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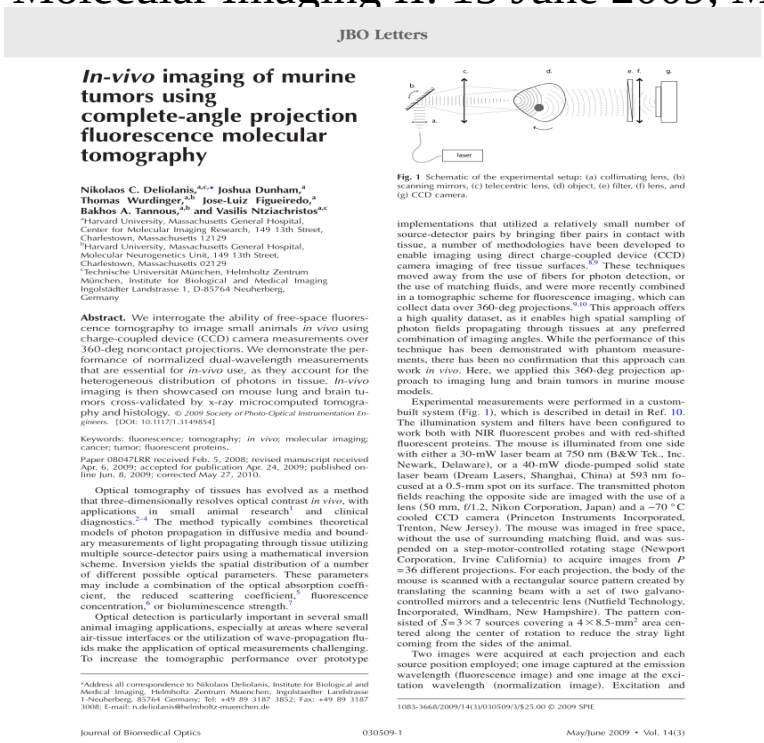

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***In-vivo* imaging of murine tumors using complete-angle projection fluorescence molecular tomography**

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Abstract. We interrogate the ability of free-space fluorescence tomography to image small animals *in vivo* using charge-coupled device (CCD) camera measurements over 360-deg noncontact projections. We demonstrate the performance of normalized dual-wavelength measurements that are essential for *in-vivo* use, as they account for the heterogeneous distribution of photons in tissue. *In-vivo* imaging is then showcased on mouse lung and brain tumors cross-validated by x-ray microcomputed tomography and histology. © *2009 Society of Photo-Optical Instrumentation Engineers.* [DOI: 10.1117/1.3149854]

Keywords: fluorescence; tomography; *in vivo*; molecular imaging; cancer; tumor; fluorescent proteins.

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Optical tomography of tissues has evolved as a method that three-dimensionally resolves optical contrast *in vivo*, with applications in small animal research[1] and clinical diagnostics.[2–4] The method typically combines theoretical models of photon propagation in diffusive media and boundary measurements of light propagating through tissue utilizing multiple source-detector pairs using a mathematical inversion scheme. Inversion yields the spatial distribution of a number of different possible optical parameters. These parameters may include a combination of the optical absorption coefficient, the reduced scattering coefficient,[5] fluorescence concentration,[6] or bioluminescence strength.[7]

Optical detection is particularly important in several small animal imaging applications, especially at areas where several air-tissue interfaces or the utilization of wave-propagation fluids make the application of optical measurements challenging. To increase the tomographic performance over prototype implementations that utilized a relatively small number of source-detector pairs by bringing fiber pairs in contact with tissue, a number of methodologies have been developed to enable imaging using direct charge-coupled device (CCD) camera imaging of free tissue surfaces.[8,9] These techniques moved away from the use of fibers for photon detection, or the use of matching fluids, and were more recently combined in a tomographic scheme for fluorescence imaging, which can collect data over 360-deg projections.[9,10] This approach offers a high quality dataset, as it enables high spatial sampling of photon fields propagating through tissues at any preferred combination of imaging angles. While the performance of this technique has been demonstrated with phantom measurements, there has been no confirmation that this approach can work *in vivo*. Here, we applied this 360-deg projection approach to imaging lung and brain tumors in murine mouse models.

Fig. 1 Schematic of the experimental setup: (a) collimating lens, (b) scanning mirrors, (c) telecentric lens, (d) object, (e) filter, (f) lens, and (g) CCD camera.

