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Polarization behavior of fluorine-labeled glucose-water solution

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Magnetic resonance imaging (MRI) with contrast agents has become an indispensable tool in medical imaging. When contrast agents such as ^{3}He gas, ^{13}C in pyruvic acid, or fluorine-labeled glucose (FDG) are used in vivo, sensitivity can increase by a factor of 10,000 or more, particularly when the nuclei are dynamically polarized.

This report presents the results of the first dynamic polarization experiments involving fluorine and hydrogen in a glucose solution doped with TEMPO.

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1. Introduction

Magnetic Resonance Imaging (MRI) with hyperpolarized contrast agents is an advanced imaging technique that significantly enhances the sensitivity of MRI. Hyperpolarization techniques, such as dynamic nuclear polarization (DNP), increase the signal strength by more than four orders of magnitude [1]. This allows for real-time, non-invasive assessment of metabolic processes in living organisms, including humans [1].

Hyperpolarized contrast agents, particularly those using hyperpolarized carbon-13 (^{13}C), enable detailed imaging of metabolic changes, which is valuable in fields like oncology, neurology, and cardiology [1]. These agents can provide high-resolution images without the use of ionizing radiation, making them safer compared to traditional imaging methods[2].

In this article, the results of dynamic polarization investigations of ^{19}FDG (Fluorodeoxyglucose) are presented. These studies aim to explore the polarization properties of FDG in different conditions, highlighting its potential for applications in advanced imaging techniques such as PET/MRI [3, 4] with hyperpolarized ^{18}F-FDG. The findings contribute to a deeper understanding of how hyperpolarized FDG can enhance diagnostic precision in oncology and other fields.

2. Materials and Methods

Initial material tests regarding the solubility of TEMPO radicals and glucose and water were investigated. According to [5], the solubility in water is 909 g/L. We chose a mixing ratio of 1 to 2. The amount of TEMPO radical was set at 0.5 percent by weight (the mixing ratio has proven to be effective for high polarization values with alcohol targets [8, 10, 11]). For further measurements, the glucose was replaced by 2-deoxy-2-fluorine-D-glucose, 95 % (FDG) by Carbolution Chemicals GmbH. Since only 100 mg of FDG was available, a total sample amount of 300 mg was prepared. In order to be able to distinguish between the protons in glucose and those in water in the polarization tests, heavy water D_2O was used here. Hence, the nuclear magnetic resonance technique nmr [7, 18] can be used to distinguish between protons, fluorine and deuterons in the different proportions when determining polarization. The proportions of the mixtures are given in table 1.

Substance	**Mass**
^{19}F-FDG (Glucose)	0.1 g
D_2O	0.2 g
TEMPO	0.0015 g

Table 1: Mixture: 0.5 % TEMPO, 66.3 % D2O and 33.2 % FDG.

The mixture was heated to 70°C to form a homogeneous liquid, then cooled in liquid nitrogen to form white beads. The left picture in figure 1 (Left) shows the frozen FDG-water beads. The mixture was examined by electron paramagnetic resonance epr [12] to control the homogeneous solution. The dynamic nuclear polarization investigation was performed with the Bochum polarized target equipment. Key system included a ^{4}He evaporator [13], a 2.5 T C-magnet, and in-house-developed Q-meter [7] and a 70 GHz microwave systems for polarization measurement.

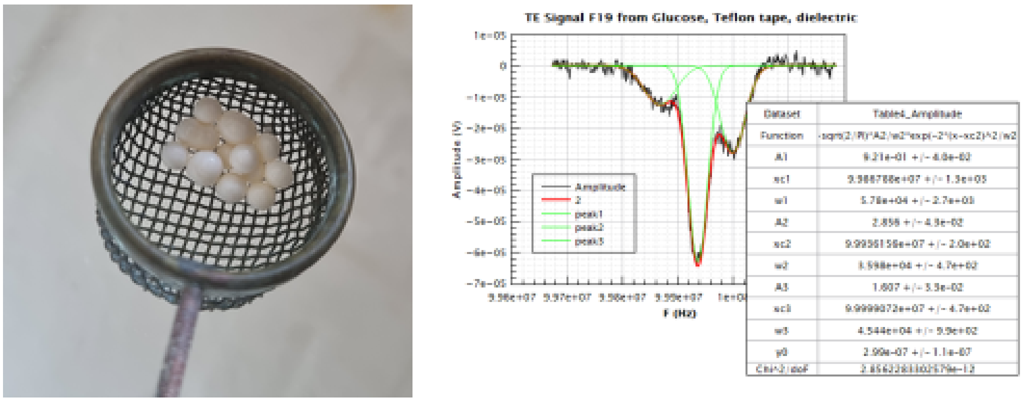

Figure 1: Left: FDG D_2O mixture frozen beads; Right: The fluorine TE signal consisting the peaks of fluorine in FDG, the target container and in the coaxial cable close to the nmr-coil.

The calibration of the measured polarization was carried out using the TE method (thermal equilibrium) at a temperature of T = 1.1 K and a magnetic field of B = 2.5 T. Figure 1 (Right) shows the TE signal with the three components in the FDG, the target container and the coaxial cable. Since only the FDG/water solution contains radicals, only the transition in the FDG will increase during dynamic polarization (Fig. 2).

