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Volumetry in magnetic particle imaging

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Abstract

In this work, we investigate the suitability of MPI as a volumetry tool for the determination of retrograde voiding cystography of the bladder. Measurements were performed in two different experimental coil settings: first with a novel gradiometer providing three orthogonal channels and second a single-channel gradiometer at varying gradient strengths. The volumes were calculated using two different approaches: a calibration approach based on the amount of SPIOs and a threshold approach. We show that with both approaches MPI volumetry is feasible. Finally we present initial in vivo results of a retrograde voiding cystography in rats.

I Introduction

Real-time imaging of urinary bladders during micturition is a standard diagnostic procedure in urology e.g. to rule out vesicoureteral reflux – a condition in which urine flows retrograde from the bladder into the ureters/kidneys. Currently, the standard procedure is ultrasound or fluoroscopy-guided voiding cystourethrography. Since these methods are either highly investigator-depended or bear the inherent drawback of ionizing radiation, our motivation was to study the potential of MPI. This imaging method has the additional advantage to deliver tomographic 3D information the filling or voiding processes. We aim to utilize this potential to also derive real-time volumetric information.

In order to determine void volumes, the pixels belonging to the void, have to be determined for each slice of the 3D dataset. Thus, the resulting accuracy depends on the pixel resolution of the 3D-data set (=voxel resolution) and on the width of the point spread function (PSF) of the structure to be mapped. In MPI, the width of the PSF varies with the tracer type, its amount dose and the gradient strength of the magnetic selection field. If the PSF is broader than one voxel it may also extend to the adjacent one which will then gain a certain intensity value. Therefore, the difficulty is to decide which voxel r_i has to be included for the volumetry.

Two different approaches to determine the volume were used. The first is based on the total amount of SPIOs $n = c_s V_I$ in the field of view, with c_s being the sample concentration. Here, the sample volume V_I is directly proportional to the summed intensity of the reconstructed dataset $\sum_s I_s(r_s)$:

$$V_I = \frac{1}{p\, c_s} \sum_s I_s(r_s) \quad \text{with} \quad p = \frac{1}{c_K V_K} \sum_k I_k(r_k) \qquad (1)$$

This "intensity" approach requires a calibration measurement K with a sample of known volume V_K and concentration c_K. Noise below the threshold σ_I is neglected in this approach. Our second alternative was a conventional "threshold" method, in which all voxels r_i with intensities $I_i(r_i)$ above a certain threshold level σ_T are summed up and multiplied with the volume of one single voxel v:

$$V_T = \sum_{i \in J} v, \quad \text{where} \quad J = \text{image voxel } i | I(r_i) \geq \sigma_T \qquad (2)$$

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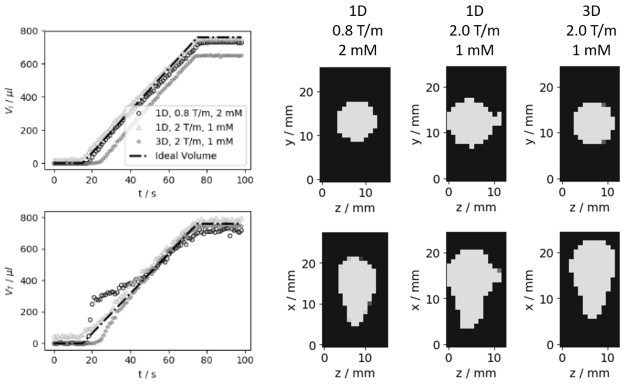

Figure 1: Dynamic MPI measurements of in vitro phantoms. Left: The determined volumes (upper: V_I, lower: V_T) are plotted against the time t. Right: Central axial and coronal slices of the reconstructed data.

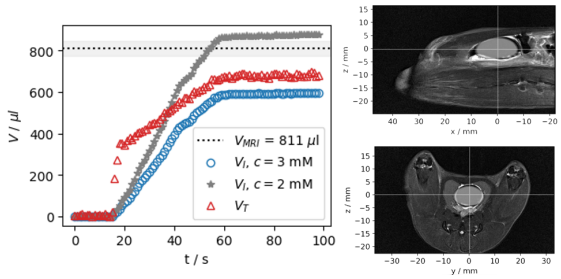

Figure 2: Dynamic MPI measurement of a retrograde cystography of the urinary rat bladder in vivo. Left: The volumes V are plotted against the time t. Right: Central sagittal and axial slices of the fused MRI-MPI data.

This approach can easily be adapted to different tracer concentrations by applying a threshold value relative to the maximum intensity in the dataset. In this work, we first used a phantom to perform the calibration measurement and to determine the threshold values in vitro. Here, we used a combination of different experimental settings using a gradiometric receive coil with a single receive channel ("1D") and a novel self-constructed coil with three orthogonal receive channels ("3D"). Experiments were performed using selection field gradients of 0.8 T/m or 2.0 T/m. In a second step, we employed a differently shaped phantom to validate our findings. Finally, we performed a retrograde cystography in which a rat bladder was filled with a SPIO solution to demonstrate the feasibility of volumetric real-time measurements in vivo.

