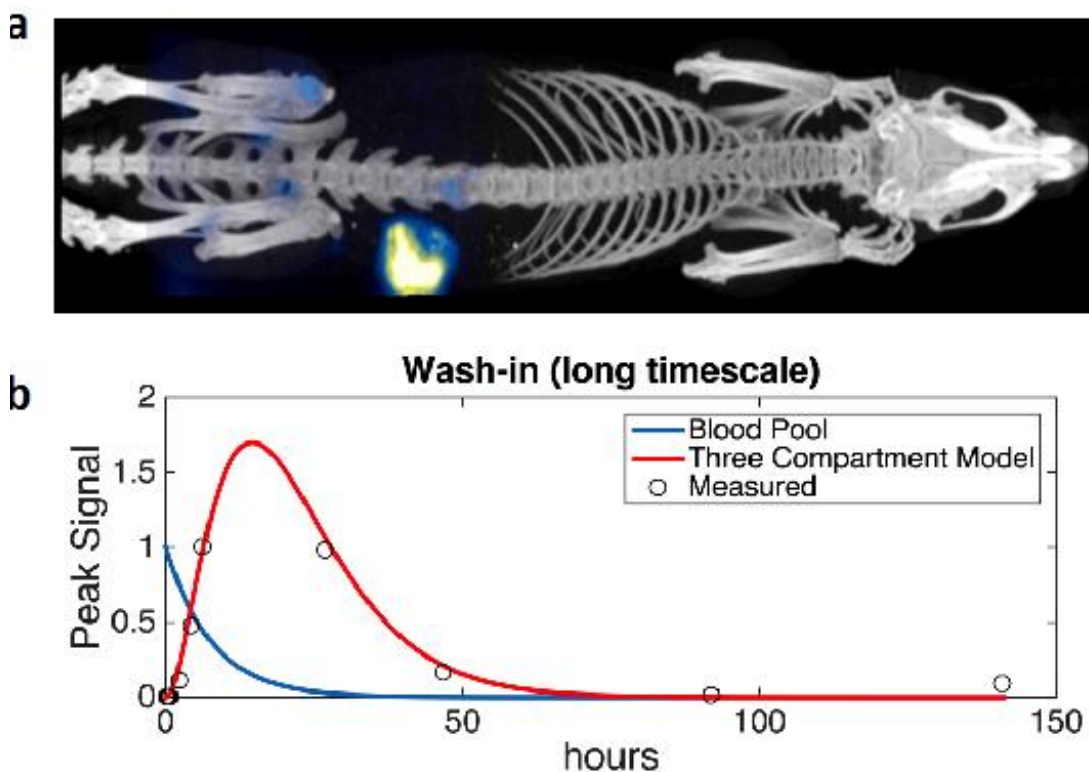


# Advances in Cancer Monitoring and Detection with Magnetic Particle Imaging

## Cancer Imaging

Multiple imaging techniques are commonly used in all phases of cancer management [1]. The early detection of cancer through image-based screening is a major contributor to reduced cancer mortality [2]. Advances in targeted imaging approaches and therapeutic agents require the development of new and improved imaging tools to assess the full spectrum of cancer tumorigenesis. One such emerging imaging modality is MPI for early cancer detection and staging. The Momentum™ MPI system is a translatable imaging technology that offers high contrast, rapid and quantitative 3D imaging capabilities without the need for ionizing radiation or toxic tracers [3].

The MPI technique enables the ultra-sensitive detection of superparamagnetic iron oxide nanoparticle (SPIO) tracers, some of which are currently used in the clinic. MPI images are “positive contrast”, a hallmark of molecular imaging techniques such as PET and Optical imaging. It produces no signal from overlying tissues, allowing robust linear quantitation of tracer in 2D, 3D and real time anywhere in the body and without depth limitations. MPI directly detects the large magnetic moment from the SPIO, potentially detecting sub-nanogram levels of iron oxide in a voxel (equivalent to about 20 cells) [3].



**Figure 1:** (a) EPR effect mediated tumor detection and biodistribution of SPIOs in a xenograft animal model of human cancer 6 hr post tail vein injection of SPIOs. (b) Quantification of tumor uptake of SPIOs and subsequent clearance of SPIOs over time.

## Cancer Screening

One of the grand challenges of cancer research is to detect tumors before the metastatic process has occurred, when surgical resection is still highly efficacious. Hence, researchers have searched for years for biomarkers with sufficient cancer sensitivity and specificity. Difficulty in diagnosis does not bode well for patients since current clinical standard of care recognizes that early and accurate diagnosis of cancer is crucial to delaying disease progression and improving patient outcome. MPI shares more with nuclear medicine than anatomic imaging with CT and MRI [4]. Hence, MPI could represent a true breakthrough in the non-invasive, sensitive and specific diagnosis of cancer. This approach could even screen asymptomatic populations since it uses a completely safe iron oxide tracer and absolutely no radiation. Additionally, MPI can provide quantitative tumor volume and shape estimates. Like PET/CT, MPI will be co-registered with an anatomic imaging technique to view organ boundaries, which are crucial for ruling out metastases. One MPI tracer, Ferucarbotran (VivoTrax™, Magnetic Insight, Inc.), is EU approved for use in humans and has been used in tens of thousands of patients with absolutely no ill effects [5].

## Mechanisms of Cancer Detection

There are a number of possible mechanisms by which MPI compatible SPIOs may be used for cancer detection. However, in order to visualize a tumor, SPIOs must either become localized to the tumor through tumor vasculature, surface, become extravagated into the tumor or enhanced permeability and retention effect (EPR) [6]. Currently cancer detection using MPI has relied on the EPR effect as shown in Figure 1. In this example, a human breast cancer xenograft animal model is injected intravenously with SPIOs that become localized in the tumor (Figure 1a).

Overtime the biodistribution of SPIOs can be monitored from initial injection, tumor localization and SPIO clearance (figure 1b). However, MPI cancer-targeted SPIOs are already in development and could be a breakthrough advancement in cancer screening, diagnosis, and staging. Other approaches that are possible are indirect tumor measures such as tumor associated macrophages (TAMs) or other cancer recruited immune cells that could be loaded with SPIOs and monitored.

## Conclusion

MPI Cancer detection is an emerging imaging tool with great potential. Rapidly acquired positive contrast images are easy to interpret and are linearly quantitative. MPI uses no radiation yet it has 1000-times greater contrast sensitivity than MRI and the high resolution of nuclear medicine. MPI is expected to make significant advances in cancer imaging capabilities and provide a new measure for cancer diagnostics.

## References

1. Mol Oncol. 2008 Aug;2(2):115-52
2. Cancer Imaging. 2011; 11(1A): S86–S92
3. Theranostics. 2016 Jan 1;6(3):291-301
4. J Magn Reson. 2013 Apr;229:116-26. doi: 10.1016
5. Adv Mater. 2012 Jul 24;24(28):3870-7
6. Adv Drug Deliv Rev. 2014 Feb;66:2-25