Not only the fluorine signal, but also the protons and deuterons in the FDG/water/TEMPO solution were investigated and behaved in accordance with the EST (equal spin theory [6, 14]). No differences in polarizability could be determined. Furthermore, only the fluorine signal is discussed.

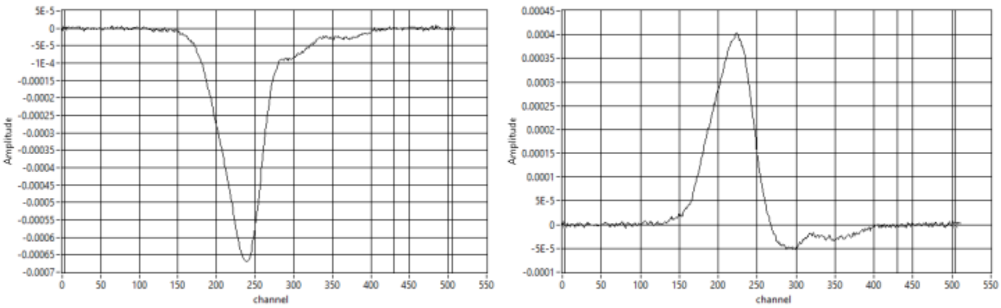

Figure 2: Left plot shows the nmr signals during positive polarization; Right plot shows the nmr signals during negative polarization. It is easily seen that the left transition shows the fluorine signal from the FDG.

Of course, these contrast agents are not injected into the body of a living being in a frozen state, but must be brought to body temperature as quickly as possible after polarization and the radicals are filtered out to extend the relaxation time. Furthermore, the entire process must meet sterile conditions [15, 16]. This is of secondary importance in this study, since the hyperpolarizability of the nuclides in FDG must first be determined. To determine the spin-lattice relaxation time T1 at room temperature of radical-free contrast agents, a glucose-water solution was investigated in a pulsed NMR apparatus [17] at B = 0.5 T.

3. Results

Dissolving TEMPO and FDG in heavy water with the mixing ratio (0.015/1/2) was carried out without any problems, and after briefly heating to 50 to 70°C, a homogeneous liquid was obtained. The X-band epr spectrum shows a line of very diluted and separated transitions of the TEMPO at room temperature. In the frozen state (77 K), the epr spectrum shows a dominant central line (see left graph in figure 3). Both spectra indicate good conditions for dynamic polarizability.

The polarization experiments with TEMPO-Glucose-D_2O at 1 K and 2.5 T resulted in polarization values for the protons of more than 15% in both negative and positive directions. Subsequently, glucose was replaced by ^{19}FDG, and the focus was primarily on fluorine in FDG. Here, the polarization values for fluorine at 1.1 K and 2.5 T were about ±10% (see figure 3 graph on the right). The polarization values in the negative direction are smaller because the microwave power decreases with frequency. The spin-lattice relaxation times were determined to be about 3 minutes.

In a further measurement, the relaxation time of the protons in pure glucose-D_2O (1/2) was determined at 1.1 K and 1.8 K and resulted in about 140 minutes and 31 minutes for T1, respectively. The relaxation time at room temperature and 0.5 T was about 1.2 seconds.

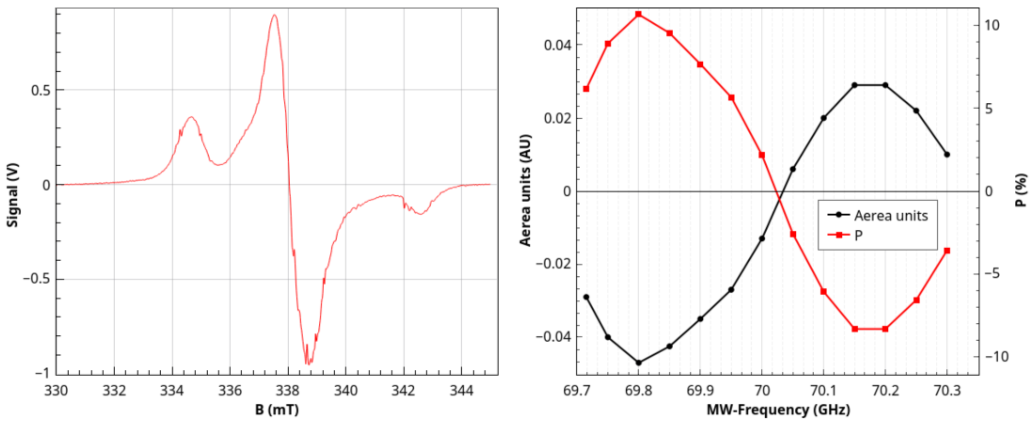

Figure 3: Left plot shows the epr signal of TEMPO radical in the Glucose - water mixture at T = 77 K; Right plot shows polarization (red) and area units (black) of fluorine versus microwave frequency.

4. Discussion

The results confirm the feasibility of using hyperpolarized MR imaging combined with ^{19}F-FDG for diagnostics. However, future studies should investigate alternative radicals, such as trityl radicals dissolvable in water, to further optimize DNP efficiency and should include testing ^{18}F-FDG polarization.

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