CORRESPONDENCE

In clinical practice, TBLC is here to stay. In our experience, most patients prefer TBLC to SLB (or indeed any "surgical" procedure) despite the lower diagnostic accuracy of TBLC. In the clinic, and in the proper clinical and radiological context, TBLC is likely to provide far more diagnostic information to the clinician than what is being projected by this study.

TBLC may have been projected to be "down" by this study, but certainly it is not out. ■

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References

- Romagnoli M, Colby TV, Berthet JP, Gamez AS, Mallet JP, Serre I, et al. Poor concordance between sequential transbronchial lung cryobiopsy and surgical lung biopsy in the diagnosis of diffuse interstitial lung diseases. Am J Respir Crit Care Med 2019;199:1249–1256.
- Katzenstein AL, Zisman DA, Litzky LA, Nguyen BT, Kotloff RM. Usual interstitial pneumonia: histologic study of biopsy and explant specimens. Am J Surg Pathol 2002;26:1567–1577.
- Rabeyrin M, Thivolet F, Ferretti GR, Chalabreysse L, Jankowski A, Cottin V, et al. Usual interstitial pneumonia end-stage features from explants with radiologic and pathological correlations. Ann Diagn Pathol 2015;19:269–276.
- Dhooria S, Agarwal R, Sehgal IS, Aggarwal AN, Goyal R, Guleria R, et al. Bronchoscopic lung cryobiopsy: an Indian association for bronchology position statement. Lung India 2019;36:48–59.
- Colella S, Haentschel M, Shah P, Poletti V, Hetzel J. Transbronchial lung cryobiopsy in interstitial lung diseases: best practice. Respiration 2018;95:383–391.

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Which Biopsy to Diagnose Interstitial Lung Disease? A Call for Evidence and Unity

To the Editor:

We read with great interest the recent article by Romagnoli and coworkers (1). This first-of-its-kind, prospective, blinded study compared the diagnostic impact of two biopsy modalities, transbronchial lung cryobiopsy (TBLC) and surgical lung biopsy, and found that they provide poor diagnostic agreement (κ = 0.22). The reasons for the low concordance between TBLC and surgical lung biopsy are unknown; however, we speculate that the unique study design, the relative size of the biopsies, technical differences in sampling methods and locations, and the impact of freezing are potential contributors.

These findings are preliminary—the sample size was small and the diagnostic process atypical—but if confirmed, they could have major clinical implications. Although previous studies have evaluated the diagnostic certainty of TBLC in patients with interstitial lung disease (ILD) (2), Romagnoli and colleagues' study demonstrates that questions remain regarding its diagnostic accuracy (3). We agree that these findings underscore the risk of early, widespread adoption of TBLC in ILD without more robust evidence (4).

What are the next steps? First, we need funding agencies and international societies to support high-quality research on the diagnostic value and safety of TBLC. Second, we need collaboration among members of the international scientific community to work toward consensus and avoid the production of discordant recommendations that poorly serve patients and providers. Lastly, we believe it is important to continue to explore the diagnostic "gold standard" for patients with ILD, including the best

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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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References

- Romagnoli M, Colby TV, Berthet JP, Gamez AS, Mallet JP, Serre I, et al. Poor concordance between sequential transbronchial lung cryobiopsy and surgical lung biopsy in the diagnosis of diffuse interstitial lung diseases. Am J Respir Crit Care Med 2019;199:1249–1256.
- Tomassetti S, Wells AU, Costabel U, Cavazza A, Colby TV, Rossi G, et al. Bronchoscopic lung cryobiopsy increases diagnostic confidence in the multidisciplinary diagnosis of idiopathic pulmonary fibrosis. Am J Respir Crit Care Med 2016;193:745–752.
- Patel NM, Borczuk AC, Lederer DJ. Cryobiopsy in the diagnosis of interstitial lung disease: a step forward or back? Am J Respir Crit Care Med 2016;193:707–709.
- 4. Raghu G, Lederer DJ, Rabe KF. Cryobiopsy for interstitial lung disease: the heat is on. *Am J Respir Crit Care Med* 2019:199:1183–1184.

- Raghu G, Flaherty KR, Lederer DJ, Lynch DA, Colby TV, Myers JL, et al.
 Use of a molecular classifier to identify usual interstitial pneumonia in
 conventional transbronchial lung biopsy samples: a prospective
 validation study. Lancet Respir Med 2019;7:487–496.
- Travis WD, Costabel U, Hansell DM, King TE Jr, Lynch DA, Nicholson AG, et al.; ATS/ERS Committee on Idiopathic Interstitial Pneumonias. An official American Thoracic Society/European Respiratory Society statement: update of the international multidisciplinary classification of the idiopathic interstitial pneumonias. Am J Respir Crit Care Med 2013;188:733–748.
- Flaherty KR, Brown KK, Wells AU, Clerisme-Beaty E, Collard HR, Cottin V, et al. Design of the PF-ILD trial: a double-blind, randomised, placebo-controlled phase III trial of nintedanib in patients with progressive fibrosing interstitial lung disease. BMJ Open Respir Res 2017;4:e000212.

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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 Twitterbased 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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