Athol Wells, M.D., Ph.D.
Royal Brompton Hospital
London, United Kingdom

Sonye Danoff, M.D., Ph.D.
Johns Hopkins School of Medicine
Baltimore, Maryland

Thomas Colby, M.D.
Mayo Clinic Scottsdale
Scottsdale, Arizona

Jay Ryu, M.D.
Mayo Clinic
Rochester, Minnesota

Venerino Poletti, M.D., Ph.D.
GB Morgagni Hospital
Forlì FC, Italy

Otis Rickman, M.D.
Vanderbilt University Medical Center
Nashville, Tennessee

Felix Herth, M.D., Ph.D.
University Hospital Heidelberg
Heidelberg, Germany

Momen Wahidi, M.D.
Duke University School of Medicine
Durham, North Carolina

Juergen Hetzel, M.D., Ph.D.
University of Tubingen
Tubingen, Germany

Moishe Liberman, M.D., Ph.D.
Universite de Montreal
Montreal, Quebec, Canada

Lonny Yarmus, D.O.*
Johns Hopkins University
Baltimore, Maryland

*Corresponding author (e-mail: lyarmus@jhmi.edu).

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Bad Performance of Lung Cryobiopsy in the Diagnosis of Interstitial Lung Diseases: Don't Throw the Baby Out with the Bathwater

To the Editor:

Multidisciplinary management is the gold standard for interstitial lung disease (ILD) diagnosis and treatment (1). In the recent American Thoracic Society/European Respiratory Society/Japanese Respiratory Society/Latin American Thoracic Association guidelines, experts did not make any recommendation for or against transbronchial lung cryobiopsy (TBLC), mostly due to a lack of strong data and the absence of standardization for the procedure. To date, most experts agree that TBLC provides a proper diagnosis in 80% of cases (2, 3), and data suggest that cryobiopsy can have a significant impact when performed in the setting of multidisciplinary management of ILD (4). In a recent issue of the *Journal*, Romagnoli and colleagues reported the first study to directly compare surgical lung biopsy (SLB) with TBLC for the diagnosis of ILD (5). After samples were read and a diagnosis was made by local pathologists, the samples were blinded and read by an external expert pathologist. The results revealed poor concordance between the two techniques as compared with the final diagnosis retained by local teams, which clearly casts a shadow on the spreading use of TBLC.

The authors must be acknowledged for conducting the first study on sequential SLB and TBLC. However, some points should be noted to preclude any hasty conclusions. First, the fact that only 21 patients were included does not allow for a strong statistical analysis. In addition, when we look at each case, some of the apparent discrepancies were expected, as we know that some patients have two different pathology patterns in their lungs (6). On the other hand, some differences between SLB and TBLC in a single patient are quite surprising (e.g., in patient #15 in the study, TBLC showed Langerhans histiocytosis and SLB showed usual interstitial pneumonia).

The authors report that TBLC would have led to a different treatment if SLB had not been performed in 11 of 21 cases (52%).

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However, when we analyze Table E3 in the online supplement of their study, this seems to be the case for only eight of 21 cases (38%).

Finally, the most striking result of the study is that neither SLB nor TBLC analysis by the blinded pathologist achieved good agreement with the final diagnosis (62% and 48%, respectively, with a wide confidence interval). This point illustrates the fact that we should consider the pathologist as one actor, among others, in the multidisciplinary assessment of ILD (7). In this regard, it would have been interesting to have the agreement between the final diagnosis and TBLC or SLB analyzed by the local pathologist, and to compare the diagnostic performance of the local pathologist (taking part in the multidisciplinary discussion) with that of the blinded expert pathologist.

In conclusion, although the study demonstrates low agreement between blinded analyses of SLB and TBLC and the final diagnosis, the results should not prevent specialists from performing TBLC in the setting of specialized multidisciplinary management of ILD. We also think that this important work by Romagnoli and colleagues paves the way for future trials comparing SLB and TBLC in a multidisciplinary setting. ■

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

Antoine Froidure, M.D., Ph.D.*
Thierry Pieters, M.D.
Cliniques Universitaires Saint-Luc
Bruxelles, Belgium

Dimitri Leduc, M.D., Ph.D.
Benjamin Bondue, M.D., Ph.D.
Hôpital Erasme
Bruxelles, Belgium

ORCID ID: 0000-0001-7133-1788 (A.F.).

*Corresponding author (e-mail: antoine.froidure@uclouvain.be).

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Surgical Lung Biopsy and Cryobiopsy in Fibrosing Interstitial Lung Diseases: One Swallow Does Not Make a Summer

To the Editor:

In a recent issue of the *Journal*, Romagnoli and colleagues presented a small prospective study comparing transbronchial lung cryobiopsy (TBLC) with surgical lung biopsy (SLB) (1). First, the authors must be complimented for the achievement of obtaining biopsies by sequentially using two different methods in the same patients, especially considering the risk of hemorrhage and acute exacerbation of an underlying fibrosing interstitial lung disease (ILD). Previous studies have shown excellent diagnostic yields with TBLC, but data regarding the accuracy of this approach have been lacking, and it is in the light of this gap that the present study is important. Regrettably, the study questions the accuracy of TBLC, as a comparison of TBLC and SLB seems to show discordant pathology findings, thus challenging the use of TBLC for diagnosing ILD.

However, the present results need to be carefully evaluated. First of all, only a small number of patients were recruited from the two centers, with only 62 patients referred for a multidisciplinary evaluation for ILD over a period of 28 months, and only 21 patients submitted to biopsy and included in the study with, at best, 11 patients at each ILD center. It was previously reported that there is a learning curve with respect to TBLC complications, and this is also true for the quality of the biopsies (2). There are no data regarding the total quantity of TBLC procedures performed in the two centers or the number of procedures performed per bronchoscopist. Training in the field of TBLC seems to be important and should be reported (2, 3).

Aside from being described as "good to excellent" in most cases, the biopsies were not defined in terms of quality (the authors judged 2 biopsies as poor, 3 as average, 13 as good, 3 as very good, and 3 as excellent). However, the criteria for making this judgment are not specified. Also, the localization of the biopsy site (i.e., central/peribronchial or peripheral) is not reported, and neither is the presence of pleura in the biopsy, a sign that shows that the biopsy is from the peripheral compartments of the lung (4). The pneumothorax rate of 9.5% was low, which also indicates that biopsies were taken from more central lung compartments. The mean size of the TBLC was 4.7 mm (range, 2.5–8.0 mm; median size, 7 mm; interquartile range, 5–8 mm). A learning curve

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