II Material and methods

For the in vitro measurements, two phantoms with voids mimicking the approximate size and shape of a filled urinary rat bladder (1 ellipsoidal, 1 pear-shaped) were designed in SolidWorks (Dassault Systems Ltd., France) and printed on a Form 2 STL printer (FormLabs, USA) using clear material. The ellipsoidal-shaped phantom was used for determining the reconstruction parameters and thresholds. It was filled with 780 µl of an aqueous Perimag-solution (micromod, Germany, iron concentration: $c_K = 3mM$). MPI measurements were performed using a preclinical system (Philips/Bruker, Germany) equipped with either the 1D or the 3D gradiometric receive coil for signal acquisition [1]. The magnetic gradient field had a gradient strengths of $G_x = G_y = -1T/m$ and $G_z = 2T/m$ or $G_x = G_y = -0.4T/m$ and $G_z = 0.8T/m$. The drive field amplitude was 12 mT for each acquisition. For the image reconstructions we used our open source reconstruction framework [2]. 46 frames ($\cong 1s^{-1}$) were averaged and the system function approach was applied by solving the least squares problem using the Kaczmarz algorithm with Tikhonov regularization. For each experimental setting, an appropriate set of reconstruction parameters (regularization parameter λ, SNR thresholding, no. of iteration steps) was determined. Using these data, the thresholds and the parameter p (cf. eq. (1)) were determined. To validate the parameters, real-time MPI measurements were performed with a pear-shaped phantom. 20 s after an MPI measurement was initialized, an injector pump (World Precision Instruments, USA) with a constant pump rate of 760 μl/min filled the phantom void with 760 μl of SPIO solutions at different concentrations ($c_s = 1mM, 2mM$) via a polyethylene tube (0.28 mm inner diam., Smiths Medical, USA). For the in vivo experiment, the urinary bladder of an anesthetized, female Wistar Unilever rat (HsdCpb:WU, Envigo; 12 weeks old) was catheterized [3] (BD Venflon Pro Safety, 22 GA, Becton, Dickinson and Company, USA) and filled manually with approximately 800 μl SPIO-solution ($c_K = 3mM$) during the acquisition of the MPI signal. Anatomical and volumetric references were obtained by MRI scans with T2w TSE sequences in sagittal and coronal orientation before and after the filling (7 T ClinScan, Bruker/Siemens, Germany).

III Results and discussion

In both volume approaches, we accounted for the noise floor by neglecting intensity values below an absolute value of $\sigma_I = 0.0005$ a.u. for measurements with $G_z = 0.8$ T/m and $\sigma_I = 0.0013$ a.u. for $G_z = 2.0$ T/m. The noise level was determined manually. By analyzing central intensity profiles and the volumes obtained for varying σ_T, the relative thresholds for V_T were chosen to be $\sigma_T = 0.28$ for $G_z = 0.8$ T/m and $\sigma_T = 0.30$ for $G_z = 2.0$ T/m. The resulting volumes V_I and V_T of the in vitro experiments as well as images of central xz- and yz-planes through the reconstructed image sets are shown in Fig. 1.

For V_T, the end volumes were determined with ab-

solute deviations of less than 41 μl (5 %). These lie well within the uncertainty range ΔV_T of -8 % and +20 % (estimated by applying σ_T to an ellipsoidal simulation). The dynamic range in which V_T is represented adequately is broader at higher gradient strength. At $G_x = 0.8$ T/m the method fails for $V_T < 300$ μl, where the SNR is probably too low for a sufficient volume reconstruction. For the intensity method, V_I could be represented with high precision showing deviations of less than 30 μl over the entire range in two cases. In the experiment using the 3D-coil, the final volume was underestimated by 108 μl (14 %). This may be explained by concentration deviations or degradation of the SPIO solution since, in contrast to the other experiments, the calibration and the dynamic measurement were not performed within one week. In terms of image quality, the visual inspection proves that the images obtained with the 3D-coil are the best of the three settings compared here. The findings from the in vivo experiment (only carried out at $G_x = 0.8$ T/m) are similar. Here, both V_I (598 μl) and V_T (680 μl) result in volumes lower than the one determined by manual segmentation from the MRI scans (811 $\pm$ 30 μl). An obvious problem here is that for V_I, we need to know the exact SPIO concentration. However, as inside the bladder, the tracer is mixed with urine, the effective concentration is decreased. By assuming a uniform mixture of residual urine and SPIOs, the volume representation is more precise (879 μl, cf. Fig. 2) but exceeds the true volume, indicating that the true concentration lies between both extremes. However, we also found that the intensity approach may fail for reconstructions that are not optimized for their visual appearance – implying that it is vulnerable to subtle changes in the experiment and the analysis.

IV Conclusions

We demonstrated MPI's potential for volumetric real-time measurements and showed that the deviation from the true volume can be determined within an uncertainty of 10 % with the threshold approach. If the exact concentration of the sample solution is known, the intensity approach may achieve even better results. This method is susceptible to experimental conditions and reconstruction parameters. With regard to our clinical motivation, our in vivo experiment represents the first step towards MPI-based retrograde cystourethrography.

Acknowledgments

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Author's Statement

The authors declare no conflict of interest. Ethical approval: The research related to animal use complies with all the relevant regulations and institutional policies and has been approved by local animal care committees (Behörde für Gesundheit und Verbraucherschutz, Hansestadt Hamburg, No. 107/16).

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