HHS Public Access

Author manuscript

JAMA Surg. Author manuscript; available in PMC 2024 June 03.

Published in final edited form as:

JAMA Surg. 2022 May 01; 157(5): 458. doi:10.1001/jamasurg.2021.6908.

Comments on Intraoperative Molecular Imaging for Localizing Nonpalpable Tumors—Reply

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In Reply

We thank Lin et al and Goto for their interest in our article.[1] They bring up important critiques, and we appreciate the opportunity to discuss them further.

Lin and colleagues point out that our evaluation of existing methods of preoperative lesion localization, particularly hook-wire placement, is overstated. The purpose of our study was not to disparage existing techniques for lesion localization, but rather to present a new technology that offers surgeons another tool in their armamentarium.

In some cases, we believe that intraoperative molecular imaging (IMI) offers advantages over hook-wire placement. It does not suffer from tip sliding, which can falsely reassure surgeons that they have resected the lesion of interest. Furthermore, IMI is able to detect synchronous lesions that may be too small to detect even on fine-cut preoperative computed tomography scan. Hook-wire localization is restricted by the inherent resolution limits of computed tomography scan and may miss lesions that IMI can identify. We have previously reported the ability of IMI to localize subcentimeter synchronous lesions not identified on computed tomography scan.[2] Ultimately, a randomized trial comparing the 2 technologies will provide a definitive answer to these questions. Furthermore, the 2 technologies may be used together as complementary approaches to lesion localization.

Lastly, Lin and colleagues question the appropriateness of wedge resection in the patients in our study with poorly differentiated or invasive cancers. We regret that we were not more clear in our article that all lesions identified by IMI were able to be initially wedge resected for frozen section analysis. Subsequent decisions on the final extent of resection were guided by pathology analysis, tumor size, and degree of invasiveness.

Goto expresses concern with the specificity of the tracer (FA-S0456) used in our study based on folate receptor alpha (FRα) expression in normal lung epithelial cells. We agree that normal lung epithelial cells express FRα but wish to clarify that this expression is only on the apical surface of the cell, precluding contact with the systemic circulation.[3] Therefore, it is only tumor cells with diffuse cell membrane expression of FRα that are exposed to and take up FA-S0456. We hypothesize that the benign lesions in our study

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took up FA-S0456 via macrophages expressing FRβ that are known to populate areas of pathologic inflammation such as granulomas or necrotizing pneumonias.

We share Goto's optimism for the role of IMI in not only guiding resection of primary lesions, but also allowing intraoperative assessment of lymphatic metastasis. In our opinion, this is the next frontier of IMI, and ongoing efforts in our laboratory are aimed at this question in particular.

We again thank the authors for their important critiques of our article.

Acknowledgments

Conflict of Interest Disclosures:

Dr Kennedy reported grants from National Institutes of Health and American Philosophical Society Daland Fellowship in Clinical Investigation during the conduct of the study. No other disclosures were reported.

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