Trimodality detection of magnetic megaparticles for simultaneous tracking of a large number of primary human cells assembled in collagen matrices

David P Cormode[1], Willem J M Mulder[2], and Erik M Shapiro[3]

[1]*Radiology, University of Pennsylvania, Philadelphia, PA, United States,* [2]*Translational and Molecular Imaging Institute, Mount Sinai School of Medicine, New York, NY, United States,* [3]*Radiology, Michigan State University, East Lansing, MI, United States*

Introduction We and others have proposed magnetic nanoparticles and microparticles for both cell labeling and targeted imaging in MRI. The success of this approach encouraged us to investigate particles of other size ranges for application in MRI-based imaging. We have developed a unique magnetic megaparticle, which we have seeded with a large number (>7 billion) of distinct human primary cell cultures assembled in collagen matrices (PCCAiCM). The megaparticle has its own magnetic field, which facilitates imaging by use of a small, simple hand-held system. In this case the system was integrated into an iPhone based user interface. The megaparticle's large size facilitates unaided optical imaging. In addition, at close ranges, we were able to simultaneously detect the megaparticle by both optical and manual methods. We herein report the synthesis of the megaparticle, its characterization, labeling and imaging.

Methods *Magnetic Megaparticle Synthesis* The megaparticle was synthesized in a previously published literature procedure.(1) In short, the particle was created in a stepwise fashion over a period of five days, as schematically depicted in panel A. On the sixth day the particle was labeled with large numbers of primary human cells, and assembled in a variety of collagen matrices. The megaparticle was allowed to incubate on the seventh day and imaging experiments were initiated soon afterwards.

Megaparticle Characterization The megaparticle diameter was determined using the Hubble Telescope. The structure of the particle was probed using seismological equipment, measuring the time of travel of refracted and reflected seismic waves. The biocompatibility of the megaparticle was investigated in a 6000 year-long study.

Megaparticle Imaging Our initial imaging system consists of a magnetized pointer free to align itself with the megaparticle's magnetic field. The system was built as a stand alone sealed instrument with a magnetized bar or needle turning freely upon a pivot and moving in a fluid, thus able to point towards the megaparticle, as shown in panel B. For clinical translation, we subsequently utilized an iPhone-based system (C) built out of three magnetic field sensors that provide data for a microprocessor. The correct heading relative to the detection device is calculated using trigonometry. For optical imaging we typically looked downwards. For simultaneous dual optical and manual detection we performed a handstand.

Results The diameter of the megaparticle was found to be 12.5762 Mm. Our seismological characterization strategy found the megaparticle to have a core-core-shell-shell-shell structure, as schematically depicted in panel D. The inner core is solid iron-nickel alloy, as it does not allow shear waves to pass through it, while the speed of travel (seismic velocity) is different in other layers. The changes in seismic velocity between different layers causes refraction owing to Snell's law, allowing the detection of the layers. We have thus far found the surface to be highly biocompatible and largely non-toxic, except for certain points at the top, bottom (too cold) and middle (too hot). Using both our initial and iPhone based detection devices, we have been able to reliably detect the megaparticle, and thus the cell culture aggregates, at ranges of up to 10 km. Detection is depicted in panels B and C. We were able to detect the megaparticle with optical imaging at close range (panel E) and also from thousands of km away via the use of satellite based telescopes.

Discussion We feel that the development of the megaparticle was highly advantageous and will be crucial to the long term survival of the primary cells. During the synthetic process it is possible that other biocompatible, magnetic megaparticles were created, although their location is currently uncertain. Some distinguished investigators have found solid proof for the existence of foreign PCCAiCM from other locations.(3) We will initiate collaborations with NASA and related agencies to extend the range of the imaging technique to 10 trillion km and over.

Conclusion Magnetic megaparticle MRI-related detection promises to be an exciting new method for tracking very large numbers of cells simultaneously. We hope to extend the range of this method to detect other magnetic megaparticles in the future.

References

1. Yahweh Y. Genesis. *The Bible* 4004 BC;**1-2**:4-24.
2. http://theresonanceproject.org