Microfabricated lenses for aberration correction in GRIN microendoscopes

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

Here we report the development and application of a new approach to correct aberrations in GRIN endoscopes using microfabricated polymer lenses. Corrective lenses were first designed using Zemax, then fabricated by two-photon polymerization [1] and finally optically aligned with the GRIN lenses to form aberration-corrected microendoscopic probes. 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.

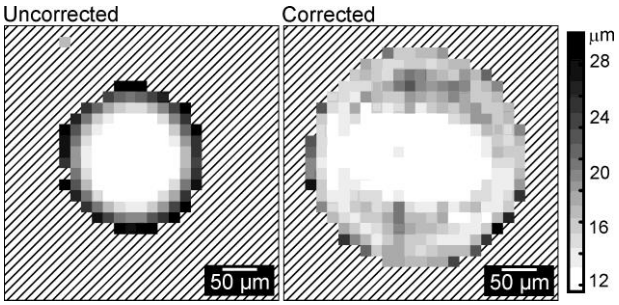

Figure 1: Axial resolution as a function of position in the x,y plane for uncorrected (left) and corrected (right) endoscopic probes (probe length: 1.86 mm; probe diameter: 0.5 mm). The grey scale indicates axial resolution values in microns measured with the technique described in [2].

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[2] Antonini, A., Liberale, C. & Fellin, T. Opt. Express, (2014).