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# Sample preparations for reproducible measurements in MPS and MPI

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**Abstract**

MPI is a promising new technology for highly sensitive medical imaging. To acquire reproducible measurements, stable scanner and sample preparations are needed for both system matrix (SM) acquisition and measurement. Therefore, it is important to analyze and subsequently minimize the influence of the scanner hardware, as well as of the preparation method. In this work, we studied the evolution of the MPI signal of particle samples using five sealing methods (tape, hot glue, silicone, silicone + tape, UV glue) in combination with two different tracers (perimag® and SHP20). In a background examination, we obtained high variations in the signal of the empty scanner over time. For the sample preparation series, we saw that for each type of tracer a different sealing method worked best. Our results offer insight to sample behavior, which is important for stable SM measurements as well as the differentiation of other factors influencing a sample measurement.

## I. Introduction

MPI is a new, tracer-based and therefore, functional imaging technique proposed by Gleich and Weizenecker in 2005. It uses the non-linear magnetization response of magnetic nanoparticles (MNPs) to an alternating magnetic field to quantitatively visualize their spatial distribution. With various advantages like a harmless tracer [1], since no radiation is used, and a sensitivity and spatiotemporal resolution that can theoretically compete or even exceed the ones of the existing imaging modalities, MPI promises a broad width of application [2]. In the field of disease diagnostic, MPI could help to determine regions of abnormal body temperature or blood viscosity [3]. With the knowledge of these two fundamental medical parameters, tumors and several diseases can be diagnosed, such as Alzheimer's disease and altered risks of cardiovascular mortality [3]. To study the particles' behavior depending on those two parameters, small plastic tubes holding the MNPs are typically used in preclinical research. During measurements with samples prepared in the containers but without any form of sealing except for the lid, dislocations of the particles within the sample have been observed over time in the form of lifted positions along the walls of the container. Furthermore, due to such interactions the liquid particle suspensions can potentially dry out and thus change their characteristics. For small changes of the environmental parameters to be visible in the MPI signal and for accurate measurements of the SM, a stable scanner hardware and a stable sample needs to be ensured. Especially for the preparation of the sample tubes, to our knowledge, no comparison of different sealing methods has been published yet.

# II. Materials and methods

To analyze the influence of the sample preparation on the evolution of the MPI signal, samples containing the same type of fluidic particle suspension have been sealed with up to five different sealing methods. For every sample, we used sample tubes provided by Bruker. As a first seal, we used plain white insulating tape that has been fitted onto the sample tube before closing it with a lid. For the second, third and fourth method, hot glue, silicone or UV glue has been inserted into the free space between particles and lid, respectively. As a last method, silicone was chosen in a combination with tape to prevent contact between the silicone layer and the iron-based particles.

Each samples was prepared with 10 µl of one of the two different types of MNPs. As a first tracer, perimag® particles (micromod Partikeltechnologie GmbH, Rostock) were used. They are characterized by a broad size distribution and we used them at a particle concentration of 25 mg ml$^{-1}$. The second tracer were SHP20 particles (Ocean NanoTech LLC, San Diego) with a narrow size distribution around the core size of 20 nm used at a particle concentration of 5 mg ml$^{-1}$.

Measurements were taken with the Bruker Preclinical Magnetic Particle Imaging scanner (Bruker BioSpin GmbH, Ettlingen), working at a drive frequency around 25 kHz. The amplitude of the drive field was set to $A_{D,x}$ = 14 mT and no gradient field was used. During each measurement, 1000 repetitions were recorded. After each signal measurement with the sample placed within the FOV of the scanner, a corresponding background measurement was performed. For the latter, the sample was completely withdrawn from the scanner via the remote controlled robot. Per sample we took five measurements a day, each with a time gap of one hour, over several days. In this work, the background needed for signal-to-noise ratio (SNR) calculation was chosen to be the sole signal of the empty scanner. That way, the time gap between signal and background measurement and thus the variation of the background signal is minimized.

To evaluate, which seal works best for each type of tracer, the signal strength and its evolution over time are compared. Therefore, the odd harmonics are filtered from the SNRs, which are calculated from the 1000 repetitions of particle and background measurement. This is done for each point of time at which measurements have been taken. For each harmonic, the average and standard deviation is calculated over the timepoints. That way, the absolute signal height, as well as the variation over time can be quantitatively compared between the different seals, with a high amplitude and a low standard deviation indicating a successful sealing method.

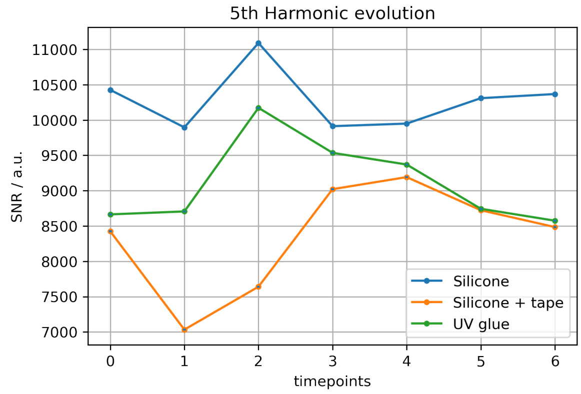


**Figure 1:** Evolution of the 5th harmonic amplitude measured consecutively with three different perimag® samples.

# III. Results and discussion

## III.I. Background

In the background examination, we found that generally the background only contributes up to 2 % to the total signal measured with sample. In terms of stability, we found that the background signal exhibits variations of up to 10 % of the background signal amplitude within one hour. To evaluate the influence of the change of the background signal between particle measurement and background measurement on the SNR, we performed a generous estimation of the error on the SNR resulting from the uncertainty on the background signal over this one hour period. Applying those errorbars to plots of the evolution of the harmonics over time (see following section) we came to the conclusion that the variation of the background signal is neglectable.

