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Postprint of: Wierzba P., Sękowska-Namiotko A., Sabisz A., Kosowska M., Jing L., Bogdanowicz R., Szczerska M., Reply to Comment on 'Nanodiamond incorporated human liver mimicking phantoms: prospective calibration medium of magnetic resonance imaging', MAGNETIC RESONANCE MATERIALS IN PHYSICS BIOLOGY AND MEDICINE, Vol. 37 (2024), pp. 315-317

Reply to Comment on 'Nanodiamond incorporated human liver mimicking phantoms: prospective calibration medium of magnetic resonance imaging'

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We express our gratitude to Prof. Panich for bringing up insightful points in his Comment [1,2]. We acknowledge his valid surprise regarding the authors' proposal of a linear dependence of the spin-lattice (T1) relaxation times on the nanodiamond concentration in the phantoms, as depicted in Figure 3 [3]. It has been unequivocally demonstrated that both proton spin-lattice and spin-spin relaxation times exhibit a hyperbolic relationship with the concentration of nanodiamonds (C_{DND}) in suspension, i.e.:

$$T_1 = \frac{1}{R_1^{solv} + r_1^{DND} \times C_{DND}} \tag{1}$$

Based on the provided Comment, the authors performed a fitting analysis using the correct function, given by (1), to the experimental data shown in Figure 3 of their paper [3]. The results of this fitting analysis are presented in Figure 1, which provides an accurate visualization of the fitted function's performance.

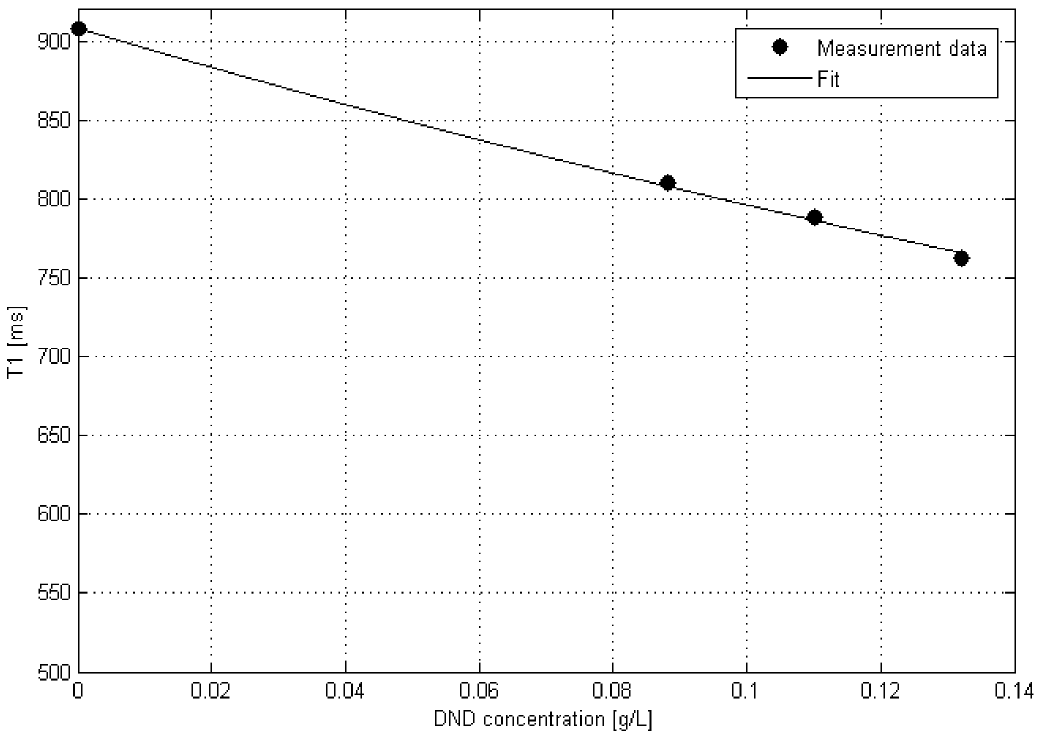

Figure 1. Spin-lattice relaxation time T_1 as a function of the nanodiamond concentration C_{DND} in suspension.

