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. ■

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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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in TBLC has been reported not only with respect to complications but also with respect to the quality and size of the biopsies. In a previous study, Almeida and colleagues assessed 100 TBLCs performed in patients with suspected diffuse lung disease (2). When they compared the first 50 TBLCs with the next 50 TBLCs, they found that the length and area of the biopsies were smaller and the diagnostic yield was lower in the first group, and all parameters improved when the bronchoscopists gained more experience. In their study, Almeida and colleagues reported a median length of 5.0 mm in the first 50 biopsies and 6.0 mm in the next 50 biopsies.

Romagnoli and colleagues reported a level of agreement between external blinded versus local pathology reports as fair to moderate, with κ values of 0.22–0.51. The κ values for individual pathologists are not presented, and as noted above for bronchoscopy, there may be a learning curve for pathologic evaluations of cryobiopsies. In support of this, previous studies (which included the same external pathologist as in the present study) reported κ values between 0.59 and 0.61 (5, 6).

With regard to the agreement between the pathologic diagnosis based on the two types of specimens and the final diagnosis at the second multidisciplinary assessment or the final treatment (Table 2 and Table E3 in the online supplement of Reference 1), there is no statistically significant difference by conventional standards between the two types of specimens in terms of performance when evaluated by a chi-square test or Fisher's exact test on simple 2×2 tables, even though there is trend in favor of SLB. This emphasizes the need for further research into this important subject before any conclusions can be made.

The TBLCs were compared with SLBs as the gold standard. However, the accuracy of SLB has never been proven, and previous studies (7) have clearly shown that SLBs can also provide discordant results when performed in different lobes; thus, the perception of SLB as the gold standard requires careful consideration.

The study by Romagnoli and colleagues certainly indicates that more research into the accuracy of TBLC is warranted, but their results cannot stand alone and should not discourage the continued use of TBLC in interstitial lung disease. ■

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Transbronchial Lung Cryobiopsy in Diffuse Interstitial Lung Diseases . . . Bent but Not Broken

To the Editor:

We read with interest the article by Romagnoli and colleagues wherein the authors demonstrate poor concordance between surgical lung biopsy (SLB) and transbronchial lung cryobiopsy (TBLC) (1). We congratulate the authors for their excellent study, given that this is the first study to perform SLB and TBLC in the same patient. There are, however, a few limitations of the study that need to be highlighted.

The authors clearly state that the study is limited by the small sample size, the use of histopathology findings in isolation to calculate concordance (without integrating clinical and imaging data), and the fact that even SLB had only 62% agreement with the final diagnosis. Despite the major limitations of the study, the authors seem to sound a death knell for TBLC, which is unjustified. If the study had had a larger sample size and a few more concordant patients in the TBLC arm, the results would have been different. The authors also consider subjects with a nondiagnostic TBLC to be discordant. In actual practice, such patients would be counseled to undergo SLB, as TBLC has not been claimed to completely replace SLB. Interestingly, the authors seem to be very hopeful about the utility of SLB even though it had a κ coefficient of only 0.51 (only slightly higher than that obtained for TBLC). It is important to understand that SLB has its own risk of sampling error (2, 3).

Also, the authors used a 2.4-mm cryoprobe on the basis that this provides larger tissues. However, the problem with the larger cryoprobe is that it provides more "central" than "peripheral" lung tissue, and this may be one important cause of a lower concordance of TBLC (4, 5).

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