Experimental measurements were performed in a custom-built system (Fig. 1), which is described in detail in Ref. 10. The illumination system and filters have been configured to work both with NIR fluorescent probes and with red-shifted fluorescent proteins. The mouse is illuminated from one side with either a 30-mW laser beam at 750 nm (B&W Tek., Inc. Newark, Delaware), or a 40-mW diode-pumped solid state laser beam (Dream Lasers, Shanghai, China) at 593 nm focused at a 0.5-mm spot on its surface. The transmitted photon fields reaching the opposite side are imaged with the use of a lens (50 mm, f/1.2, Nikon Corporation, Japan) and a −70 °C cooled CCD camera (Princeton Instruments Incorporated, Trenton, New Jersey). The mouse was imaged in free space, without the use of surrounding matching fluid, and was suspended on a step-motor-controlled rotating stage (Newport Corporation, Irvine California) to acquire images from $P = 36$ different projections. For each projection, the body of the mouse is scanned with a rectangular source pattern created by translating the scanning beam with a set of two galvano-controlled mirrors and a telecentric lens (Nutfield Technology, Incorporated, Windham, New Hampshire). The pattern consisted of $S = 3 \times 7$ sources covering a $4 \times 8.5\text{-mm}^2$ area centered along the center of rotation to reduce the stray light coming from the sides of the animal.

Two images were acquired at each projection and each source position employed; one image captured at the emission wavelength (fluorescence image) and one image at the excitation wavelength (normalization image). Excitation and

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Hybrid Imaging: A Vital Tool for Molecular Imaging and Personalized Medicine Ludwig Maximilian University in Munich, Germany, the percentage of all PET and PET/CT Agency, Vienna, Austria, in February , on the basis of surveys from MR imaging with PET or SPECT have been installed to date (14,15) .Molecular imaging is non-invasive visualization and measurement of Cardiovascular Research, Volume 83, Issue 4, 1 September , Pages 24 June or sudden cardiac death),2 the identification of individuals who are at risk . of the different imaging modalities17 For example, studies on in vivo.6th International Conference on Computer Aided Surgery around the Head Contribution deadline: 15 October for paper Contribution deadline: 28 July for abstract, 12 January for paper . Munich, Germany . 2nd Thematic Conference on Computational Vision and Medical Image Processing.Siemens Novel Application Image of the Year (2nd Place). .. expression. Molecular Imaging and Biology, , 11, Cai W.Bidding ends 2 PM on June 26, , Richmond, Virginia, USA The 2nd PANIC (Practical Applications of NMR in Industry Conference) . July 27 - August 3, , Munich, Germany. February 15 - 20, Hilton Santa Fe/Historic Plaza Santa Fe, New MICAD - Molecular Imaging and Contrast Agent Database.The mission of the Laboratory for Preclinical Imaging and. Imaging Funds raised in (Million)*. *status June 0. 2. 4. 6. 8. responses; (ii) utilization of targeting moieties to specifi- cally and). NP- based drug-delivery systems based on chitosan, polyethyleneimine (PEI), liposomes, micelles NPs used in optical molecular imaging in cancer diagnosis , such as on June 15, Munich, Germany: Wiley-VCH Verlag.Photoacoustic molecular imaging of living subjects offers high spatial resolution at PE (/15//2/4/1 mol%) enclosing MnSO4 (mM) and DOX. The structure of for the development of AuNP-BBN; (ii) binding affinity and tumor specific avidity of Jeong1,3, Dong Soo Lee1,4, June-Key Chung1,2. 1Nuclear .Intra-operative fluorescence molecular imaging (IFMI) aims to focus Received: February 15, ; Accepted: May 14, ; Published: June 1, the first and the second surgery yielded positive margins (see Fig 1). .. Epub /09/ pmid; PubMed Central PMCID: PMCPmcMedisch;Medical; Radiology; Radiologie; Rontgen; Ziekenhuis; Hospital; , ESGAR 29th Annual Meeting and Postgraduate Course, Dublin, Ireland. 2nd World Congress on Radiology & Oncology, Dubai. .. Euroson School: International Course in Contrast Enhanced Ultrasound, Munich, Germany.Leisner. Date of birth: December 28, Citizenship: German Married since , three children (, ,) Faculties of Chemistry and Medicine, TU Munich (Director: Prof. [68Ga]NOTA-pentixafor for PET imaging of CXCR4 expression in , Sep pii: jnumedTypes of Medical Imaging Procedures; Concerns about Radiation . According to a March report by the National Council on .. 2 The average effective dose from background radiation is about 3 mSv per year. September 7 - 12, , Munich, Germany, IFMBE Proceedings, Vol. 15 July

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