Nonlinear multimode fiber photonics for biomedical applications

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***Abstract*—Nonlinear propagation effects in multimode optical fiber-based endoscopic probes permit for a novel teragnostic approach combining real-time biopsy with cold-plasma treatment of cancer cells.**

***Index Terms*—nonlinear optics, optical fibers, endoscopy**

I. Summary

Cancer diagnosis and treatment in gastrointestinal (GI) endoscopy remain constrained by a disconnect between real-time visual inspection and pathological diagnosis. Despite major advances in endoscopic imaging, conclusive cancer diagnosis still relies on ex-vivo histopathology, requiring tissue excision, laboratory processing, and delayed reporting. This introduces significant time lags between detection and treatment and increases healthcare costs. These limitations are particularly critical in the management of early-stage GI cancers and dysplasia, where rapid, accurate decision-making can substantially improve clinical outcomes. Novel developments in the research on nonlinear effects in multimode optical fibers permit integrating real-time, label-free optical biopsy with immediate therapeutic intervention in a single endoscopic platform. By exploiting nonlinear light self-organization or spatial beam cleaning, one may overcome long-standing technical barriers that have prevented high-resolution, robust in-vivo optical biopsy from clinical translation [1]–[3].

We present a disruptive, physics-driven approach that enables stable multimodal nonlinear imaging (second harmonic generation, nonlinear fluorescence and M-CARS spectroscopy) through fibers suitable for clinical endoscopy. Our approach integrates cold atmospheric plasma (CAP) therapy directly into the same fiber-based endoscopic probe, enabling a seamless transition from detection to treatment. By combining optical biopsy with controlled plasma delivery, our theragnostic approach will allow clinicians to diagnose, treat, and monitor tissue response in real time during a single procedure.

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We integrate multimodal nonlinear imaging with cold atmospheric plasma generation at the fiber tip. Based on novel hollow-core, multimode, and hybrid optical fibers for broadband transmission, we exploit beam self-cleaning and plasma compatibility. By supercontinuum generation and nonlinear experiments, we validated the feasibility of multiplexed imaging and spectroscopy in an endoscopic configuration.

We developed a compact endoscopic head with piezoelectric fiber-tip scanning, enabling spiral scanning with micrometric resolution over sub-millimetric fields of view [4]. Plasma generation at the fiber tip was successfully demonstrated using both optoelectronic and electronic excitation, with controllable pulse parameters and reproducible operation. On the biological side, standardized 3D bioprinted spheroids and organoids (healthy and tumoral) were produced and integrated into the technological workflow. M-CARS hyperspectral microscopy experiments demonstrated the ability to discriminate healthy versus cancerous organoids with high accuracy using machine-learning analysis, identifying key diagnostic spectral regions.

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