Secondly, we found that compared to the empty scanner signal, hot glue shows its own MPI signal, while for every other material no significant difference was observed. These results have to be considered, especially when analyzing the samples sealed with hot glue.

## III.II. Particle measurement

In Figure 1 the evolution of the amplitudes of the $5^{th}$ harmonic are exemplarily shown for three perimag® samples prepared with silicone, silicone + tape and UV glue together with their corresponding uncertainties including the background signal variation over one hour. To prevent further external influences to the MPI signal, at each point of time all three samples were measured consecutively.

With this plot, one can see that the variation of each amplitude has very unlikely been caused by shifts of the background but rather seems to be of statistical origin. Furthermore, no sample exhibits signs of sample change since no consistent tendencies are observable. Therefore,

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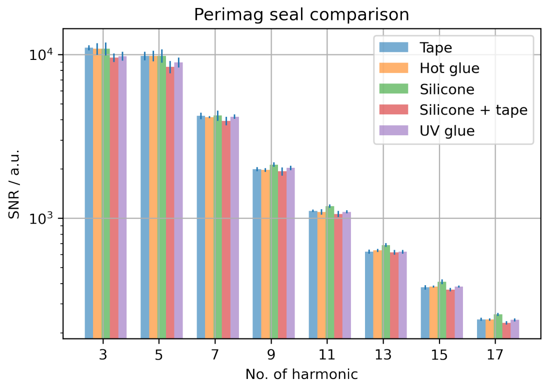



**Figure 2:** Mean SNR of six timepoints at which perimag® samples have been measured together with the standard deviation at odd harmonics 3 - 17.

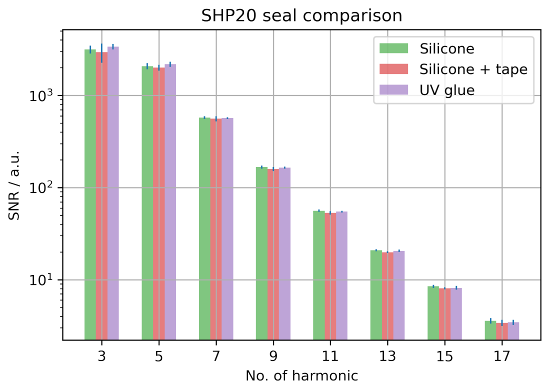
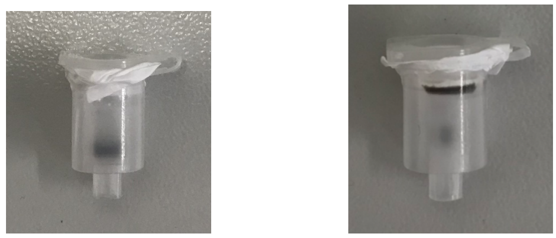



**Figure 3:** Mean SNR of the 15 timepoints (tape) and 10 timepoints (silicone, silicone + tape and UV glue) at which corresponding SHP20 samples have been measured together with the standard deviation.

it was sufficient to calculate the mean amplitude of a sample at each harmonic and its standard deviation to compare all samples.

With perimag®, samples with all five sealing methods have been prepared. The analyzed data can be seen in Figure 2. For better insight on the data, only the harmonics up to the 17$^{\text{th}}$ are plotted. The sample sealed with silicone exhibits overall the highest signal amplitudes but also the highest variation over time. The sample sealed with tape yields the second highest signal amplitudes but generally the lowest variation over time, which is why tape resulted to be the best sealing method for samples containing perimag® particles.

With SHP20 particles, three of the five sealing methods were tested. Their comparison can be seen in Figure 3. The signal amplitudes of the samples sealed with silicone and UV glue are comparable. In terms of signal variation, again the silicone sample exhibits high variation over time, while the sample sealed with UV glue shows the lowest variation among all four samples. Therefore,



**(a)** SHP sample sealed with tape.

**(b)** perimag® sample sealed with tape.

**Figure 4:** Sample tubes sealed with tape containing different types of tracer.

based on the results of the measurements executed in this work, UV glue seems to work best as seal for SHP20 samples.

The tape sealing was also tested with SHP20 particles but can not be compared to the other samples due to differing measurement influences. However, another interesting result was obtained with the SHP20 particles and tape sealing. While other samples only showed light dislocations as seen in Figure 4a, both SHP20 samples containing tape showed much stronger dislocations as exemplarily shown in Figure 4b for the tape sample. This behavior could also explain the reduced signal amplitude and increased signal variation of the silicone + tape sample in Figure 3.

# IV. Conclusion

In this paper, we have shown the importance to investigate the sample preparation depending on the used tracer. We did see an interesting and potentially significant influence of the sealing method to the signal of MPI and thus found that for different particles the optimal sealing method may vary. This result has especially been observed with tape working best for perimag® particles, while leading to strong, unwanted reactions when used in combination with SHP20 particles.
To confirm the impact of the sealing material on the signal of MPI, extended experiments are needed, which includes measurements with various samples of each sealing as well as measurements at numerous points of time. For further optimization, the reasons for these unequal reactions between different tracers will be examined. Furthermore, reasons for the differences in the background signal between varying days should be analyzed to reduce its contribution. In the background examination, we found that the background signal generally only contributes up to 2 % in amplitude to the sample signal. In this work, the variation can therefore be neglected, but it needs to be considered, when analyzing sample variations that lie within the 2 % range of the total signal, which could happen due to different environmental factors.

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## Author's statement

Conflict of interest: Authors state no conflict of interest.

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