3D printing of microlenses for aberration correction in GRIN microendoscopes

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Two-photon fluorescence microscopy provides high resolution information on the anatomy and function of cellular structures located several hundreds of microns deep within biological tissues. However, light scattering poses a fundamental limit to imaging of deeper areas (> 1.5 mm). Implantable microendoscopic probes based on graded index (GRIN) lenses are widely used tools to perform two-photon fluorescence microscopy in otherwise inaccessible regions[1], but the optical performances of with these probes are limited by intrinsic aberrations.

Here we report the development and application of a new approach to correct aberrations in GRIN endoscopes using microfabricated lenses. Corrective aspheric lenses were first designed using Zemax, with the goal to maximize the extent of the aberration free Field of View (FOV) of the microendoscope. We then fabricated polymer microlenses, according to previously determined sag, with high precision Direct Laser Writing based on two-photon polymerization [2]. The microlenses were finally aligned with the GRIN rods to form aberration-corrected microendoscopic probes. Optical characterization of the final probes showed an improvement of the effective FOV up to 9 folds when compared to the GRIN rods without corrective lenses. The method that we developed can be applied to several types of GRIN lenses that differ in length and diameter, allowing the functional investigation of biological tissues between 1 and 4 mm depth. As proof-of-principle, corrected microendoscopes were implanted in the brain of rodents *in vivo* and high resolution functional imaging on hundreds of hippocampal cells expressing activity-dependent fluorescent indicators was performed.

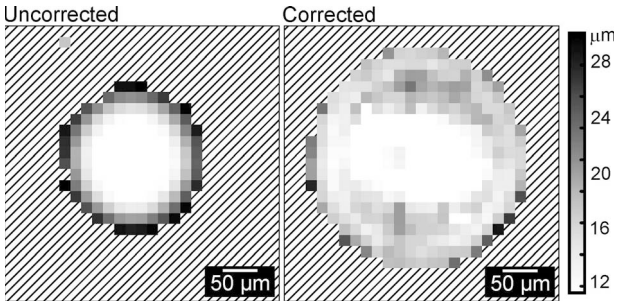

Fig. 1 Axial resolution as a function of position in the x,y plane for uncorrected (left) and corrected (right) endoscopic probes (probe length: 1.86 mm; probe diameter: 0.5 mm). The grey scale indicates axial resolution values in microns measured with the technique described in [3].

References

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