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Executive Summary: Magnetic Particle Imaging – A parallel to MRI

Gleich, B. and Weizenecker, J. Tomographic imaging using the nonlinear response of magnetic particles. *Nature*. **435**: 1214-1217 (2005).

In a Letter to the journal *Nature*, Gleich and Weizenecker propose a novel method for imaging magnetic nanoparticles (MNPs) with a high degree of spatial sensitivity. They hypothesized that the nonlinear response of certain ferromagnetic materials and their saturation at specific field strengths can form the basis of a tomographic imaging modality. In a manner analogous to nuclear magnetic resonance imaging, they proposed that selective saturation of a collection of MNPs in combination with an applied oscillating field allows discrimination of the MNPs through their time varying magnetization. In an elegant “proof of principle” experiment, the authors demonstrated an ability to image a commonly used magnetic tracer (Resovist) in a phantom with a high degree of spatial resolution. In their conclusion, they also proposed future directions for the technology to grow into a biomedical imaging technique.

Magnetic contrast agents have been used with great efficacy in MRI to enhance imaging capabilities. However, MRI is only sensitive to the intrinsic magnetic signal of tissue (usually protons) and magnetic contrast agents only modify this signal. Techniques have been used to measure the magnetic field intensity of MNPs after application of an external applied field. For example, Romanus *et al* employed magnetorelaxometry to measure and spatially resolve the relaxation of MNPs after application of an applied field. However, this technique lacks appropriate resolution needed in biomedical imaging. Direct measurement of the magnetic field of MNPs is possible, but no method to date has been able to demonstrate spatially sensitive detection.

Gleich and Weizenecker have overcome this issue by developing a method for spatially selective measurements of the magnetic field. Ferromagnetic materials have long been known to display hysteresis in their ensemble magnetization when an external field is applied. Such materials do exhibit a nonlinear response when magnetized from a zero field value. By applying a time-invariant spatially varying gradient magnetic field of appropriate amplitude to an object containing MNPs, most of the sample is saturated, while a limited portion around the zero field point (termed field-free point (FFP) by the authors) is not. These regions respond nonlinearly to an applied oscillating magnetic field. This produces a time varying magnetization signal that can be decomposed into higher harmonics of the applied field frequency. By filtering out the base frequency, the MNPs can be directly imaged at that point by averaging the remaining harmonics to obtain a signal.

There are two fundamental ways for spatial encoding during MPI image acquisition proposed by the authors. The first is that the object can be mechanically moved around the FFP and spatially registered signal collected at each point. The second demonstrates analogy to MRI by proposing that, in addition to the static field, the use of three driving fields that are oscillating at different frequencies allows the FFP to be moved throughout the sample by the fields. In the proof-of-principle experiment, the authors perform two techniques by (i.) manually moving the sample with a robot and (ii.) mechanically moving the sample in the horizontal direction while attempting vertical selection by modulating the drive field. The former technique provided a higher resolution, but took longer (18 minutes). The latter was faster (~1 minute), but because of the increased measurement speed had decreases signal to noise (SNR) and thus lower resolution.

According to the authors’ theoretical calculations, the resolution of MPI is directly proportional to the ratio of the field strength at which MNPs produce significant harmonics and spatial derivative of the gradient field. For this study, the resolution was about 0.3 to 0.5 millimeters as determined by the fields applied. The field of view (FOV) for MPI measurements follows a similar relationship with the minimal field strength required for nonlinear response replaced by the actual amplitude of the driving field used. Further enhancing the resolution is the large signal of MPI in relation to the background noise. This differs from MRI, where there is significant background noise and signal is improved by increasing the static magnetic field strength.

MPI may prove to be another excellent biomedical imaging technique. It does not measure intrinsic signal e.g. MRI, but it does measure the signal of an applied agent that would permit superb contrast in an *in vivo* imaging setting due to the lack of other confounding signals. Additionally, it uses longer radio frequency wavelengths that may permit deeper imaging in tissue. The future is certainly expansive for MPI and it will be interesting to see whether it someday proves an equal to MRI.