Temperature monitoring through nanoparticle-activated proton relaxation for magnetic resonance imaging application

A D Mironova¹,², https://orcid.org/0000-0003-2533-6873, Yu V Kargina¹,², https://orcid.org/0000-0001-7477-5579, A M Perepukhov³, https://orcid.org/0000-0001-8623-4147, O S Pavlova²,⁴, https://orcid.org/0000-0002-2574-1978, M V Gulyaev⁴, https://orcid.org/0000-0003-4684-2484, Yu A Pirogov², https://orcid.org/0000-0001-8518-6323, V Yu Timoshenko⁵

¹ National Research Nuclear University “MEPhI”, Phys-Bio Institute, 115409 Moscow, Russia
² Lomonosov Moscow State University, Faculty of Physics, 119991 Moscow, Russia
³ Institute of Physics and Technology, Dolgoprudny, 141700 Moscow Region, Russia
⁴ Lomonosov Moscow State University, Faculty of Fundamental Medicine, 119991 Moscow, Russia
⁵ Lebedev Physical Institute of the Russian Academy of Sciences, 119991 Moscow, Russia
a) E-mail: navonorim@mail.ru

Abstract. An effect of temperature on the proton relaxation times in aqueous suspensions of solid-state nanoparticles (NPs) is comparatively investigated for the NPs’ composition varied from pure silicon (Si) with natural isotope content to Si with iron impurities as well as for Si NPs enriched with Si-29 isotope. For all types of the investigated NPs both the longitudinal and transverse relaxation times become shorter compared with that for pure water because of the interaction of electron spin centers in those NPs with nuclear spins of the protons in water molecules. The obtained results allow us to evaluate the temperature sensitivity of NP-based systems for their biomedical applications in magnetic resonance imaging (MRI).

1. Introduction

In recent years, silicon-based nanomaterials have been in the focus of attention for biomedical applications due to their biocompatibility, biodegradability, and surface modification opportunities [see for example 1,2]). Recently, among various contrast agents for MRI [3], different types of solid NPs based on silicon (Si) oxide with an admixture of gadolinium (so-called AGuIX [4]), as well as pure Si NPs [5-7] have been considered.

The nuclear magnetic resonance (NMR) phenomenon, which is used in MRI, is known to be temperature-sensitive [3]. Therefore, it is possible to observe the temperature fields inside the investigated object using MRI. It can be used to realize a thermographic control, which plays an important role in hyperthermia - local heating of tissues inside the body to suppress or activate ongoing processes [8].

One of the methods of temperature control using MRI is the T₁-relaxation method [9]. The amplitude of the signal in the T₁-weighted image makes it possible to judge the temperature distribution in the sample. A decrease in the signal amplitude with increasing temperature occurs both due to an increase in T₁ and due to a decrease in the value of the equilibrium magnetization. Therefore, when constructing temperature maps of temperatures, it is necessary to use calibration curves of the dependence of the
longitudinal relaxation time on temperature or use the known data for each type of tissue. The accuracy of this method is estimated at ± 1 °C.

In our paper the temperature effect on proton relaxation times in aqueous suspensions of Si-based NPs is comparatively investigated for both pure Si NPs with natural isotope content and Si NPs with iron impurities as well as for Si NPs enriched with Si-29 isotope.

2. Materials and methods
To measure relaxation times, we used a Bruker Minispec NMR relaxometer equipped with a magnet of 0.5 T. The corresponding operating frequency for protons is about 20 MHz. To regulate and maintain a constant sample temperature, the sample tube was blown with dry air. The temperature near the sample was measured with a thermocouple. The temperature was adjusted using a special program. For selected samples the temperature dependence of the proton magnetization was investigated by using with a 7.05T Bruker BioSpec 70/30 USR MR scanner driven by a ParaVision® 5.0 console and equipped with a 105 mT/m gradient amplitude device.

To study the temperature dependence of proton relaxation, Si NPs were dispersed in water. Si NPs with different atomic iron (Fe) content, i.e. 0.2, 2.5, 5, and 10% at % Fe, were obtained by using a plasma-ablative synthesis described in Refs. [5,6]). Also, the following S-based NPs were studied: porous Si prepared by using a ball-milling of electrochemically grown por-Si films [4] and crystalline Si (c-Si) ones obtained by mechanical grinding of c-Si wafers enriched (99%) with Si-29 isotope. To obtain a uniform distribution of NPs in water, all samples were exposed to ultrasound for 30 minutes and sedimented in a centrifuge set at 8000 rpm.

The proton magnetization relaxation times were measured for pure de-ionized water and aqueous suspensions of NPs in glass cylindrical ampoules with a base diameter of 1 cm placed into the NMR relaxometer. The ampoules were filled with 800 μL of water or aqueous suspensions of the studied NPs. The samples were kept in a water thermostat at a given temperature for 15 minutes before the ampoule being placed into the relaxometer. The temperature range was from 22 to 60 °C with a step of 5 °C with ± 0.1 °C accuracy of temperature maintenance.

