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Multispectral Fluorescence Imaging for Tumor Detection and Molecular Biology

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1. Introduction

Optical techniques, such as fluorescence imaging, are of particular interest for visualization of various superficially located epithelial tissues, such as the skin or the mucosa of interior hollow organs including easily reachable areas, such as the oral cavity or genital tract, besides the endoscopically accessible organs. The feature that fluorescence changes early in the development of certain types of malignant lesions and the utility for identification of premalignant lesions is of particular clinical interest. Obvious advantages with fluorescence detection are the minimally invasiveness and real-time aspect. In the clinic this means that LIF can be utilized interactively during the procedure and give up-dated information during the diagnostic procedure. Spectroscopic characterization is based on very early biochemical as well as morphological changes in the tissue. Multispectral fluorescence imaging can also be used for identification of early lesion and for delineating tumours based on exogenous fluorescent tumour markers.

For tumor detection located inside solid organs, such as liver, kidney and breast parenchyma, fluorescence techniques are not equally favorable and straight forward due to poor penetration and multiple scattering of light in tissue. A currently very interesting field of research for deep lesion characterization is based on fluorescence mediated tomography, of interest especially for longitudinal small animal investigations, where a fluorescence labeled lesion can be studied for treatment evaluation; as well as for studies of molecular interactions *in vivo*. Also fluorescence-based optical mammography is presently investigated by several groups. As the tomographic reconstruction is complex and relatively mathematically ill-conditioned, any additional knowledge is welcome to improve the reconstruction and can potentially speed it up and/or make it more robust. The data presented here suggest that multispectral detection can be used for both these purposes[1,2].

2. System outline

The multispectral detector unit consists of a CCD-camera (Hamamatsu C4742-80-12AG) for CW detection or an ICCD-camera (ANDOR Corp., DH734-18F-73) for gated detection, a liquid crystal tunable filter (Varispec LCTF VIS 20-35) adapted to a standard camera objective lens. The camera and the filter is controlled by a user-developed software making it possible to rapidly acquire images at a preset number of arbitrary wavelengths, with individual setting of the acquisition parameters. The excitation source used varied with the application, being a matrix of LEDs at 405 nm or a diode laser at 652 nm.

3. Multispectral imaging during clinically PDT of skin tumours

A clinically adapted setup of the multispectral system was used during photodynamic therapy of skin lesions. The photosensitizer (mTHPC) was applied topically onto skin lesions four hours prior to the treatment session. The fluorescence emission emitted from the lesions induced by continuous wave excitation light at 405 nm was monitored pre-treatment and post-treatment. Thus the spatial extent of the lesion and photobleaching of the photosensitiser during the treatment could be retrieved using image processing of the spectrally resolved images. The multispectral imaging system was in this way utilized to monitor the treatment progression yielding valuable information to clinicians.

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4. Experimental studies of fluorescence in small animal models and phantoms

Extensive studies have been conducted to evaluate the possibilities of multispectral imaging to localise small fluorescence volumes located deeply into tissues, without utilizing tomographic reconstruction algorithms as also shown in Refs 1-3. This method could thus be used as a quick way to obtain a rough estimation of the position of a lesion inside tissue. This estimate could, if necessary, be used in a subsequent tomographic analysis as an initial guess, thus speeding up and making this algorithm more robust. This has been demonstrated in modelling and experimental phantom measurements. In one series of experiment the concentration of mTHPC was investigated in nude mice following intravenous injection of mTHPC containing sensitizer. The fluorescence imaging system was used to acquire fluorescence images from mTHPC. The aims of these *in vivo* measurements were to evaluate the pharmacokinetics of mTHPC concentration following systemic administration. The experimental setup and example images are shown in figure 1.

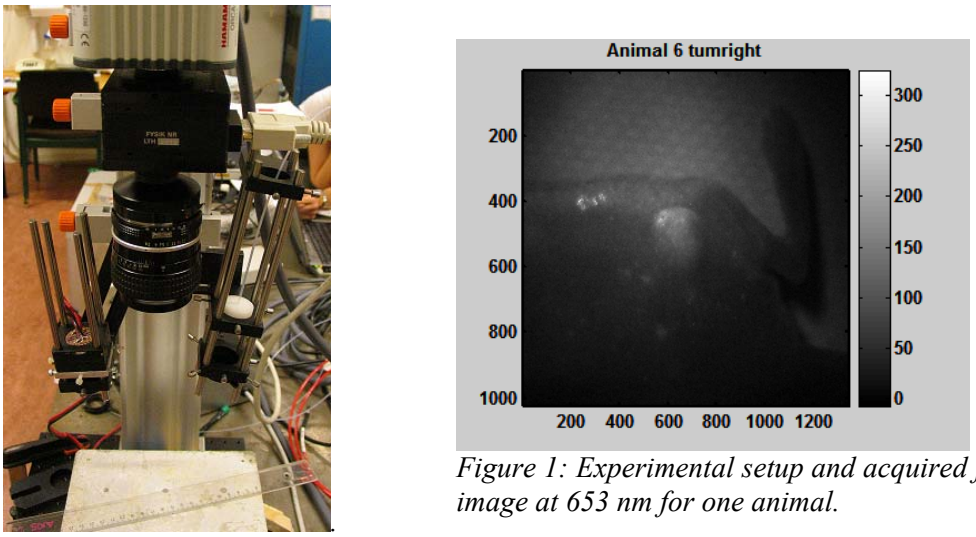

Figure 1: Experimental setup and acquired fluorescence image at 653 nm for one animal.

5. Conclusions

The use of a multispectral imaging system provides possibilities to map all information encoded in the spectral fingerprint of an exogenous or endogenous chromohpore in biological media. The spectral information has been used to demarcate the spatial extent of superficial skin tumours. Monitoring the fluorescence emitted from the photosensitzer over time yield information about the photodynamic treatment progression. The multispectral approach will also enable depth estimation of a lesion and thus allow quantitative measurements of a fluorophore as shown by the results presented.

6. Acknowledgements

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