ON-LINE APPENDIX

MPI Physics

Selection Field. The core invention that underlies MPI is the ability to spatially encode a position of a SPION using a strong magnetic field gradient (typically 2–6 T/m) known as a selection field (On-line Fig 1*B*). The gradient field "selects" nanoparticles by passing through a zero magnetic field in the FFR (FFP or FFL). Within the FFR, SPIONs are free to rotate, while away from the FFR they are locked into position. The FFR position is moved rapidly throughout the imaging volume to produce an image,

Excitation Field. The excitation field or drive field is a low-amplitude homogeneous field that rapidly shifts the mean position of the FFR using an oscillating magnetic field (typically 20–45 kHz at 20 mT). The FFR can be moved in trajectories such as the one shown in On-line Fig 1*C*. For example, 3D scanning can be achieved through 3 orthogonally oriented drive fields. However, due to magnetostimulation and sample heating (specific absorption rate) limitations, the scanning region is limited from a few millimeters to a couple of centimeters, depending on the gradient strength. To increase the scanning region and hence the FOV, some scanners incorporate an additional field called a slow-shift or focus field.

Slow-Shift/Focus Field and Mechanical Translation. Focus fields are homogeneous, high-amplitude, low-frequency fields (typically 50–200 mT at <100 Hz) that slowly move the mean position of the FFR to cover the desired FOV (On-line Fig 1*D*). For example, moving the FFR by 3 cm in a 6 T/m gradient requires a 180-mT field, or an equivalent 3-cm mechanical translation. Application of a slow-shift field and/or mechanical translation of the field is typically performed simultaneously with application of the drive field. The small regions scanned by the limited extent of the drive field can be stitched together to produce a single extended FOV.

Scanner Construction

General Principles and Typical Setup. A few different fields are required for MPI scanning, including homogeneous/inhomogeneous and high-frequency/low-frequency/static fields. Different types of scanner setups may be used to generate these fields. Electromagnetic coils driven by an electric current are commonly used and allow high-frequency field generation. Homogeneous fields are typically generated using a cylindric coil or a Helmholtz coil pair (parallel coils with currents flowing in the same direction). Inhomogeneous fields can be generated using a Maxwell coil pair (parallel coils with currents flowing in opposite directions). Several coil sets are often combined to generate the fields in all 3 anatomic axes to construct a scanner (On-line Fig 2). With the static/slow-frequency field requirement, selection/gradient coils and focus coils are often combined (On-line Fig 2, blue). One set of selection coils (often a Maxwell pair) is needed to create an FFP. The focus field can be superimposed on this set of coils to move the FFP. Two other orthogonal coils (1 cylindric, 1 Helmholtz pair) generate focus fields in the other 2 anatomic directions. Drive/excitation fields are often realized through a cylindric coil and 2 Helmholtz pairs (On-line Fig 2, orange). Receive coils are constructed in a manner similar to that on the drive-field coils (On-line Fig 2, red).

Main Magnet Subsystem: Selection Field and Slow-Shift Fields. The main magnet is the core of the magnetic particle imager and the most expensive single component. Typically, it produces both the selection field and the slow-shift fields. The main magnet is often constructed with water-cooled electromagnets, permanent magnets, soft magnetic field returns, and combinations thereof. For example, several coil sets can be combined to generate the fields in all 3 anatomic axes (On-line Fig 2). Frequently, the current amplifiers that generate the main field gradient are also used to shift the main magnetic field by sharing the same electromagnets (On-line Fig 2, blue). The strength of the selection field drives the native resolution of the system, which is defined as the resolution that arises solely from the interaction between the main magnetic field gradient and the magnetic nanoparticle. As a gradient gets stronger, the resolution improves; doubling the gradient strength improves resolution by a factor of two.

Transmit/Receive Subsystem: Drive Field, Receiver Coils, and Electronics. All MPI scanners must deal with a technical challenge: direct feedthrough from the drive coil to the receiver. The nanoparticle induces nanovolts of signal into the receive coil. On the other hand, the drive field is >10 million times stronger than the nanoparticle signal, inducing hundreds of volts in a receiver coil. System designers typically use 3 techniques to isolate the nanoparticle signal from the drive signal: First, they make the drive signal a pure sinusoid by building an aggressive low-pass filter that lets only the drive frequency into the transmit coil. Second, the receive coil is wound as a gradiometer to reduce the drive-field pickup voltage by 1~2 orders of magnitude. Last, the remaining 5 orders of magnitude of drive signal are "notched" out using an analog filter so that only the nanoparticle signal makes it to the preamplifier. Drive/excitation fields are often constructed in cylindric coils and 2 saddle coil pairs (On-line Fig 2, orange). Receive coils are constructed in a manner similar to that in the drive-field coils (On-line Fig 2, red).

Control Console: Pulse Sequences and Reconstruction. The imaging process is controlled by a real-time computer. Much like MRI, MPI relies on pulse sequences. A typical pulse sequence will control the trajectory that the FFR travels through real space, including the drive-field trajectory, the slow-shift field trajectory, and any mechanical translation. Furthermore, the pulse sequences can be built to tease out nanoparticle behavior, enabling new applications such as "color" MPI.[1-3] Once the data are acquired, the console reconstructs the image. Numerous reconstruction techniques have been invented, including x-space reconstruction[4,5], harmonic space reconstruction,[6] and single harmonic imaging.[7]

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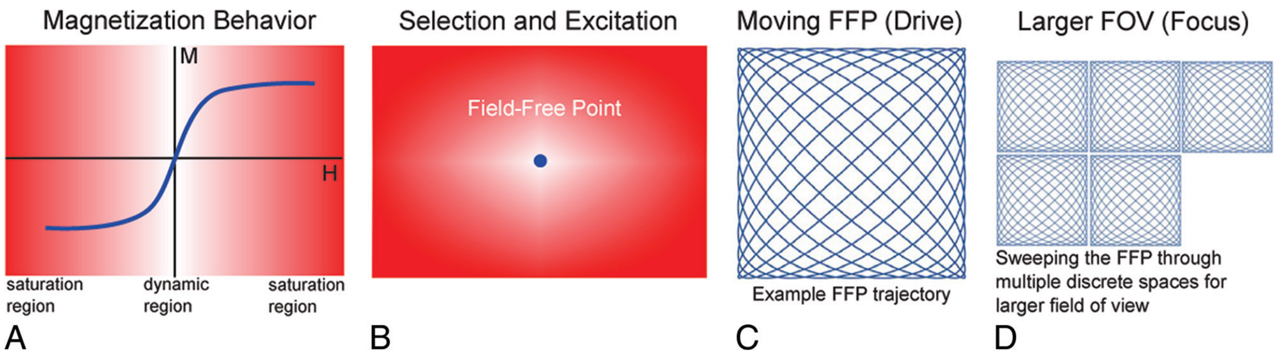

ON-LINE FIG 1. MPI physics. The behavior of superparamagnetic nanoparticles (SPIONs), which are tracers used in MPI, can be explained by the Langevin theory, in which particle magnetization (M) increases with external field strength (H) until it saturates (*A*). A selection field generates an inhomogeneous field containing an FFP (*B*). Magnetic particles at the FFP can be excited through the excitation field to generate signal. To scan through space, one moves the FFP through the drive field (*C*). A larger FOV can be achieved through a focus field (*D*).

ON-LINE FIG 2. Multiple coil sets are combined to generate all required fields in the 3 anatomic axes, including selection/focus-field coils (blue), drive-field coils (orange), and receive coils (red).