Tracking magnetotactic bacteria using an MRI system for future in-vivo therapeutic targeting

O. Felfoul[1], and S. Martel[1]

[1]Biomedical engineering, École Polytechnique de Montréal (EPM), Montreal, Quebec, Canada

Introduction

MC-1 magnetotactic bacteria (MTB) [1] are studied for their potential use as bio-carriers for applications such as drug delivery through the human blood circulatory network. Combining both the flagella and an induced directional torque on a chain of nanoparticles named magnetosomes embedded in each bacterium could enable both propulsion and steering of these carriers in small diameter blood vessels. However, tracking for the purpose of guiding these MTB towards a target located deep in the human body remains a great challenge. The magnetosomes embedded in each MC-1 MTB are Fe_3O_4 single magnetic domain particles of a few tenths of nanometers in sizes. Similar to the superparamagnetic contrast agents, they cause a local distortion of the magnetic field increasing thus the relaxation rates R_1 and R_2 values proportionally to its concentration; however, the effect on R_2 is often much higher [2]. In order to study the contrast generated by the MTB on the MRI, T_1, T_2 and T_2* images of different concentrations have been taken. We demonstrate the application of this technique for the tracking of the bacterial concentration for future drug delivery applications.

Method

Seven concentrations, as given in the legend of fig.1, of MC-1 MTB have been prepared for the experiment. Qualitative observation of bacterial motility and response to the magnetic field before and after concentrating was performed using a Zeiss Imager.Z1 microscope in order to validate the vitality and magnetotaxis after centrifugation. A 1 ml of every sample of the three materials was inserted into a 2 ml Progene microtube. Images were run under a Siemens Avanto 1.5 T scanner using the wrist antenna. T_2*-weighted Flash sequence parameters are as follow: TR = 776 ms, and a flip angle = 90°. T_2-weighted TSE sequence parameters are as follow: TR = 5620 ms, and an echo train length = 27. T_1-weighted FLAIR sequence parameters are as follow: TR/TE = 9000/90 ms. A pixel spacing = 0.254/0.254 mm was used for the three imaging sequences.

Results and discussion

Samples containing MTB show signal enhancement compared to the medium in T_1-weighted images for low bacterial concentration as depicted fig.1. However, this signal enhancement is inversed for higher concentration that could be due to the important signal loss from field inhomogeneity. The effect of the concentration of MTB on the MR-signal is more evident on T_2* as well as T_2-weighted images. As the concentration of the bacteria increases, the relaxation rates R_2 and R_2* increase proportionally to the concentration as given by fig.2.

Conclusion

R_2 values could be converted to concentration, [MTB], according to equation 1, where α is the relaxivity constant and $R_{2,0}$ is the R_2 of pure medium, enabling thus real-time tracking of MTB using an MRI system.

$$[MTB] = \frac{1}{\alpha}\left(R_2 - R_{2,0}\right) \qquad (1)$$

Acknowledgment

Natural Sciences and Engineering Research Council of Canada (NSERC), Fond Québécois de la recherche sur la nature et les technologies (FQRNT), Canada Research Chair (CRC) in Micro/Nanosystem Development, Fabrication and Validation.

References

[1] R. P. Blakemore, Science, v190, n4212, (1975)

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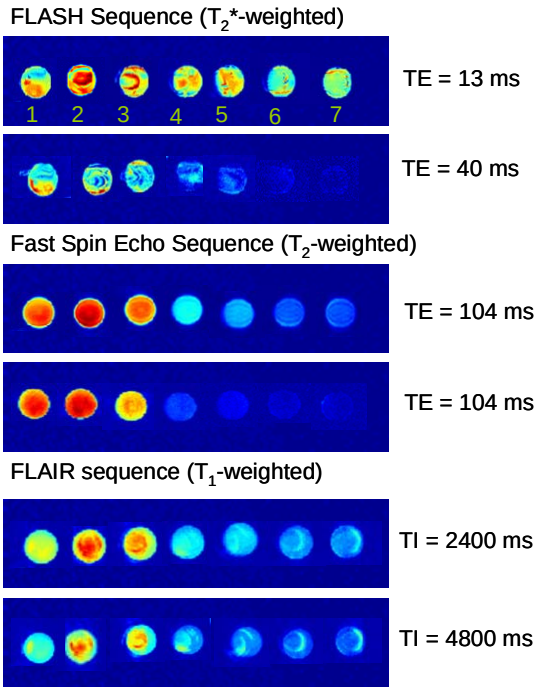

Fig. 1: FLASH, FSE, and FLAIR sequence imaging of several samples of MTB of different concentrations. From 1 to 7 the concentrations are 0, 1.9, 3.0, 5.1, 7.3, 8.4, 9.0 × 10^8 cells/ml. The sequence parameters are given in the text.

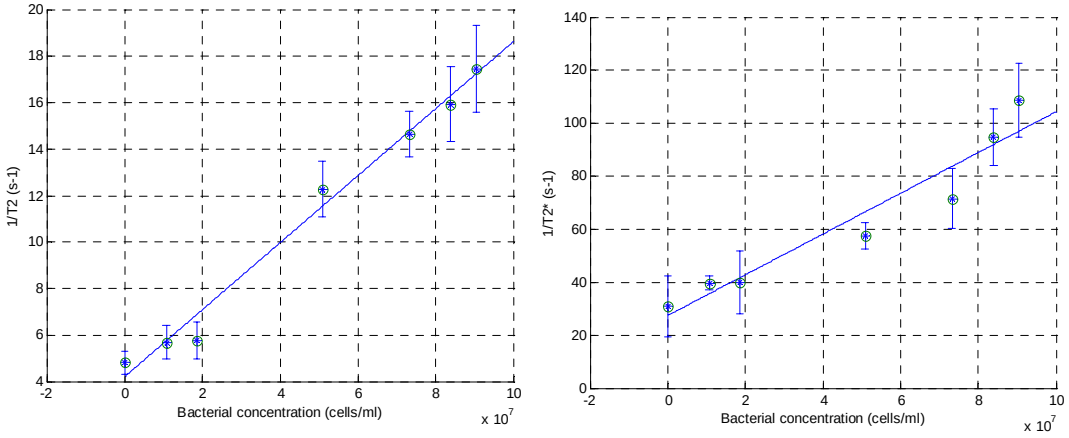

Fig. 2: Proton T_2^* (right) and T_2 (left) relaxation rates at 1.5 T as a function of the bacterial concentration.