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Rigid endomicroscopic system for multiphoton imaging and tissue ablation in the head and neck region

Chenting Lai^a, Bernhard Messerschmidt^{*a}, Karl Reichwald^a, Sven Flämig^a, Tino Eidam^b, Fabian Stutzki^b, Matteo Calvarese^c, Hyeonsoo Bae^c, Tobias Meyer-Zedler^{c,d}, Michael Schmitt^d, Herbert Gross^e, Franziska Hoffmann^f, Orlando Guntinas-Lichius^f, Juergen Popp^{c,d}

^aGRINTECH GmbH, Otto-Eppenstein-Str. 7, 07745 Jena, Germany; ^bActive Fiber Systems GmbH, Ernst-Ruska-Ring 17, 07745 Jena, Germany; ^cLeibniz Institute of Photonic Technology, Member of Leibniz Health Technologies, Member of the Leibniz Centre for Photonics in Infection Research (LPI), Albert-Einstein-Str. 9, 07745 Jena, Germany; ^dFriedrich Schiller University Jena, Institute of Physical Chemistry, Helmholtzweg 4, 07743 Jena, Germany; ^eFraunhofer Institute for Applied Optics and Precision Engineering, Albert-Einstein-Str. 7, 07745 Jena, Germany; ^fJena University Hospital, Department of Otorhinolaryngology, Am Klinikum 1, 07747 Jena, Germany

ABSTRACT

Here, we present a new handheld multiphoton endomicroscopic system for tumor diagnosis in the head and neck region. It consists of an approx. 25 cm long rigid endomicroscopic probe with two variants (0° and 45° bended tip), connected to a handheld scan-head. The system can achieve a field of view > 600 µm for coherent anti-Stokes Raman scattering (CARS) and other nonlinear imaging techniques by a non-descanned detection channel, and laser confocal imaging with indocyanine green (ICG) by a descanned detection channel. Furthermore, high-power femtosecond laser pulses can be transmitted through the system for precise tissue ablation without the risk of damaging the optical components.

Keywords: CARS and multiphoton endoscopy, non-linear endomicroscopy, fs laser ablation, indocyanine green imaging, laryngeal cancer

1. INTRODUCTION

Multiphoton imaging as a highly potential diagnostic technique for delineating tumor margins has advantages of high accuracy, label-free, and in-depth imaging.^{1, 2} Combining it with endomicroscopy can allow in-vivo and in-situ imaging identification of tumorous tissue, and is noninvasive compared to ex-vivo histopathology, which requires resection of suspicious areas from patients.³⁻⁶ Here, we present a new endomicroscopic system with a field of view (FOV) > 600 µm, aiming to achieve not only tumor diagnostics by multimodal imaging based on single photon or multiphoton absorption processes, but also tumor treatment by femtosecond laser surgery. The system consists of a scan-head and a long rigid endomicroscope. The scan-head with a Galvanometer scanner inside and dimensions of approx. 10 cm × 12 cm × 6 cm, contains a non-descanned detection channel for nonlinear imaging of two-photon fluorescence (TPEF), second harmonic generation (SHG), and coherent anti-Stokes Raman scattering (CARS), as well as a descanned detection channel for laser confocal imaging with indocyanine green (ICG). The endomicroscopic tube is about 25 cm long and 6 mm in diameter. An initial straight version was complemented by an angled version with a 45° bended tip providing better access to the relevant tissue areas in the head and neck region.

^{*}messerschmidt@grintech.de; phone +49 3641 55417-0; Grintech.de

2. RESULTS

The optical design of the endomicroscopic tube was optimized to generate all intermediate foci in air, applicable to transmit high-power femtosecond laser pulses for tissue ablation without damaging the optical components. The laser source is composed of two air-cooled turnkey fiber lasers that are optically coupled into a hollow-core transport fiber of 30 μm mode field diameter and an NA of 0.021 in 830 nm. The first laser, the imaging source, is based on a wavelength tunable picosecond oscillator. Its pulses are amplified and frequency converted in a photonic-crystal fiber via degenerated four-wave mixing.⁶ This compact all-fiber setup allows to generate pulses with tunable energy separation that are, additionally, temporally and spatially overlapped. The second laser, the ablation source, is based on a femtosecond oscillator that is amplified in a fiber based chirped-pulse amplification scheme. After compression, up to 10W of average power, 10 μJ of pulse energy and a variable pulse duration between 300fs and 10ps are available.

