

Proceedings Article

Quasi-simultaneous magnetic particle imaging and navigation of nanomag/synomag-D particles in bifurcation flow experiments

F. Griese^{1,2,*} · P. Ludewig³ · C. Gruettner⁴ · F. Thieben^{1,2} · K. Müller⁴ · T. Knopp^{1,2}

¹Section for Biomedical Imaging, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

²Institute for Biomedical Imaging, Hamburg University of Technology, Hamburg, Germany

³Department of Neurology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

⁴micromod Partikeltechnologie GmbH, Rostock, Germany

*Corresponding author, email: f.griese@uke.de

© 2020 Griese *et al.*; licensee Infinite Science Publishing GmbH

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Abstract

Magnetic Particle Imaging (MPI) is used to visualize the distribution of superparamagnetic nanoparticles within 3D volumes with high sensitivity in real time. Recently, MPI is utilized to navigate micron-sized particles and micron-sized swimmers, since the magnetic field topology of the MPI scanner is well suited to apply magnetic forces. In this work, we analyze the magnetic mobility and imaging performance of nanomag/synomag-D for Magnetic Particle Imaging/Navigation (MPIN). With MPIN the focus fields are constantly switching between imaging and magnetic force mode, thus enabling quasi-simultaneous navigation and imaging of particles. In flow bifurcation experiment with a 100 % stenosis on one branch, we determine the limiting flow velocity of 1.36 mL/s, which allows all particles to flow only through one branch towards the stenosis. During this experiment, we image the accumulation of the particles within the stenosis. In combination with therapeutic substances, this approach has high potential for targeted drug delivery.

1 Introduction

Magnetic Particle Imaging (MPI) takes advantage of the non-linear magnetization characteristics of superparamagnetic nanoparticles to resolve the distribution of them in 3D at high temporal resolution [1]. Usually, the highest sensitivity is achieved with particles in the magnetic core size range of 15 nm to 30 nm [2]. However, micron-sized devices attached with soft-magnetic spheres have been imaged and tracked with MPI [3]. These devices can also be moved to target areas by the magnetic force of MPI [3]. Using a similar principle rotational magnetic fields

are utilized to selectively control helical micro-devices [4]. Bakenecker *et al.* use rotational focus fields to control the actuation of magnetically coated swimmers and have moved them through bifurcations while sequentially imaging and magnetically navigating them [5]. Further, micron-sized magnetic particles are moved and imaged quasi-simultaneously with the Magnetic Particle Imaging/Navigation (MPIN) method with a temporal resolution of 2.9 Hz [6].

The ability to navigate and image magnetic particles can be deployed in potential medical application such as acute stroke therapy. Usually, thrombolytic medications,

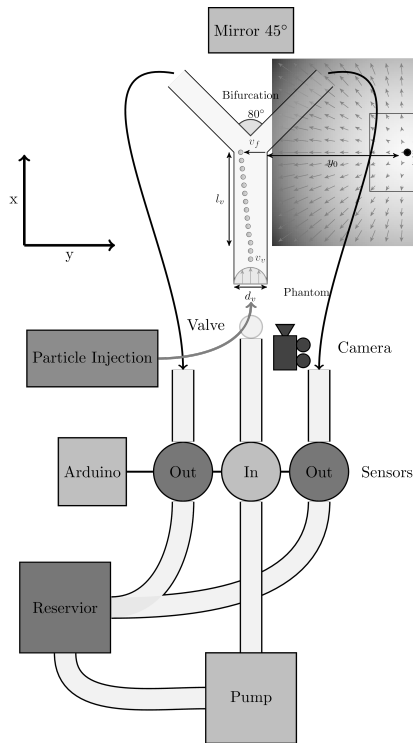


Figure 1: Schematic image of the flow measurement setup with bifurcation phantom visible inside the mirror placed inside the bore, Arduino attached to flow sensors, light source and camera.

e.g. tissue plasminogen activator (tPA), are injected to clear vessel occlusions in the bifurcation between external carotid artery and internal carotid artery [7]. However, the tPA does not dissolve the blood clot effectively, because the blood flows mainly through the unblocked branch between the external carotid and internal carotid artery. Consequently, the blood clot is cleared in a risky, invasive procedure using a catheter. With the MPIN method, functionalized magnetic particles would be navigated towards the vessel stenosis and thus resolve the blood clot. With that in mind, the usage of functionalized magnetic particles could help reducing the dose or even make an invasive procedure superfluous. In this work, we analyze the nanomag/synomag-D particle characteristics in terms of magnetic manipulability and imaging performance for MPI. Additionally, we set up inflow bifurcation experiments to determine the flow velocity, up to which it is possible to navigate the particles to one side of the bifurcation towards a 100 % stenosis.

II Material and methods

For the MPIN method, the gradient field induces a magnetic force by appropriately adjusting the location of the FFP with the focus fields. The magnetic force at all time

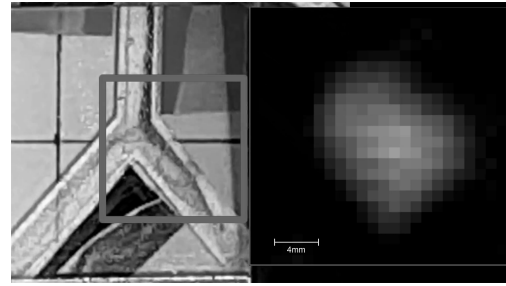


Figure 2: In this snapshot of the acquired video [8] most of the particles are navigated into the right branch towards the 100 % stenosis at a flow velocity of 1.36 mL/s while the MPI imaging mode (rectangle in left image) shows the distribution of the particles.

