Experiment Proposal

Experiment number GP2024007

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Experiment title	The use of NMR spectroscopy to characterize phantom materials for neutron therapy		
MRF Instrument	NMR 600 MHz	**Days requested:**	2
Access Route	Direct Access	**Previous GP Number:**	GP2023069
Science Areas	Medicine, Technique Development	**DOI:**	-
Sponsored Grant	None	**Sponsor:**	-
Grant Title	-	**Grant Number:**	-
Start Date	-	**Finish Date:**	-
Similar Submission?	-		
Industrial Links	-		

Non-Technical Abstract

We propose a an experiment to establish and validate a quantitative procedure using nuclear magnetic resonance (NMR) spectroscopy to provide patient-specific neutron scattering libraries for neutron capture therapy. In particular, using chemical shift spectra from 1H-NMR, the idea is to reconstruct the relative concentrations of organic functional groups in standard samples, and use these data to build the sample-specific macroscopic cross section at thermal neutron energies using the Average Functional Group Approximation. Therefore, we propose to further collect NMR spectroscopy data on samples prepared in a controlled procedure and previously characterized using neutron transmission measurements at the ISIS Neutron and Muon Source. Samples are hydrogel systems composed of semi-interpenetrated polymer networks(SIPN) to be suggested and used as radiation protection standards. This proposal builds on the promising results from a training proposal (GP2023069) previously approved.

Publications

Fluorinated borono-phenylalanine for optimizing BNCT: Enhancing boron absorption against hydrogen scattering for thermal neutrons G Romanelli et al., Medical Physics (2023)
Neutron thermal cross sections of 3D-printing organic polymers using the Average Functional Group Approximation, G. Romanelli et al., EPJ Web of Conferences (2023)

Sample record sheet

Principal contact   Dr Giovanni Romanelli, University of Rome Tor Vergata, ITALY
MRF Instrument   **NMR 600 MHz**   **Days Requested:** 2
Special requirements:

SAMPLE

Material	pHEMA+H2O	-	-
Formula	Poly(2-hydroxyethyl methacrylate)	-	-
Forms	Solid		
Volume	2 cc		
Weight	2 g		
Container or substrate	-	-	-
Storage Requirements	-	-	-

SAMPLE ENVIROMENT

Temperature Range	300 - 300 K	-	-
Pressure Range	- 1000 mbar	-	-
Magnetic field range	- T	-	-
Standard equipment	None	-	-
Special equipment	-	-	-

SAFETY

Prep lab needed	Yes	-	-
Sample Prep Hazards	-	-	-
Special equip. reqs	-	-	-
Sensitivity to air	No	-	-
Sensitivity to vapour	No	-	-
Experiment Hazards	-	-	-
Equipment Hazards	-	-	-
Biological hazards	-	-	-
Radioactive Hazards	-	-	-
Additional Hazards	-	-	-
Additional Details	-	-	-
Sample will be	Disposed by IS	-	-

Background and Context

Neutron capture therapy [1] is a cancer-treatment technique based on the irradiation of the human body with epithermal neutrons, their moderation within organic matter, and their eventual absorption by suitable drugs, often rich in boron, taken by the patient and delivered to the cancer region. Following neutron absorption, the heavy ions produced in the nuclear reaction deliver a large amount of energy over small regions of few micrometres, destroying cancer cells without affecting heathy ones. At present, the transport and moderation of neutrons in the human body is modelled using well-characterized materials, such as polymethyl methacrylate (pMMA) phantoms, in a crude simplification of the complexity of the human body. A possible way forward would be to reconstruct the chemical and physical composition of the region of interest in a patient-specific manner, using phenomenological libraries specific of the actual molecular composition. Proton magnetic resonance spectroscopy [2] methods can provide a quantitative information on the molecular composition of human body (e.g., see the case of fat and water in Ref. [3]), by relaxometry and chemical-shift-based approaches. In both cases, properties related to the presence of hydrogen atoms in specific functional groups are related to their abundance in any voxel of the volume under investigation. While the thermal neutron cross section of specific organic systems is known only for a handful of materials, a method was recently presented, referred to as the Average Functional Group Approximation (AFGA) [4], that allows the accurate prediction of the mass attenuation factor at thermal neutron energies of hydrogen-rich materials by a simple rationalisation of its constituent functional groups. Within this framework, one can hypothesize a procedure whereby the information on the abundances of hydrogen-containing functional groups, provided, e.g., by NMR spectroscopy or chemical-shift imaging, is given as an input to a transport code where the position-specific neutron attenuation functions are calculated using AFGA. If reliable, such procedure would allow safer, patient-specific, and more efficient treatments in the case of neutron capture therapy.