The endomicroscopic tube was initially tested by coupling in both pump (799 nm) and the Stokes (1031 nm) beam through a commercial confocal-microscope (SP 8 Falcon, Leica) with homebuilt CRS functionality to the endomicroscope. Multiphoton signals, i.e., CARS, SHG, and TPEF were epi-detected by three hybrid detectors embedded in the Leica microscope. The lateral resolution of the endomicroscope was shown to be less than one μm in the nonlinear imaging application. Recently, the endomicroscopic tube was connected to the described mobile scan head using the 2-axis-galvanometer scanner 6210H (Cambridge Technology) to provide a fiber-coupled stand-alone device, which can be freely positioned to access the tissue of interest. It allows simultaneous CARS, SHG and TPEF imaging and confocal indocyanine green (ICG) imaging through a confocal channel. Figure 1 (a) shows a trimodal CARS/TPFE/SHG image of unprocessed human head and neck tissue section recorded through the endomicroscopic tube.

High-energy laser pulses with a central wavelength of 1030 nm, repetition rate of 190 kHz and 360 fs in time duration were transmitted through the endomicroscope, and used to ablate a square area on a slice of chicken meat as shown in Fig. 1 (b). The square was ablated by exposing the tissue to 290nJ pulses at different focal planes. After 5 consecutive scans at the focus, the sample was moved towards the probe with steps of 4 μm , until reaching 12 μm in depth, to optimize the ablation volume.

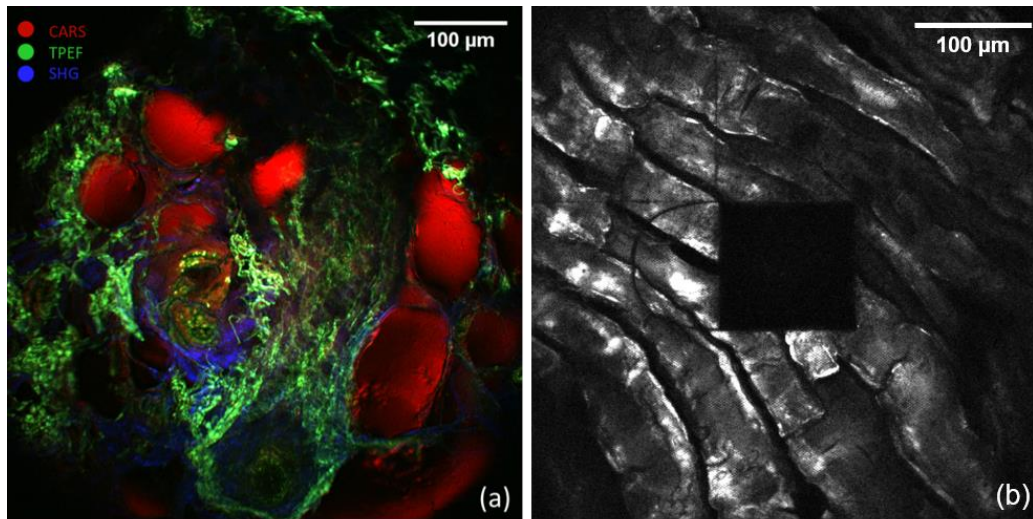


Figure 1. (a) Human tissue section from the head and neck region, imaged by multimodal nonlinear endomicroscope; red is CARS at 650 nm, green is TPEF, and blue is SHG, providing contrast for methylene groups abundant in lipids and protein, autofluorescence below 495 nm and collagen content at 514, 3 nm bandwidth, respectively; (b) square area ablated on a chicken meat slice with 290nJ pulses, 5 scans per focal plane at four different focal planes (0, -4, -8 and -12 μm into the sample). The figure is a CARS image at 2850 cm^{-1} .

3. ACKNOWLEDGEMENT

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