

STAND-ALONE, VERSATILELY APPLICABLE, FLEXIBLE, MINIMALLY INVASIVE ONE-PHOTON-EPIFLUORESCENCE ENDOMICROSCOPE

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Minimally invasive in-vivo imaging using one-photon-fluorescence endomicroscopy represents a challenging topic in medical and biomedical fields. Rigid and flexible endoscopes dominate the market to observe regions that are unreachable by optical microscopy. Rigid probes achieve small diameters and hence assure minimal destruction of tissue. However, their inflexibility forecloses access to hardly accessible regions. The flexible counterparts reach regions deep inside the living organism but suffer mostly from a large distal tip caused by the incorporation of complex scanning mechanisms.

We demonstrate a flexible stand-alone, minimally invasive endomicroscope with an outer diameter of less than 2.0 mm that enables surgeons or biologists to image hardly accessible regions in-vivo in epifluorescence mode. Based on previously published, highly promising design concepts [1], the device overcomes spatial limitations of state-of-the-art objectives by combining gradient index lenses and tiny spherical lenses with a side fire fiber and an extremely miniaturized chip-on-the-tip camera. A large field of view of around 200 μm in diameter and a numerical aperture of 0.7 enable a submicrometer resolution and hence guarantee the observation of subcellular structures, assure a bright and high-contrast image and enable the user to keep an overview during the intervention. The endoscope illuminates the region under examination at a wavelength below 490 nm utilizing a side-fire-fiber and captures the polychromatic image at video-rate above 510 nm.

The development can in the future support surgeons at endoscopic interventions or early cancer detection at hardly accessible areas or help biologists performing intravital microscopic research like long-term observations of brain regions in freely moving animals. Finally, in-vivo observations in genetically modified mice and bead measurements confirmed the expected functionality of the presented probe.

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References

[1] Matz, G., Messerschmidt, B., & Gross, H., „Design and evaluation of new color-corrected rigid endomicroscopic high NA GRIN-objectives with a sub-micron resolution and large field of view,” *Opt. Express* 24(10), 10987-11001 (2016).