 10 mM PEG signal is evident (top row) upon application of the filter, whereas the control (blanked carbon pulses in the HMQC) proves the signal is due to PEG (as it removes PEG signal, but has no influence on water.

Conclusions

^{13}C-edited ^{1}H imaging is feasible for in vivo experiments on small animals, for region-specific detection of pegylated drug delivery systems or therapeutics.

Acknowledgements

AMRIS facility and NHMFL seed money ($5k).