As anticipated, the fit is not perfect, mirroring the results shown in Figure 1 of the Comment. Values of coefficients R_1^{solv} and r_1^{DND} (with 95% confidence bounds) are listed in Table 1. Notably, values of both coefficients differ substantially from those presented in the Comment. In the case of relaxation rate R_1^{solv} this disparity is initially observed as different spin-lattice relaxation time T_1 in phantoms without nanodiamonds (C_{DND}=0). In our bare phantoms, T_1 is measured at 908 ms [3], whereas in the referenced Comment T_1 is 3800 ms [1,2]. However, those values might differ significantly due to the fact that the phantoms tested in the original article[3] consisted not only of water, for which the aforementioned relaxation time in the Comment[1,2] was measured, but also of agar, carrageenan and dimethyl sulfoxide (DMSO) suspension of detonation nanodiamonds.

Table 1. Relaxation rate R_1^{solv} and relaxivity r_1^{DND} of the produced phantoms.

Name	Value	95% confidence bounds
R_1^{solv}	1.101 s^{-1}	(1.085·s^{-1},1.116·s^{-1})
r_1^{DND}	1.551 $L·g^{-1}·s^{-1}$	(1.374 $L·g^{-1}·s^{-1}$,1.728 $L·g^{-1}·s^{-1}$)

Although such a substantial difference is certainly concerning, it is important to note that this observation is not exclusive to our paper. For instance, spin-lattice relaxation time T_1 for a phantom with 2% of agar, reported in [4], was 1669.5 ms (c.f. [4], Table 1, Phantom 1). Moreover, results presented in Table 1 of [4] for Phantoms 7-10 indicate that inclusion of biological materials such as milk or wood can reduce T_1 considerably, down to 837.5 ms for Phantom 10. Furthermore, the spin-lattice relaxation time T_1 measured by Ohno, S. et al.[5] in phantoms containing carrageenan, agarose and gadolinium chloride as T_1 modifier was within the range of 921.1 ± 33.8 ms and 911.7 ± 26.7 ms, for two created phantoms respectively. This observations suggests that in addition to agar and carrageenan our phantoms may have unintentionally included some biological contaminants, such as bacteria, that were not easily detectable in our experiments.

Relaxivity r_1^{DND} of nanodiamonds also differs substantially, being 1.551 $L \cdot g^{-1} \cdot s^{-1}$ for our phantoms [3] and 175 $L \cdot g^{-1} \cdot s^{-1}$ for the phantoms referenced in the Comment [1,2]. While a portion of this variation can be ascribed to distinct relaxation rates, it is important to acknowledge that additional factors could have played a role in influencing these differences. Therefore, a comprehensive understanding of the underlying factors influencing the observed variations is crucial for a thorough analysis of the results.

In conclusion, we agree with the perspective of Professor Panich that materials incorporating nanodiamond particles hold significant potential as MRI phantoms. However, the practical implementation of these phantoms and the assurance of long-term stability of their relevant properties necessitate further research and testing. To enhance the reliability and reproducibility of these phantoms, not only improvements should be made to their preparation process but also rigorous quality control measures should be implemented. Attention must be given to refining the fabrication methods to ensure consistent results and minimize the presence of contaminants that may affect the phantom's performance. Additionally, it is crucial to conduct comparative measurements using various types of MRI scanners. Such a comprehensive analysis will shed light on the dependence of the measurement results on the specific equipment used. By examining multiple MRI scanners, potential variations in the obtained imaging data can be identified and accounted for, allowing for a better understanding of the performance and compatibility of the nanodiamond-based phantoms with different imaging systems. Further research efforts should be directed towards addressing these aspects, enabling the realization of the full potential of nanodiamond-based materials as MRI phantoms. By perfecting the preparation process, ensuring repeatability, and conducting comparative measurements on diverse MRI scanners, we can establish a solid foundation for the practical application of these phantoms in the field of magnetic resonance imaging.

References

1. Panich, A. M. Can detonation nanodiamonds serve as MRI phantoms? *Magn Reson Mater Phy* **35**, 345–347 (2022).
2. Panich, A. M. Universal Dependence of Nuclear Spin Relaxation on the Concentration of Paramagnetic Centers in Nano- and Microdiamonds. *Materials* **15**, 5774 (2022).
3. Sękowska, A. *et al.* Nanodiamond phantoms mimicking human liver: perspective to calibration of T1 relaxation time in magnetic resonance imaging. *Sci Rep* **10**, 6446 (2020).
4. Antoniou, A. *et al.* MR relaxation times of agar-based tissue-mimicking phantoms. *Journal of Applied Clinical Medical Physics* **23**, e13533 (2022).
5. Ohno, S. et al. Production of a human-tissue-equivalent MRI phantom: optimization of material heating. *Magn Reson Med Sci* 7, 131–140 (2008).