Reply to Wand et al.: Role of Transbronchial Cryobiopsy in Interstitial Lung Diseases – An Ongoing Tale

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Reply to Wand *et al.*

From the Authors:

We read with interest the letter to the editor from Wand and colleagues, who highlighted some concerns about the findings in our recent article, which showed a poor concordance between lung histology from sequential transbronchial lung cryobiopsies (TBLC) and surgical lung biopsies (SLB) obtained prospectively from the same patient during the same surgical procedure.

We obviously agree with the authors regarding the critical importance of multidisciplinary assessments (MDAs) in the diagnostic evaluation of interstitial lung diseases (ILDs) (1, 2), despite the reported low agreement among MDAs for ILDs that are not idiopathic pulmonary fibrosis (3). However, the role of MDAs was not the main focus of our study. Our goal was to assess the concordance of pathological diagnoses *per se* obtained by two different procedures (TBLC and SLB) performed in the same patient, blinded to any clinical information—something that has never been done before. We do believe that our blinded histology approach was somewhat artificial, and we agree that it was outside the routine clinical workflow, as clearly stated in our article (1). However, we

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also believe that this was the only way to compare pathological outcomes from the two techniques while avoiding significant bias.

We had considered assessing the concordance between the blinded pathologist and the other two local pathologists but concluded that this was not an appropriate comparison because the methodologies used in these two contexts were different (e.g., blinded vs. nonblinded). In fact, the two nonblinded pathologists were not only informed about clinical and radiological information but were also "biased" by the fact that they were simultaneously assessing both TBLC and SLB for the same patient at the same time. Although the agreement level of 57.1% Wand and colleagues calculated from the provided data is correct, we considered this calculation problematic because the two approaches (blinded vs. nonblinded) cannot be directly compared, and we decided not to include it in our report. If anything, this would indicate that all pathologists involved held to a high diagnostic standard.

We also considered involving two or more blinded pathologists but, based on discussions with the statistician (N.M.), concluded that the addition of another blinded pathologist would have introduced more confusion than improvement in data readability. Indeed, the community should keep in mind that concordance among experts in this domain is traditionally fair to poor, and the cases involved are inherently difficult to diagnose.

Our study demonstrates that in several cases, TBLC alone would have led to a completely different diagnosis. One of these cases, chronic lymphocytic leukemia (at blinded TBLC) versus desquamative interstitial pneumonia (at SLB), can be discussed as an insightful example of poor concordance. Clearly, this case is related to a sampling issue and would likely have been sorted out in MDA discussions even with the TBLC alone (considering the patient's history of smoking and lymphoproliferative disease, among other factors).

The suggestion by Wand and colleagues to discuss either sampling technique in a separate MDA is interesting. We are planning to conduct such an analysis and will report our findings.

In conclusion, we definitely do not completely reject the role of TBLC in the assessment of ILDs. However, our findings suggest that for now, TBLC should not be considered interchangeable with SLB in the management of ILDs (1, 2). Although we all agree that we need further studies and data, we suggest that TBLC in patients with ILD should not be encouraged in routine clinical practice (4) and should only be performed in the setting of registered, ethically approved clinical trials involving clearly informed patients (5), or in patients who deliberately refuse or are not suitable for SLB. ■

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

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