

# ***In Vivo* Cellular Imaging using Magnetic Nanoparticles: From MRI Contrast Agents to MPI Tracers**

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Labeling of cells with magnetic nanoparticles<sup>1</sup> has been applied for in vivo magnetic resonance imaging (MRI) cell tracking for over 30 years, having resulted in a dozen or so clinical trials<sup>2</sup>. These superparamagnetic iron oxide (SPIO) nanoparticles are biodegradable and can be broken down into elemental iron, and hence the tolerance of cells to magnetic labeling has been overall high. Cell tracking is expected to play a key role in evaluating the efficacy of cell therapy in clinical trials of immunotherapy and regenerative medicine (“Did the cells get there?”. “Did the cells stay there and for how long?”). MRI-guided injections will be a major add-on in advanced clinical cell therapy settings, being able to verify the accuracy of targeted cell injection in real-time, with a temporal resolution of <1 sec.

More recently, magnetic particle imaging (MPI) has emerged as non-invasive imaging modality that can also be applied for cell tracking<sup>3</sup>. It can use the same SPIO nanoparticles as those used with MRI, but instead of MRI contrast agents these formulations act as MPI tracer agents to provide “hot spot” signal without tissue background signal, and true cell quantification<sup>4</sup>. A historical perspective will be presented from the very first MRI test tube cell labeling studies<sup>5</sup> to the first in vivo clinical<sup>6</sup> study, followed by some of the early pre-clinical MPI cell tracking studies. At the end, advantages and disadvantages of MPI and MRI will be discussed as compared to a more recent approach to detect unlabeled cells with MRI<sup>7</sup>.

## **References**

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- <sup>5</sup>Bulte, JWM et al., *Magn. Reson. Med.* **1992**, 25: 148-157.
- <sup>6</sup>de Vries IJM et al., *Nat. Biotechnol.* **2005**, 23, 1407-1413.
- <sup>7</sup>Y. Yuan Y et al., *Nat. Biomed. Eng.* **2022**, 6, 658-666.