Proposed Experiment

We propose an experiment to perform a series of measurements to complement the results obtained during a training activity held at the IM@IT – Milano-Bicocca unit (GP2023069), using the NMR spectrometer (Bruker Avance III 600 MHz NMR spectrometer). We aim to show the accuracy and/or limitations of ^{1}H-NMR spectroscopy in the gel phase, using High-Resolution Magic Angle Spinning (HR-MAS), to establish the effect of the relaxation times on the evaluation of the functional-group populations in the final applications. In particular, we propose to carry out the measurements on 4 samples of polyhydroxyethylmethacrylate (pHEMA) at different hydration levels (10%, 20%, 30%, 40%) to explore the dependence of the peaks relative intensities and chemical shifts to the hydration level. Since D_2O needs to be introduced inside the sample container to perform ^{1}H-NMR measurements, the samples will be hydrated with D_2O, to control their hydration level. Similar samples, hydrated with H_2O, were previously characterized with neutrons (see Figure 2). pHEMA represents a material with a similar stoichiometry to pMMA yet with the possibility of including some amounts of water, as a first step to better reproduce human body.

The need of an NMR spectrometer is dictated by the final applications related to NMR imaging at medical facilities and its availability at the IM@IT unit of Milano-Bicocca represents an opportunity to consolidate cooperation across different units of the ISIS@MACH ITALIA Research Infrastructure, as well as the ISIS Neutron and Muon Source.

Summary of previous proposals and characterizations

Two sets of samples were previously synthesized at the IM@IT – CSGI unit in Florence, the first set is composed of 4 pHEMA samples, hydrated with H_2O at 4 different hydration levels (10%, 20%, 30%, 40%), the second is composed of two samples of pHEMA+PVP, the relative concentrations of pHEMA and PVP were chosen in order to have the maximum level of hydration at 50% and 60% respectively. The first set of samples were characterized at the ISIS Neutron and Muon Source using neutron transmission experiments (ISIS Proposal RB 2310166 carried out in July 2023) to measure their mass attenuation factors as functions of the incident neutron energy. The second set of samples were characterized by NMR spectrometer (Bruker Avance III 600 MHz NMR spectrometer) during a training activity carried out at the IM@IT – Milano-Bicocca unit. Preliminary results for pHEMA+PVP samples are reported in Figure 1 and show that the contributions of different functional groups are distinguishable, and their relative concentration can be extrapolated.

Justification of experimental proposals request

We request 2 days of time to use the **NMR spectrometer (Bruker Avance III 600 MHz NMR spectrometer)** available at the IM@IT – Milano-Bicocca unit. Having discussed the training plan with the instrument scientist, we envisage 0.5 days for the measurement of each sample. Therefore, we request 0.5x4 = 2.0 days of instrument time.

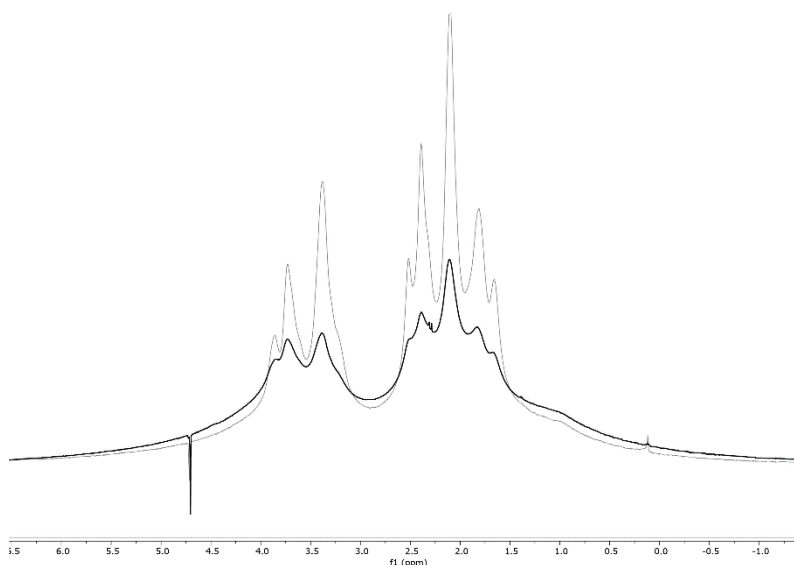**Figure 1.** High-Resolution Magic Angle Spinning (HR-MAS) ^{1}H-NMR spectra are reported for pHEMA+PVP+50%H_2O (dark gray) and pHEMA+PVP+60%H_2O (light gray). Both samples are hydrated at their maximum hydration level, which depends on the relative concentration of pHEMA and PVP. While the relative intensity of the peaks changes as a consequence of the different relative concentrations of pHEMA, no chemical shift is observed.

References

[1] Z.P. Zagorski, Radiation Physics and Chemistry 56, 559–565 (1999).
[2] Nuclear Magnetic Resonance Spectroscopy, J.B. Lambert and E.P. Mazzola (2004).
[3] H. H. Hu and H. E. Kan, NMR Biomed., 26(12), 1609–1629 (2013).
[4] G. Romanelli et al., J. Phys.: Condens. Matter 33, 285901 (2021).