A fiber-based optical excitation-emission fluorescence spectrometer for MR-guided in vivo tissue characterization

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Introduction: Excitation emission spectroscopy (EES) has been used in the past to characterize many different types of tissue [1-3]. This technique involves the use of multiple excitation wavelengths with a complete optical spectrum being sampled for each, yielding an excitation-emission matrix (EEM). Using EES it is possible to determine the presence of more than one optical contrast agent since these dyes tend to have characteristic spectra that can be separated [4]. Furthermore, the extra information contained in the EEM can be used to determine relative fluorescent dye concentrations, if background autofluorescence is either subtracted or previously characterized. In this work, we present a new fiber-based EE spectrometer intended for interventional use under guidance with MRI. We demonstrate the spectrometer using a vascular phantom and real-time MR guidance with an in-room console.

Methods: EES The spectrometer (LaVision Biotec, GmbH, Bielefeld, Germany) has been previously described and characterized in [4] (Fig 1). Briefly, excitation is performed with a high pressure Xenon lamp (300W, 280-1100nm) in combination with a fast filter wheel equipped with six customizable excitation bandpass filters. The filters were chosen to span most of the visible light spectrum and a portion of the near infrared spectrum. Light is fed into a **6.0m long** fiber optic cable with outer diameter of 720µm and inner core diameter of 600µm. For interstitial applications, the probe collects light from an area of ~1.0mm^2 tip and to a depth of approximately 6mm. Fibers intended for intravascular applications are capped with a 500µm-wide prism to allow "sideways" measurements [4]. Fluorescence returning from the sample is detected with a -60˚C cooled, back-illuminated CCD camera providing an effective spectral resolution of 5nm. Every rotation of the filter wheel produces one EEM, a plot excitation wavelength vs emission wavelength with optical signal intensity represented with color, (Fig 3) and every individual spectrum in the EEM takes ~1ms to acquire.

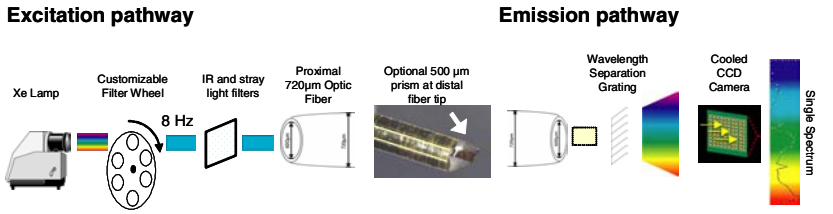

Figure 1: Pictorial schematic of the excitation emission pathways of the optical spectrometer. The fiber tip is optionally capped with a prism for intravascular applications (white arrow). The system utilizes a wide-band Xe lamp with a rotating filter wheel to select up to 6 different excitation wavelengths. After filtering, an optical fiber is used to both excite and collect the fluorescent light. A cooled CCD is used to measure light intensity with minimal noise.

Methods: MRI All imaging took place on a 3T Achieva (Philips Medical Systems, Best, The Netherlands). The optical fiber was attached to an active tracking catheter which permits interactive tracking as well as real-time update of the slice containing the catheter tip. To demonstrate the EES's ability to perform with MR guidance, a vascular phantom was used containing three different combinations of optical contrast agent-doped agar gels (Fig 2): (1) 5.0mM Rho(damine), (2) 3.3mM Rho+3.4mM Ox(azine), (3) 3.3mM Rho+3/4mM Ox+3.1mM HITC Iodide in 1% Agar (dyes from Exciton, Dayton OH). The phantom was submerged in $CuS0_4$-doped water and imaged using standard surface coils (Flex-M). To facilitate MR guidance a KVM extender was used to place a keyboard and mouse within the scan room in combination with a projector and screen. Similarly, a second keyboard and mouse were placed beside the console for the EES (Fig 2).

Results: Figure 3 displays three separate EEMs along with the corresponding MR images obtained while tracking catheter position. The EE spectrometer was able to adequately characterize each gel. The dotted circles in Fig 3 represent the areas of the EEM where each dye is expected to have a signature. Note that though the Oxazine signature is not directly visible in the middle EEM, post-processing of the optical data can be performed to extract its relative concentration [4].

Conclusion: We have presented a fiber-based excitation-emission spectrometer specifically designed for MR guidance applicable in both interstitial and intravascular procedures. The 6.0m-long, 720µm-diameter fiber, optionally equipped with a 90° prism at the tip, fits into the lumen of a 4F diagnostic catheter. In this case, an active catheter was navigated to the point of interest for a successful in vitro optical measurement. This technology can be used complementarily with MRI in regard to spatial resolution and functional parameters that can be visualized. Optical fluorescence spectroscopy, as demonstrated here, could be used for the characterization of cancerous tissues [5] and atherosclerotic plaques [3]. Furthermore, other optical technologies such as polarized backscattering spectroscopy for multiparametric interrogation of neoplasia could be further developed for integration with MR guidance.

References: 1 Li, B et al. World J Gastroneterol 2005 **11**(25) :2931-3934. 2 JiJi, R et al. Analytica Chimica Acta 2004 **397:** 61-72. 3. Christov Am et al. Photochem and Photobio 2000 **72**(2): 242-252. 4 Krueger S, et al NIH Bench to Bedside Optical Imaging (abstract) Sept 2006. 5. Sokolov K, et al. Curr Op Chem Biol 2002 **6**: 651-658.

Figure 2: (a) Interactive setup for simultaneous control of the EES (left) and MRI (right). A projector also permitted control of the MR system from within the scan room. (b) Vascular phantom loaded with three differently-doped agar gels.

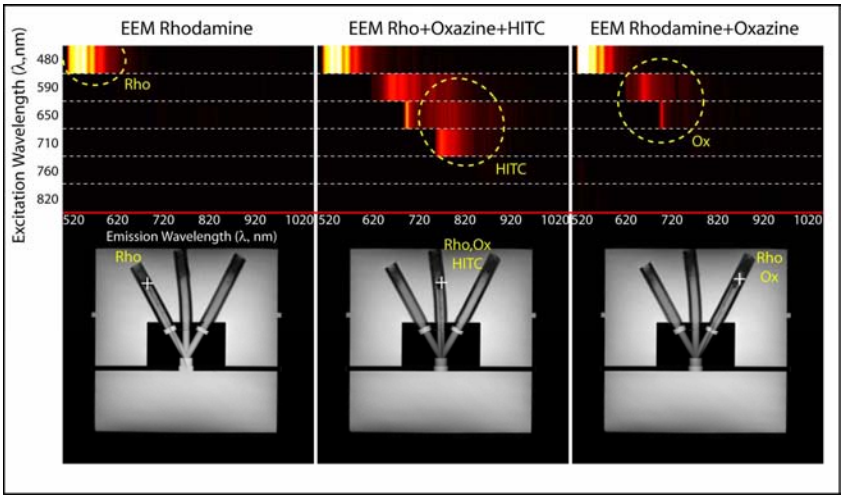

Figure 3: MR images of a vascular phantom with three branches each containing an agar gel doped with different mixtures of optical contrast agents. Excitation-emission matrices (top row) obtained from each of the gels. Plus signs estimate tracking coil position of active catheter at the time of EEM acquisition. Optical imaging tip was approximately 2.0mm in front of the tracking coil. Dotted circles mark the expected dye signatures according to reference spectra.