Microfabricated lenses for aberration correction in GRIN microendoscopes

Andrea Antonini[1,2], Serena Bovetti[1], Claudio Moretti[1], Francesca Succol[1], Vijayakumar P. Rajamanickam[1,2,3], Carlo Liberale[2,3], Tommaso Fellin[1*]

[1]Neuroscience and Brain Technologies Department, Istituto Italiano di Tecnologia, Genova, Italy
[2]Nanostructures Department, Istituto Italiano di Tecnologia, Genova, Italy
[3]Biological and Environmental Sciences and Engineering Division (BESE), King Abdullah University of Science and Technology (KAUST), Thuwal 23955-6900, Saudi Arabia
E-Mail: **tommaso.fellin@iit.it**

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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 polymeric lenses. Corrective optical elements 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 aberration-corrected optical investigation of biological tissues at depth 1-4 mm. 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.

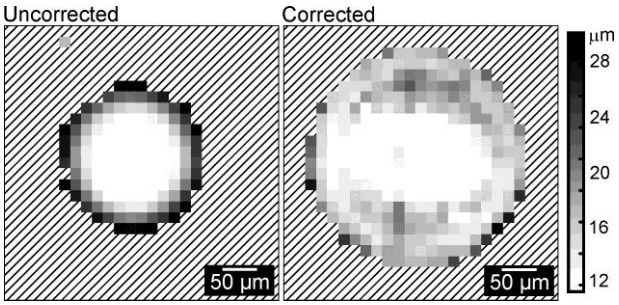

Figure 1: Axial resolution as a function of position in the x,y plane for uncorrected (left) and corrected (right) endoscopic probes (probe length: 1.86 mm; probe diameter: 0.5 mm). The grey scale indicates axial resolution values in microns measured with the technique described in [2].

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