Fast 3D tracking of 19F labeled small capsules for combined morphology and real-time flow studies in the gastrointestinal tract

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Introduction: The gastrointestinal (GI) tract is a large, complex three dimensional organ with non-uniform peristaltic motion. Shape, transit and function are difficult to image by conventional anatomical and dynamic MR imaging. This holds in particular for the small bowel due to its complex structure and motility. A new approach in mapping GI structure, introduced by Schwarz et al[1], is to follow a fluorine labeled capsule through the intestine by means of 19F NMR. The background fluorine signal from the human body is virtually zero, yielding a high contrast to noise ratio of the exogenously introduced capsule. The collected 3D data might eventually be used in combination with interleaved conventional 1H MRI and segmentation methods to generate a high-resolution 3D anatomical model of the entire GI tract. At the same time, real-time tracking of capsules might provide additional physiological information such as flow quantification. To allow for this, the size of the capsules should be minimized in order to truly describe the passage of food through the GI tract. Additionally, the fluorine containing substance has to be non-toxic and the carrier system should not interact with the human body. Therefore, in this study we discuss the use of small-sized capsules containing Perfluoro-15-crown-5-ether (15C5) and Hexafluorobenzene (HFB) for real-time projection sequences to map structural and functional information in the GI tract.

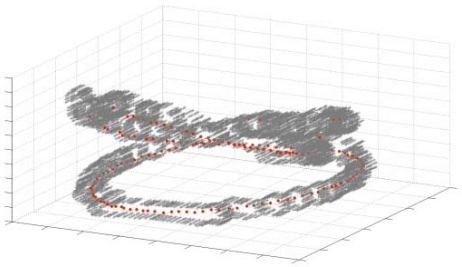

Figure 1 Phantom 1 with 3D capsule coordinates

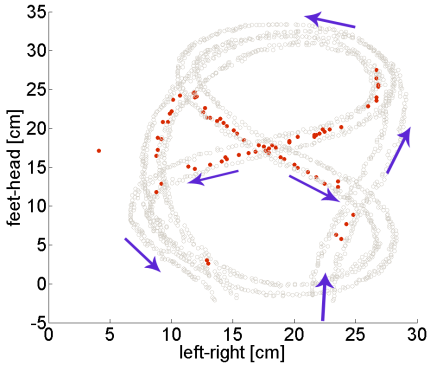

Figure 2 Phantom 2 with capsule coordinates

Methods and Materials: *Data acquisition:* All experiments were performed on a 3T whole-body Achieva MR system (Philips Healthcare, Best, The Netherlands). For 19F imaging, a single-loop transceiver coil (14*21 cm^2) developed in-house and a commercial Helmholtz coil (PulseTeq Ltd, UK) with 22cm diameter were used. A modified balanced FFE sequence with 3 stacks for three orthogonal projections was performed with phase encoding gradients switched off (FOV 20*20cm^2, slice thickness 15cm, NSA 30, scan percentage 1.14% or FOV: 35*35cm^2, slice thickness: 30cm, NSA 16, scan percentage 1.14%). Spatial resolution was 2.3 mm or 1.99 mm and temporal resolution 0.252s or 0.192s, respectively. The flip angle was adjusted to maximize signal. The center frequencies were tuned to the 15C5 and HFB resonances. *Data processing:* The maximum intensity in each projection scan was extracted to localize the capsules. False coordinates were rejected if the signal was below 11% of the maximum signal intensity or below an SNR of 5 and if the calculated velocity was unrealistic (>15cm/s). In case of concurrent tracking of two capsules the starting coordinates were selected manually, based on the time-course for each coordinate, Figure 3. *Phantom experiments:* A cylindrically shaped glass container with 19cm diameter was used (phantom 1). The container was filled with Agar and a PVC tube with 2 turns was immersed. A second phantom mimicking the abdomen with a cubic shape (25*13*40cm^3) was built in addition (phantom 2). This phantom was filled with distilled water and TX151 and a 2m long small intestinal phantom tube with 15mm inner diameter was fixed. Both phantoms were placed in the center of the coils. Water was thickened with Polyacryl Acid (PA) and pumped through the tubes with velocities < 10cm/s simulating expected gastric flow conditions[2]. Different capsules were tested: For the small phantom, tracking of one and two in-house produced cylindrical PMMA capsules of 4mm length and 4mm diameter, containing a hollow sphere of 3mm diameter, filled with 15C5 (99%, Exfluor Research, USA) and sealed with Dichloromethane and Parafilm was performed. For the large phantom, HFB (99%, Apollo Scientific Ltd, UK) was filled in capsules of volume 0.5ml, 0.2ml, 0.05ml and 0.01ml. Additionally, the use of different HFB volumes and lowered spatial resolution for increased tracking efficiency was tested: HFB fluids were positioned in phantom 2 in the centre of the coil sensitivity. Using the above described tracking sequence for HFB, the SNRs of the extracted coordinates for the different stacks were determined.

