A Transcatheter MR-guided Fiber Optical Confocal Microscopy System

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Objective: Molecular imaging with MRI is gaining momentum due to the rapidly increasing understanding of molecular processes. One way of approaching this challenging field has been to combine modalities in order to use strengths of different modalities. Optical fibre-based confocal microscopic fluorescence imaging has a high specificity when used in combination with targeted contrast agents as well as extremely high resolution [1,2]. Problems caused by the limited penetration depths for optical signals in biological tissue are avoided by the localized, direct-contact imaging approach. However, the optical microscopy technique can be difficult to apply in vivo without additional guidance [3].

MRI has the capability of generating excellent anatomical images that can be used for both tissue characterization as well as guidance in an interventional setting without the need for radiation exposure. MRI currently has lower sensitivity in terms of targeted molecular agents [4], making true imaging of molecular processes difficult. In this work, we demonstrate a multi-modality imaging system that combines the strengths of MRI for imaging and catheter guidance, with a fiber optic confocal microscopy catheter (Cellvizio, Mauna Kea Technologies, Paris, France) for profiling of optically active targeted markers ("fingerprinting"). The system is demonstrated in a simulated vascular setting with tissues and agar gels imaged optically with the use of targeted agents after active guidance with real-time MRI.

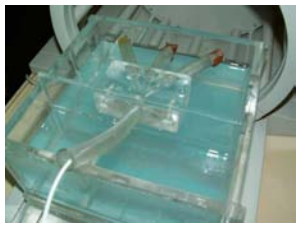

Fig. 1a

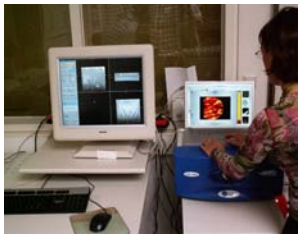

Fig. 1c

Material and Methods: MRI: All imaging was performed on a 1.5T Achieva system (Philips Medical Systems, Best, The Netherlands) using a standard head coil. A vascular phantom (Fig 1a) composed of an entry port with a three-way branch was imaged while submerged in a $CuSO_4$ doped solution. An RF-safe active tracking catheter [5] was steered through the three different pathways in the vascular phantom under MR-guidance. A $CuSO_4$-agarose gel phantom (T_1~500ms, T_2~3-4ms) doped with FITC (fluorescein isothiocyanate, Vector Laboratories, Burlingame, CA, 4.3 mmol dilution) was placed at the end of one plastic tube vessel. The gel was used to mimic an MR-visible tissue labelled with an unspecific optical agent. The other two vessels contained pieces of muscle tissue from a chicken. One piece was bathed in FITC-Lectin (Vector Laboratories, Burlingame, CA, 3.3 mmol dilution) for 5-10min. This targeted agent highlights the underlying vasculature (capillary network) of the tissue [6,7].

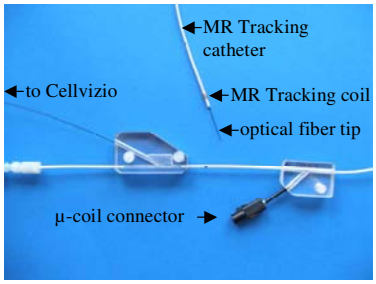

Fig. 1b

MR imaging was demonstrated in two different modes. In one mode, both, images and catheter position were refreshed in real time, while, in the second mode, a roadmap image was acquired, and the catheter position was detected in real time. Image refresh rates were 3.2 fps (256mm FOV, 1mm^2 resolution, TR = 4.7ms, TE = 2.1ms, $\alpha = 30°$), while the catheter position was updated every 200ms. Optical imaging was performed with a fiber-based confocal microscope (Cellvizio, Mauna Kea Technologies (MKT), Paris France) and a 6m long probe (Proflex S300, MKT, Paris France). The fiber optic probe is composed of a series of 10000 optical fibers that are used to obtain an imaging resolution of 5µm in the lateral and 15µm in axial direction and a FOV of 300µm at a frame rate of 12 fps [2]. The miniaturized fiber optic probe (outer ∅400 µm) was introduced through a catheter sheath of a 6F catheter equipped with an active tracking coil (Fig 1b). An RF-safe transmission line for tracking signal readout was used to avoid RF heating of the catheter tip [5]. The tip of the fiber optic probe was manually pushed out through the catheter when approaching a sample.

Results and Discussion: In Fig 2a, a sample frame from a real-time MRI movie demonstrates clear visualization of the trifurcation of the simulated vessel phantom. The catheter position is automatically marked by the scanner with a '+' sign. Optical images acquired simultaneously show direct correspondence to the imaged sample tissues. A sample image from the FITC-doped agar gel can be seen in Fig 2b. As expected, there is no defined structure in the gel, though a bright signal was obtained. Fig 2c demonstrates a sample image obtained from the FITC-Lectin labelled chicken. The capillary network is clearly visible. No signal was obtained from the unlabelled chicken (results not shown).

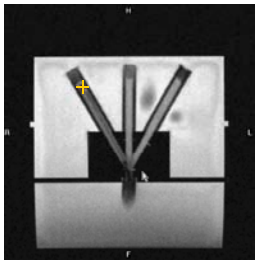

Fig. 2a

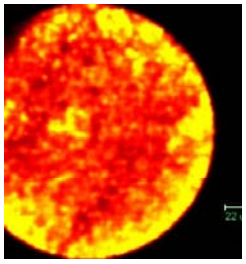

Fig. 2b

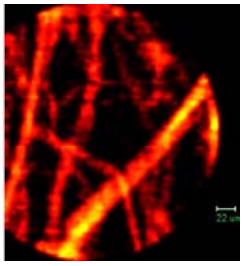

Fig. 2c

Conclusion and Outlook: As molecular imaging advances as a field of research, more robust combinations of different imaging modalities will be possible. Here we demonstrate the use of MR, a modality with a resolution of ~1mm, used in anatomical imaging at an organ or tissue level, in combination with a fibre-based confocal microscopy technique offering high resolution, sensitivity and selectivity. These results demonstrate a possible scenario for the diagnosis and treatment of atherosclerotic lesions with MR, relying on the highly specific optical imaging component to "fingerprint" suspicious lesions and even target them for localized therapy delivery.

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