Fully-Integrated MR–Optical Imaging Concept for Pre-Clinical Applications

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Objective
We propose a method for single-procedural integrated three-dimensional time-resolved non-contact optical (bioluminescence/fluorescence) and magnetic resonance small animal imaging.

Background
Intrinsically fused anatomical (MRI) and molecular (optical) imaging through simultaneous detection of in vivo distributions of fluorescent or bioluminescent probes and magnetic resonance signals is of high desire. While integrated approaches were proposed recently for MRI-PET [1], MRI-optical imaging has only been accomplished so far through sequential imaging [2], which is problematic due to animal/organ movement, co-registration, and kinetics recovery. Another approach employs fiber-conjoint optical detectors where the photon sensor is placed outside the MR bore and the fiber tips are in direct contact with the imaged object [3]. This inevitably limits the number of applications and yields insufficient spatial resolution for two-dimensional imaging.

Methods
To completely avoid these limitations, a novel fully MR-compatible optical detector has been developed. It is made of a rectangular optical sensor (25 mm×50 mm sensor size with a 512×1024 silicon photodiode matrix at 48 µm pixel pitch), a microlens array for field-of-view definition (55×105 plano-convex lens matrix with 480 µm lens diameter and pitch, 2.2 mm focal plane distance at which the sensor is aligned), and a septum mask (55×105 borehole aluminum matrix with 400 µm hole diameter, 480 µm pitch, and 2.1 mm thickness), positioned between the sensor and the microlens array. The septum mask suppresses cross-talk between the pixels and is additionally used for RF shielding. The entire detector, depicted in Fig. 1, possesses an effective thickness of less than 5 mm. A separate detector electronics unit and the photon sensor are completely RF-shielded. In the electronics unit the sensor signals are transformed into a USB-compliant signal stream and transmitted through an optical fiber connection to an external data and control PC. As pictured in Fig. 2, one or several such photon detectors are mounted on a common gantry which also has a mounting support for a Helmholtz coil. The Helmholtz coils used in this proof-of-concept study have diameters of 17 cm each and are distanced 15 cm. For dual-modality imaging the entire setup was placed in a 1.5 Tesla whole body MR system (Magnetom Symphony, Siemens, Erlangen, Germany). To study the mutual compatibilities of the optical and MR setups, 3D FLASH images (flip angle: 30 °, TR = 26.1 ms, TE = 8.2 ms, bandwidth: 40 Hz/pixel) of a Derenzo phantom (Ø: 32 mm, plexi glass rods ranging in diameter from 1.0 mm to 2.0 mm in 0.2 mm steps) filled with a 1/100 Gd-DTPA/H_2O solution were acquired together with optical images.

Results
In the optical images no artifacts or nor interferences caused neither by the magnet field nor by high frequency components were seen. To illustrate the performance of the optical detector, planar projection data for assessment of intrinsic spatial resolution versus object-detector distance is shown in Fig. 3. Within the variance of the photon distribution results are identical for the optical detector inside or outside the MR system. In the MR images only minor susceptibility and eddy-current related artifacts were seen. The transverse partitions of the 3D data set, Fig. 4, acquired with and without optical detector in operation exhibit similar SNR and image resolution, and no visible RF artifacts.

Discussion
We present a blueprint of a novel fully integrated MR-optical imaging approach, the impact of which rivals that of the MRI-PET concept for small animal applications. While using a Helmholtz-coil for proof-of-concept and relying so far on phantom experimental measurement due to the novelty of this approach, small animal studies are being under preparation. Because optical imaging in vivo – while still in the early stages of laboratory use – possesses a number of potential advantages over PET (less costly, advanced probes, no radiation) it might become the preferred method of choice for small animal pre-clinical imaging. As the very same optical detector is also compatible with PET imaging [4], the development and use of generalized multi-modal reporter probes becomes now feasible, hence fostering molecular target translational research.

References
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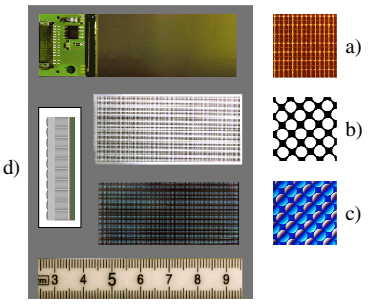

Fig. 1 *Elements of the optical detector: a) CMOS sensor, b) septum mask, c) MLA (right-hand-side images are regional magnifications of the corresponding images to the left, respectively); d) Cross-sectional detector rendering (not to scale).*

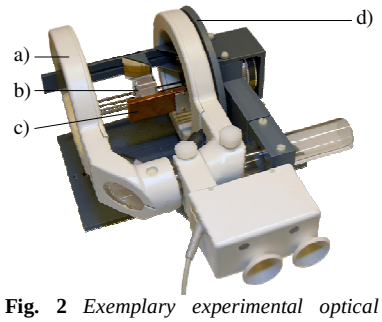

Fig. 2 *Exemplary experimental optical detector / Helmholtz coil unit: a) coil, b) imaged object, c) optical detector as shown in Fig. 1, d) rotatable gantry. This setup is put into a light-proof enclosure and placed into the MRI bore.*

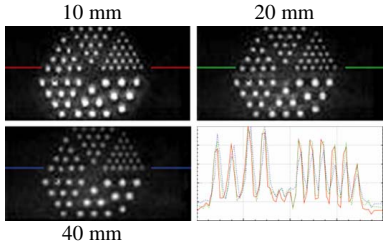

Fig. 3 *Optical intrinsic spatial resolution (regardless of insertion into MRI) versus object-detector distance using a Derenzo-like planar pattern of circles (TA = 1.0 s).*

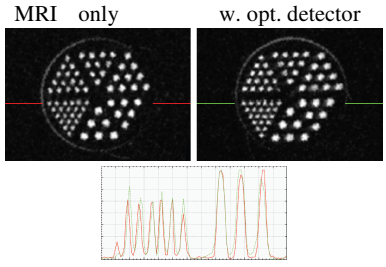

Fig. 4 *MR images and profiles of a 3.2 mm Ø Derenzo phantom experiment without (l) and with (r) optical setup inserted.*