3. Results and discussion
Transients of the longitudinal and transverse components of the proton magnetization in pure water are shown in Figures 1 and Figure 2, respectively. The obtained curves were approximated by using a single exponential function. The larger temperature the faster recovery of the longitudinal magnetization occurs (see Fig.1). Also, at higher temperature the transverse magnetization falls off faster. Therefore, with increasing temperature both the longitudinal and transverse relaxation become slower.

![Figure 1](image1.png)  **Figure 1.** Spin-lattice relaxation curves for pure water at different temperatures.

![Figure 2](image2.png)  **Figure 2.** Spin-spin relaxation curves for pure water at different temperatures.
The addition of Si NPs in aqueous solutions shortens the proton relaxation times. NPs of porous Si and Si-29 enriched c-Si are less effective in this regard. Among Si NPs, the sample with 5 at. % of iron exhibit stronger shortening of the relaxation times, which account above 50% and 76% for T_1 and T_2, respectively.

To characterize the temperature sensitivity of the proton relaxation we introduce a value, which is defined as a relative temperature sensitivity of the relaxation time, as follows:

\[ S_{1,2} = \left( \frac{\Delta T_{1,2}}{\Delta t} \right) \cdot \frac{T_{1,2}}{\% / ^\circ C} \tag{1} \]

where subscripts 1 and 2 are related to the temperature sensitivity of the longitudinal (T_1) and transverse (T_2) relaxation times, respectively.

The temperature sensitivity of pure water and aqueous suspensions NPs for the longitudinal and transverse relaxation are summarized in Tables 1 and Table 2, respectively.

**Table 1.** Temperature dependences of the longitudinal relaxation for pure water and aqueous suspensions of different Si-based NPs with concentration of 1 mg/mL.

| Sample  | T_1, ms | ΔT_1/Δt, ms/°C | S_1, %/°C |
|---------|---------|----------------|-----------|
| Water   | 4760    | 98             | 2.06      |
| 0.2 at. % Fe | 1980    | 36              | 1.82      |
| 2.5 at. % Fe | 2270    | 45              | 2.00      |
| 5 at. % Fe  | 1710    | 17              | 0.97      |
| 10 at. % Fe | 2180    | 28              | 1.29      |
| por Si   | 3350    | 44              | 1.32      |
| Si-29    | 3480    | 27              | 0.78      |

**Table 2.** Temperature sensitivity of the transverse relaxation for pure water and aqueous suspensions of different Si-based NPs with concentration of 1 mg/mL.

| Sample  | T_2, ms | ΔT_2/Δt, ms/°C | S_2, %/°C |
|---------|---------|----------------|-----------|
| Water   | 3170    | 35             | 1.1       |
| 0.2 at. % Fe | 362     | 11             | 3.0       |
| 2.5 at. % Fe | 1050    | 19             | 1.8       |
| 5 at. % Fe  | 628     | 6              | 1.0       |
| 10 at. % Fe | 780     | 6              | 0.8       |
| por Si   | 2330    | 16             | 0.7       |
| Si-29    | 2015    | 19             | 0.9       |

By comparing the obtained values, one can conclude that Si NPs with 0.2 at. % and 2.5 at. % of iron are the most sensitive to temperature changes. For more detailed study of the temperature sensitivity of aqueous solutions of NPs, samples 0.2 at. % Fe with NPs’ concentrations of 0.5, 1, and 2 mg/mL were analyzed by using the MRI scanner with a field strength of 7 T. The temperature of the samples was changed by heat exchange with plastic tubes with water of a given temperature wrapped around the phantoms with aqueous suspensions of Si NPs.

Temperature dependences of the longitudinal and transverse proton relaxation times in aqueous suspensions of NPs are shown in Figure 3 and Figure 4, respectively. An increase of the relaxation times with increasing temperature was found and the effect was observed even at high NPs’ concentration about 1-2 mg/mL.
Figure 3. Temperature dependences of the longitudinal (a) and transverse (b) relaxation times in aqueous solutions of NPs with 0.2 at. % Fe at various NPs’ concentrations.

By using the obtained experimental data, the temperature sensitivities of the proton relaxation times in NPs suspensions in the concentration range of 0.5 – 2 mg/mL were calculated. A comparison of the temperature sensitivities of the longitudinal and transverse relaxations is shown in Figure 4. The obtained results indicate higher sensitivity of the transverse relaxation time to temperature changes than that for the longitudinal one. This fact can be related to peculiarities of the interaction of proton spins of water molecules and paramagnetic center in Si NPs [5-7].

Figure 4. Sensitivities of the longitudinal (T₁) and transverse (T₂) relaxation times at different concentrations of Si NPs with 0.2 at. % Fe.

4. Conclusions
The longitudinal proton relaxation and transverse one in an aqueous medium depend on temperature and they are very sensitive to the presence of Si NPs. The stronger reduction in the relaxation times is observed in the case of an aqueous suspension of Si NPs with iron impurities. The highest temperature sensitivity of both the longitudinal and transverse proton relaxation times is found in the aqueous suspensions of Si NPs with 0.2 at. % and 2.5 at. % of iron. It was found that the spin-spin relaxation is
more sensitive to temperature changes than the spin-lattice one. The obtained results indicate that Si-based NPs are promising for the MRI-guided temperature monitoring in biomedical purposes.

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