IVYSPRING INTERNATIONAL PUBLISHER

Theranostics

2018; 8(13): 3691-3692. doi: 10.7150/thno.27454

Editorial

Take a Deep Breath – Monitoring of Inhaled Nanoparticles with Magnetic Particle Imaging

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Received: 2018.05.24; Accepted: 2018.05.26; Published: 2018.06.11

Abstract

Magnetic Particle Imaging (MPI) is a new imaging modality based on the visualization of Superparamagnetic Iron Oxide Nanoparticles (SPIONs) using magnetic fields. The potential of MPI was recently evaluated in numerous *ex vivo* and *in vivo* studies and the technique can now be considered as an established preclinical imaging modality with a promising perspective of clinical applications.

Key words: Magnetic Particle Imaging, Nanoparticles, Preclinical Imaging, Clinical Imaging

Introduction

More than 10 years ago Magnetic Particle Imaging (MPI) emerged as a completely new imaging modality. The basic principle of MPI - the visualization of the spatial distribution of Superparamagnetic Iron Oxide Nanoparticles (SPIONs) using oscillating magnetic fields - was first described by Gleich and Weizenecker in 2005 [1]. The technique provides a high temporal and spatial resolution combined with a high sensitivity and due to its electro-magnetic properties, the MPI signal penetrates tissue unrestrictedly. MPI acquires quantitative, hot-spot images with positive contrast similar to PET and SPECT, except that MPI avoids the use of radiochemicals. The sensitivity of MPI to an optimal iron oxide contrast agent is predicted to be two to three orders of magnitude greater than that of MRI. Furthermore, MPI is much faster than MRI, because the signal can be detected immediately after the excitation, whereas the MRI signal (echo) occurs after a considerable waiting time in the range of 1 to 100 ms. MPI therefore opens the way to new radiation-free applications in real-time imaging, molecular diagnostics and therapy-monitoring.

Especially the field of cardiovascular imaging was intensely evaluated in several proof-of-principle studies in the last decade. The quantification of stenosis, vascular flow-measurements and MPI-guided catheter interventions have been successfully performed in several preclinical studies [2–5]. Safety limits of interventional devices were evaluated and recently first real-time experiments were published [6–9]. Additionally, the detection of bleeding and ischemic events were taken into account in small animal studies [10–12].

As cardiovascular applications take advantage of the high temporal resolution of MPI, it is the excellent sensitivity which predisposes MPI for molecular imaging applications. *Graeser et al.* recently demonstrated a detection limit of 5 ng iron in MPI using a gradiometric receive coil [13]. In 2009, first preclinical experiments on MPI guided sentinel lymph node biopsies have been published [14]. Additionally, it is possible to load erythrocytes with SPIOs [16] and *Zheng et al.* depicted neuronal cells for 87 days in rat brains [17]. Furthermore, stem cells [15,18] as well as cancer cells [19] can be tracked by MPI. Another interesting application is the conjugation of SPIONs with molecules, which bind to specific cell surfaces. Thus, the conjugation of lactoferrin with SPIONs to detect glioma cells is an

impressive example for a new approach of MPI based cancer imaging [20].

In this issue of *Theranostics* an excellent article titled "In Vivo Tracking and Quantification of Inhaled Aerosol using Magnetic Particle Imaging towards Inhaled Therapeutic Monitoring" was published by *Tay et al.* [21]. In a well-designed and innovative study the authors showed that inhaled nanoparticles can be visualized by MPI in mice with accuracy comparable to radiolabeled aerosols. The inhalation parameters such as aerosol particle size have major impact on the particle distribution, and due to quantitative MPI measurements the described method can be applied for MPI-based drug monitoring. This concept was first described in the article and the authors validated their results by means of fluorescence imaging. Another interesting aspect of the study is the *in vivo* visualization of the mucociliary clearance. The clearance pathway of SPIONs in mice was shown for 13 days and the transport function of the alveolar cells was successfully demonstrated with MPI. Last but not least, the authors addressed potential safety concerns and pointed out options for human applications.

Taken together with recent results from *Zhou et al.* [22], demonstrating the possibility of lung perfusion imaging with MPI, the authors completed the proof of concept of an MPI-based perfusion-ventilation mapping [21]. Perfusion-ventilation mapping is widely used in clinical routine for the diagnosis of pulmonary embolism and the preoperative evaluation of the lungs. Without the use of ionizing radiation, MPI may overcome important disadvantages of nuclear medicine techniques.

In conclusion, the article by *Tay et al.* shows the huge potential of MPI for basic research in a very illustrative way. The quantitative *in vivo* visualization of inhaled particle aerosols as well as SPION labeled drugs combined with the analysis of the mucociliary clearance provides an effective tool for the investigation of numerous scientific questions.

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