Results: 3D coordinates were correctly identified. Figure 1 and Figure 2 show the overlays of tracked 3D coordinates of the capsules (marked red) and segmented 3D plots of the tubes for phantom 1 (15C5) and phantom 2 (0.5ml HFB) with the flow direction being indicated by arrows. For the first phantom, coordinates could be tracked along the lower loop. Tracking efficiency decreased with increasing height and distance from the center, as expected. Tracking of two 15C5 capsules correctly identified the two separate capsule trajectories. Figure 3 shows an exemplary time course of two capsules in one dimension. For the 0.5ml HFB capsule in phantom 2, one coordinate was determined wrong. Figure 2 shows clearly an area of high coil sensitivity of roughly 15*15cm^2. Outside this high sensitivity field tracking was not feasible using the Helmholtz mode coil setup. For 0.2ml HFB, the 3D trajectory of the capsule in the sensitive volume could still successfully be generated. For 0.05ml HFB, the SNR was too small and no coordinate could be extracted. Measuring different volumes of HFB in the center of the coil sensitivity field yielded SNRs of 10.1, 9.5 and 6.9 (stacks 1,2,3) for 0.05ml volume HFB. Increasing the voxel size in encoding direction from 2mm to 4mm resulted in increased SNRs for the 3 stacks: 11.4, 10.3, 10.2. The coordinate of the 0.01ml HFB volume was not detectable.

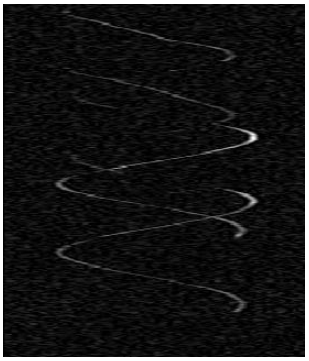

Figure 3 1D tracking of two capsules

Discussion: Real-time tracking of small-sized capsules in small and large phantoms is possible using the proposed protocol. Tracking of one or more small capsules in vivo bears potential for gaining structural and functional information at the same time and potentially determining abnormal gastric function in vivo. Both 15C5 and HFB bear potential for in vivo capsule tracking. Concurrent tracking of several capsules is possible, however delineation of the capsules gets more sophisticated with more capsules and the use of automatic trace detection techniques like active contours should be studied. Lowering the spatial resolution allows to track even smaller capsules with a lower limit being 0.01ml HFB. The coverage volume of the Helmholtz coil pair for in vivo measurements has to be carefully taken into account; however, the described sensitivity is expected to be sufficient for tracking capsules through the stomach and parts of the small intestine. For an increased sensitivity area the use of coils in quadrature mode should be examined.

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References: [1] Schwarz et al. MRM 48 :255-61 (2002) ; [2] Pal et al. Proc.R.Sc.Lond.B 271:2587-94 (2004)