points is given by

$$F_{(m,y)}(y, t) = \frac{4}{3} \pi \mu_0 r_m^3 \Delta \chi G_y^2 y s(t) \quad (1)$$

with $i = 1, \dots, n$ and

$$s(t) = \begin{cases} 1, & \text{if } t \in [T(i-1)N_{nc} + TiN_{ic}, Ti(N_{nc} + N_{ic})] \\ 0, & \text{else} \end{cases} \quad (2)$$

where μ_0 is the vacuum permeability, $\Delta \chi$ the difference in magnetic susceptibility between particles and surrounding medium, r_m the magnetic core radius, G_y the gradient in y -direction and y the distance to the FFP in y -direction. N_{nc} is the number of navigation drive field (DF) cycles, N_{ic} is the number of imaging DF cycles and $T=0.021$ s is the time span for one acquisition cycle [8]. The customized nanomag/synomag-D particles (micromod) have a hydrodynamic diameter of about 700 nm (iron core 500-600 nm) and a dilution series is set up to analyze their linear behavior with respect to the particle concentration. The imaging characteristics of the nanomag/synomag-D particles are investigated with our custom-built Magnetic Particle Spectrometer (MPS) [9] and the magnetic mobility properties are determined with a magnetic separation device (SEPMAG Q 100 ml). For the flow experiments, a bifurcation phantom with a crossing angle of 80°, a quadratic cross section with a side length of 3.54 mm and 100 % stenosis in one branch is 3D printed by a Forms 2 stereolithography printer. The flow experiment setup can be seen in Fig. 1 with bifurcation phantom, pump, flow sensors, Arduino, valve for particle injection and 45° mirror inside the bore to see the phantom from outside the scanner.

For the quasi-simultaneous imaging and navigation, the number of imaging DF cycles is set to $N_{ic} = 1$, while the number of navigation cycles is set to $N_{nc} = 20$. Thus, MPI takes a snapshot every 2.15 s of the particle distribution at the 100 % stenosis. The bifurcation phantom is moved 8 mm away from the center, while the FFP position for the navigation mode is adjusted 14.16 mm in the

opposite direction, making a total distance of 22.16 mm between FFP and particles in flow.

III Results and discussion

The analyzed nanomag/synomag-D particles generate up to 35 harmonics above the noise level, which is sufficient enough for imaging. The regression of the signal strength through the dilution series results in a coefficient of determination of 0.997 for the linearity. The nanomag/synomag-D particles yield a half-separation time (time when half of the turbidity is reached) of 75 s, which underlines its navigation capabilities when comparing it to 500 nm nanomag-D with a half-separation time of 194 s. Altogether, the nanomag/synomag-D particles provide a good compromise between imaging ability and magnetic mobility. In the bifurcation experiment with the 100 % stenosis in one branch, it is possible to successfully navigate the particles towards the stenosis with a flow velocity of up to 1.36 mL/s (108 mm/s), as seen in Fig. 2. The concentration of the particles is increasing in the MPI image during the measurement. In a control experiment without magnetic forces the particles do not reach the stenosis, since they are pulled towards the other clear branch by the flowing current.

IV Conclusions

In this work, we have shown the imaging and navigation capabilities of nanomag/synomag-D for MPIN. The MPIN method is successfully used to maneuver the particles to towards the 100 % stenosis as the flow moves with 1.36 mL/s. During the measurement, we image the particles' distribution in the stenosis every 2.15 s. The goal of future experiments will be to functionalize the particles in order to resolve a blood clot in a stenosis, while monitoring the liquidation with MPIN.

Author's Statement

F.G., F.T. and T.K. thankfully acknowledge the financial support of the German Research Foundation (DFG, grant number KN 1108/2-1) and the Federal Ministry of Education and Research (BMBF, grant number 05M16GKA). This work is supported by the BMBF under the frame of EuroNanoMed III (grant number: 13XP5060B, T.K, P.L.). Authors state no conflict of interest.

References

- [1] B. Gleich. Tomographic imaging using the nonlinear response of magnetic particles. *Nat.* 435, 1214–1217 (2005). DOI 10.1038/nature03808.
- [2] R. M. Ferguson. Optimization of nanoparticle core size for magnetic particle imaging. *J. magnetism magnetic materials* 321, 1548–1551 (2009). DOI 10.1016/j.jmmm.2009.02.083.
- [3] N. Nothnagel. Steering of magnetic devices with a magnetic particle imaging system. *IEEE Transactions on Biomed. Eng.* 63, 2286–2293 (2016). DOI 10.1109/TBME.2016.2524070.
- [4] J. Rahmer. Remote magnetic actuation using a clinical scale system. *PLoS ONE* 13 (2018). DOI 10.1371/journal.pone.0193546.
- [5] A. C. Bakenecker. Actuation and visualization of a magnetically coated swimmer with magnetic particle imaging. *J. magnetism magnetic materials* (2018). DOI 10.1016/j.jmmm.2018.10.056.
- [6] F. Griese. Imaging and moving magnetic beads with magnetic particle imaging for targeted drug delivery. In 2018 IEEE 15th International Symposium on Biomedical Imaging (ISBI 2018), 1293–1296. DOI 10.1109/ISBI.2018.8363808.
- [7] Declerck PJ, Gils A. Three decades of research on plasminogen activator inhibitor-1: a multifaceted serpin. *Seminars in Thrombosis and Hemostasis.* 39 (4): 356–64 (2013).
- [8] F. Griese. Simultaneous Magnetic Particle Imaging and Navigation of large superparamagnetic nanoparticles in bifurcation flow experiments. In: *J of magnetism and magnetic materials* (2020). DOI:10.1016/j.jmmm.2019.166206.
- [9] S. Biederer, et al. Magnetization response spectroscopy of superparamagnetic nanoparticles for magnetic particle imaging, *J. Phys. D: Appl. Phys.* 42 (2009) 1–7.