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EDITORIAL

Optical imaging in lung cancer—follow the light, towards molecular imaging–guided precision surgery

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Lung cancer is one of the most common and lethal neoplasms, representing the leading cause of cancer-related death [1]. Despite advancements in non-invasive approaches, thoracic surgery still remains the most effective therapeutic option. Nonetheless, the goal of a definitive resection is hampered by several issues, including the identification of small lesions and the complete excision of primary tumors, with local recurrence still representing the Achilles heel of cancer surgery [2]. Intraoperative molecular imaging definitely represents the most promising tool to overcome these hurdles, holding the ability to empower recognition of small malignancies undetectable on preoperatory imaging, localization of lesions amidst parenchymal distortions, and assessment of residual disease and surgical margins directly in the operatory room [3].

In this setting, various preoperative techniques have been described for lung cancer, aimed to improve image-guided localization of pulmonary nodules during surgery, such as computed tomography–guided modalities, preoperative placement of hook wires, or radiotracers [4]; however, despite supporting the localization of the primary lesion, these techniques demonstrated insufficient resolution to precisely determine resection margins. Therefore, in thoracic surgery, a real-time, safe, and reliable intraoperative imaging technique still represents a major unmet clinical need.

Optical imaging is particularly suited to overcome several of these issues, as the real-time visualization of underlying molecular phenomena provides to the surgical operators a precision, rapidity, and confidence unmatchable by other techniques.

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In this encouraging and evolving scenario, compelling challenges are yet to be solved as there is no clear consensus on the best tracer to be employed and on the cohort of patients who will derive the greatest clinical benefit from this technology.

Many fluorescent agents have been developed and tested in preclinical settings of lung diseases, although little in-human data are available.

Recently, pafolacianine (OTL38), a fluorescent imaging agent composed of a folate receptor-alpha (FRa)–targeting ligand conjugated to a fluorescent near-infrared (NIR) dye, has been tested in clinical trials for its ability to identify FRα-expressing tumor cells.

Pafolacianine has been approved by FDA in November 2021 as effective tool for detecting malignant lesions in patients with ovarian cancer; starting from March 2022, FDA also granted the approval for the use of OTL38 as imaging drug to identify lung lesions during surgery.

Recently, Azari et al. prospectively evaluated the possibility to preoperatively assess folate receptor density on bioptical specimen in order to predict intraoperative pafolacianine (OTL38) fluorescence [5]. The results regarding both the overall performance of the tracer and the predictive power of the preoperative receptor density evaluation are encouraging, although more data are needed to confirm these findings in larger cohort of patients. This approach is particularly interesting as it recognizes the limitations of currently available tracers—namely the lower sensitivity related to the possibility of cancer histotypes not expressing the specific target—and successfully employs a rational solution driven by the paradigms of precision and personalized medicine.

The same group provided significant contributions to the discipline during the last years, accruing valuable experience to guide future advancements and exploring different tracers even in multicentric protocols [6, 7].

Pafolacianine came forth as the most promising tracer, also thanks to its favorable wavelength [8], and their newest contribution is the last milestone in a thorough and compelling evaluation of this tool in clinical scenarios [9–11].

Research in the field is blooming worldwide, covering ground in many directions, with numerous promising drugs under development in the preclinical setting [12–15].

Optical imaging represents a luminous beacon of hope and promises to drive significant improvements in the surgical management of lung cancer. Moreover, the integration of technology, molecular imaging, and surgery by its nature encourages strong multidisciplinary collaborations between medical imaging and surgery: from the development of the sentinel lymph node technique onwards, a proven recipe for success and mutual enrichment, to the benefit of cancer patients. The scientific community of nuclear medicine should be embracing this opportunity to further broaden its focus towards molecular imaging on the whole, securing its place on the driver seat of this exciting novel approach that holds a bright future and promises to shed light on new paths in the surgical management of cancer patients.

From technological advancements to bedside, the future of precision surgery is here: follow the light, and keep your eyes open.

Declarations

Ethical approval Institutional Review Board approval was not required because the paper is an Editorial.

Informed consent Not applicable.

Conflict of interest The authors declare no competing interests.

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