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Endobronchial Optical Coherence Tomography: Shining New Light on Diagnosing Usual Interstitial Pneumonitis?

To the Editor:

In 15–30% of patients with a fibrotic interstitial lung disease (ILD), tissue acquisition is indicated, as the diagnostic confidence based on clinical and radiological investigations does not justify a specific treatment allocation (1). However, surgical lung biopsy and transbronchial cryobiopsy are associated with considerable risks of morbidity and even mortality (2). Minimally invasive imaging techniques have the potential to obviate the need for tissue biopsy in at least a proportion of these patients (3).

Therefore, we are excited by the work of Nandy and colleagues and congratulate them on their work on endobronchial optical coherence tomography (EB-OCT) in fibrotic ILD (3). With histopathology of surgical lung biopsy as reference standard, EB-OCT convincingly distinguished usual interstitial pneumonitis (UIP) from non-UIP disease in patients with unclassifiable ILD. In addition, non-UIP ILD diagnoses were identified with EB-OCT with high concordance with histopathological diagnosis (3).

To fully appreciate the added value of EB-OCT to the current diagnostic workup (clinical evaluation, high-resolution computed tomography, and BAL), it is important to have additional insights in patient characteristics and selection. A description of the high-resolution computed tomography patterns and a clinical-radiological diagnosis, as assessed by a multidisciplinary discussion, in Table 3 would have been helpful. Can the authors provide more details on this aspect?

Our study group has EB-OCT experience from more than 50 patients, and we have learned that adequate and reproducible EB-OCT imaging can be challenging. First, subpleural probe placement is of key importance to differentiate between UIP and non-UIP disease. Nandy and colleagues report that the presence of pleural resistance confirmed subpleural positioning. In our experience, especially in patients with extensive fibrotic changes, it can be difficult to reach the subpleural space, and in general when the OCT probe hits a carina, this can resemble pleural resistance. Therefore, a validated method for correct EB-OCT probe positioning seems needed. We have noticed that in a subset of patients, we were able to visualize the pleura and/or thoracic wall and thereby confirmed subpleural placement of the EB-OCT probe (4). We question if this "subpleural sign" could be used for probe positioning. Second, in our experience, EB-OCT alveolar image quality improves when flushing with saline just before the OCT pullback; do the authors have a similar experience? Third, it is not clear whether the same airway segments were measured multiple times, and therefore image reproducibility is not addressed. Furthermore, can the authors comment on image interpretation: was it based on all cross-sectional images (1,340 images per pullback) or on the three-dimensional reconstructions of the entire pullback, or both? In this respect, what were the EB-OCT image interpretation training requirements?

For future direction, the authors postulate that EB-OCT, given the low-risk nature of the procedure, can be used for longitudinal measurements. Indeed, in addition to identification of EB-OCT patterns, quantifying the amount of fibrosis would be helpful to evaluate treatment response or disease progression. Polarization-sensitive OCT (PS-OCT) could provide the contrast to quantify fibrosis; this is currently being explored by our study group to strengthen the potential of EB-(PS)OCT in respiratory diseases (5, 6).

We warmly encourage further studies investigating the diagnostic potential of EB-(PS)OCT, with the aim of improving safe and minimally invasive diagnostics for the vulnerable population of patients with ILD. ■

Author disclosures are available with the text of this letter at www.atsjournals.org.

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Reply to Kalverda *et al.*

From the Authors:

We thank Kalverda and colleagues for their letter regarding our recently published paper (1), and we appreciate the opportunity to provide additional clarity on the points they raise about the work. Below we address the questions asked by Kalverda and colleagues.

This study was funded in part by the NIH (grant numbers K23HL132120, R01HL152075, and P41EB015903), an investigator-initiated study (IIS) grant from Boehringer Ingelheim Pharmaceuticals, Inc. (BIPI), and the LUNGevity Foundation. BIPI had no role in the design, analysis, or interpretation of the results of this study. Boehringer Ingelheim was given the opportunity to review the manuscript for medical and scientific accuracy as it relates to BIPI substances, as well as intellectual property considerations.

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Enrollment Criteria

Our primary objective was to conduct a blinded, prospective study to evaluate the diagnostic accuracy of endobronchial optical coherence tomography (EB-OCT) for microscopic diagnosis of interstitial lung disease (ILD) compared with concurrent surgical lung biopsy (SLB) and clinical follow-up diagnosis. Our inclusion criteria were *1*) age > 21 years; *2*) fibrotic ILD on the basis of high-resolution computed tomography (HRCT) with unclear diagnosis; *3*) SLB required for ILD diagnosis on the basis of the clinical decision of the treating pulmonologist, and *4*) ability to give informed consent. Therefore, in our patient cohort, there was no high-confidence clinical-radiologic diagnosis before SLB. Our institution does not routinely use BAL as part of the ILD diagnostic workup, which is consistent with the practice of many academic ILD centers in the United States. The clinical follow-up diagnosis for each patient was determined by the treating pulmonologist on the basis of clinical, HRCT, SLB, and serology data and was provided in Table 3 in our paper (1). Formal presentation in a multidisciplinary discussion conference was conducted after SLB as deemed necessary by the treating pulmonologist and was performed in ∼60% of the cases in our cohort.

EB-OCT Probe Placement in Subpleural Lung and Reproducibility

To reach the subpleural lung, the flexible EB-OCT catheter was advanced through the bronchoscope working channel and extended beyond the visualized region of the bronchoscope until resistance was met in the subpleural lung at each imaging site. This method for reaching the subpleural lung was developed and validated in our prior *ex vivo* studies of EB-OCT in whole explanted lungs, including lungs with end-stage ILD, using visual and tactile inspection to confirm subpleural catheter placement (2, 3). In the present *in vivo* study, fluoroscopy was performed in two subjects and also confirmed the subpleural location of the catheter in both cases (1). In this study, an individual with experience in EB-OCT interpretation was present during the procedure to confirm subpleural positioning of the EB-OCT catheter at the beginning of each scan and to ensure adequate data quality and sampling of anatomic sites for diagnosis. Occasionally, the catheter would hit a branchpoint, creating a sensation of resistance similar to that of the subpleural lung, but these instances were infrequent and readily recognizable during the intraprocedural adequacy assessment. This is reflected in our average time of 9.5 minutes per patient for EB-OCT imaging, which included the time needed for intraprocedural EB-OCT adequacy evaluation and instances requiring catheter repositioning. We did not perform repeat imaging in the same airway segment unless there was a need to reposition the catheter. We believe our ability to reach the correct anatomic location in the subpleural lung is reflected in our data, which demonstrated 100% sensitivity and specificity for histopathologic usual interstitial pneumonia (UIP) and strong agreement (weighted kappa = 0.87) with SLB for diagnosis of fibrotic ILD pattern.

We agree with Kalverda and colleagues that the described "subpleural sign" mentioned in their letter (4) is consistent with the appearance of pleura and chest wall tissues, which we have also seen in our EB-OCT imaging data. In our experience, we have found that the imaging angle of side-viewing EB-OCT catheters, such as the catheter used in our study, does not allow pleura and chest wall tissues to be within the imaging field of view in many anatomic locations within the lung (i.e., where the imaging beam is parallel to