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Title: Light-guided sectioning for precise in situ localization and tissue interface analysis for brain-implanted optical fibers and GRIN lenses

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Abstract: Optical implants to control and monitor neuronal activity in vivo have become foundational tools of neuroscience. Standard two-dimensional histology of the implant location, however, often suffers from distortion and loss during tissue processing. To address that, we developed a three-dimensional post hoc histology method called "light-guided sectioning" (LiGS), which preserves the tissue with its optical implant in place and allows staining and clearing of a volume up to 500 µm in depth. We demonstrate the use of LiGS to determine the precise location of an optical fiber relative to a deep brain target and to investigate the implant-tissue interface. We show accurate cell registration of ex vivo histology with single-cell, two-photon calcium imaging, obtained through gradient refractive index (GRIN) lenses, and identify subpopulations based on immunohistochemistry. LiGS provides spatial information in experimental paradigms that use optical fibers and GRIN lenses and could help increase reproducibility through identification of fiber-to-target localization and molecular profiling.