Commentary: Following the (near-infrared) light? Don’t throw out your other navigational tools just yet…

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Ishiwata and colleagues at the University of Toronto report their preclinical experiences involving a novel application of intraoperative molecular imaging (IMI) to improve yield of transbronchial biopsy for peribronchial lung lesions. IMI is an emerging technique that involves systemic delivery of optical contrast agents that preferentially accumulate in tumors. During procedures, these agents emit light when stimulated with a known quantity of energy (in this case, near infrared light). IMI has been evaluated by thoracic surgeons for several applications both during open and video-assisted thoracoscopic surgery/robotic-assisted thoracoscopic surgery; however, this report provides some of the first data supporting a role during endoscopic procedures.

The authors utilized the recent Food and Drug Administration-approved drug pafolacianine, a folate analog that is linked to a near-infrared (NIR) fluorophore. Our group at Penn began working with this drug nearly a decade ago, and studies have demonstrated accumulation in >90% of all adenocarcinomas and 60% of squamous cell carcinomas. These results have been corroborated in multicenter Phase 2 (ClinicalTrials.gov identifier: NCT02872701) and Phase 3 (ClinicalTrials.gov identifier: NCT04241315) trials. These experiences have suggested clinical utility in localizing peripheral lesions, assessing margins during sublobar resection, and identifying additional lesions.

Although many have proposed applications of IMI during endoscopic procedures as a means to improve screening, enhance early diagnosis, and deliver intratumoral treatments; this technology has not yet been pursued. Ishiwata and colleagues begin to nicely address this gap and describe encouraging preclinical results using a technique they call “molecular-targeted NIR-guided bronchoscopy” for peribronchial tumor localization. They utilize pafolacianine as a study drug and an engineered, ultrathin composite optical fiber endoscope as an imaging device. Using pafolacianine-labeled xenografts, the authors found their device successful in localizing 100% of murine flank tumors and pseudo-orthotopic tumors in swine pulmonary explants. This well-performing prototype is among the first described for this application.

The presented proof-of-concept data are exciting; however, the performance of molecular-targeted NIR-guided bronchoscopy in human beings with lung cancers remains uncertain. As the authors astutely point out, their murine flank tumors and peribronchial tumors in swine pulmonary explants are quite different than the early-stage, subsolid lesions for which this technology may be most useful. Such adenocarcinoma spectrum lesions present unique challenges given heterogeneity in folate receptor expression patterns. From an engineering perspective, perhaps the most obvious hurdle for advancement involves creating miniaturized accessories that simultaneously allow white light, NIR light, and multiple light sensors to function within rigid and, even more challenging, flexible bronchoscopic platforms.

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Disclosures: The authors reported no conflicts of interest.

The Journal policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

Received for publication Oct 24, 2022; accepted for publication Oct 24, 2022; available ahead of print Oct 27, 2022.

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J Thorac Cardiovasc Surg 2023;165:252-3
0022-5223/$36.00
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https://doi.org/10.1016/j.jtcvs.2022.10.027
Notwithstanding uncertainties, molecular-targeted NIR-guided bronchoscopy has a unique opportunity to complement current navigational modalities. We envision this as a modality to not only improve diagnostic yield by providing real-time feedback at a cellular level, but also to potentially guide future therapies that can be delivered bronchoscopically. Success of this technology within the airways could be applied to other tumors that rely on endoscopy for screening and diagnosis. We believe that the future is bright for molecular-targeted NIR-guided bronchoscopy, and we are excited to see forthcoming human data that will provide a better understanding of how this approach performs in patients with lung cancer.

References