methodology to obtain tissue for histopathology and new diagnostic paradigms such as the use of molecular profiling of transbronchial biopsy samples (5) and behavioral classifications (6, 7). As this study shows, we need to use a deliberative process when investigating novel approaches to improve our diagnostic methods.

While we await additional data, the current study should give clinicians pause before they consider further implementation of TBLC in ILD. Despite the frustration inherent in this approach, increasing diagnostic confidence, minimizing adverse outcomes, and lowering barriers against substantive progress will remain our community's common goals. ■

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Cryobiopsy for Diagnosis of Interstitial Lung Disease: Discussion from the University of Toronto Respirology Journal Club

To the Editor:

We had the pleasure of discussing Romagnoli and colleagues' recent publication, "Poor Concordance between Sequential Transbronchial Lung Cryobiopsy and Surgical Lung Biopsy in the Diagnosis of Diffuse Interstitial Lung Diseases" (1), at our Twitter-based journal club (@RespandSleepJC, #rsjc) on April 25, 2019. Although previous studies have demonstrated a diagnostic yield of transbronchial lung cryobiopsy (TBLC) for the diagnosis of interstitial lung disease (ILD) of 80% or higher (2), this study was the first of its kind to examine the concordance between TBLC and surgical lung biopsy (SLB) performed sequentially in the same patients. The results were disappointing, with histopathologic diagnoses from both biopsy techniques being concordant in only 8 of 21 cases. Our discussants raised several interesting points both in person and online.

Some of our participants expressed apprehension about the rapid uptake of TBLC despite insufficient evidence, noting that many may be confusing diagnostic yield with diagnostic accuracy. The fact that TBLC has essentially replaced SLB in the European IPF Registry since 2016 was cause for concern (3).

Other participants believed it was difficult to draw any conclusions from the trial, noting that it may have been underpowered to achieve its primary objective (4). Furthermore, many commented on the loss of external validity that comes with the use of a blinded pathologist providing a single preferred diagnosis. Agreement between blinded pathologists interpreting lung histopathology is known to be low (5) and not representative of real-world practice. Although it was not explicitly discussed in the article, it is noteworthy that diagnostic concordance between the routine pathology samples reported locally at each institution

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(presumably with access to clinical information as well as both TBLC and SLB specimens) and the final diagnosis made at the second multidisciplinary assessment (MDA2) occurred in 17 of 21 cases. This is better than the concordance observed between both blinded SLB and MDA2 (13/21 cases) and TBLC and MDA2 (10/21 cases). Although the additional tissue that local pathologists would have had may be responsible for this difference, we wondered if access to clinical information may have been the major driver.

Finally, if an MDA meeting is taken as the gold standard for ILD diagnosis, both blinded SLB and TBLC performed poorly, and the difference in concordance between pathology specimens and MDA2 (13/21 cases for SLB vs. 10/21 cases for TBLC) did not appear dramatic. Given the potential morbidity associated with either biopsy approach, many questioned whether lung biopsy of any kind truly leads to meaningful improvements in clinical outcomes in ILD (6, 7).

In conclusion, we commend the authors for their well-done study, and acknowledge our ongoing confusion about the utility of lung histology for ILD diagnosis. Despite the poor concordance between TBLC and SLB, we hope cryobiopsy remains an area of study, as this paper has not completely "cooled off" our interest in this new and less invasive diagnostic technique. ■

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Comparing Transbronchial Cryobiopsy and Surgical Biopsy in Idiopathic Pulmonary Fibrosis

To the Editor:

In 2018, the Fleischner Society (1) and American Thoracic Society/European Respiratory Society/Japanese Respiratory Society/Latin American Thoracic Association (2) guidelines for idiopathic pulmonary fibrosis were published. The American Thoracic Society/European Respiratory Society/Japanese Respiratory Society/Latin American Thoracic Association biopsy recommendations were made only for surgical lung biopsy (SLB), indicating that there was a lack of evidence to make a recommendation for or against performing transbronchial lung biopsy or transbronchial lung cryobiopsy (TBLC) (2).

Large studies evaluating TBLC have shown it to be an accurate and safer alternative to SLB (3). The concerns about the TBLC are related mostly to the substantial procedural variability among centers and the consequent variable diagnostic yields and complication rates (4).

Comparing two methods with a nonnegligible rate of complications in the same patient raises considerable ethical concerns about the possibility of duplicating the harms of each method without offering more benefit (5).

Romagnoli and colleagues (6) report the results of a prospective study designed to compare histopathological features in paired lung biopsy specimens from TBLC and SLB obtained sequentially from the same patient. The authors conclude that the tissue samples obtained for evaluation of interstitial lung disease demonstrated poor concordance, and that consequently, TBLC has not only lower sensitivity but also lower accuracy than SLB. However, some factors impose important limitations on the study.

The first factor is the high proportion of patients who were excluded by nonconsent. Among the initial 62 patients, 29 had autoimmune features; therefore, only 33 patients were actually eligible, and 12 of these patients (36%) were excluded by nonconsent. It is plausible that the excluded patients were different from those who were finally included in the study, confounding the accuracy of the analysis ("spectrum bias"). Additionally, TBLC was nondiagnostic in four cases, which therefore had to be excluded from the analysis, leaving only 17 cases.

Also, taking into account the spatial heterogeneity of idiopathic pulmonary fibrosis and the frequent overlap of different patterns of

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