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Authors' Reply

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We thank Hardavella and Navani [1] for their comments regarding our study comparing endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) with and without rapid on-site cytologic evaluation (ROSE) for the diagnosis of lung cancer [2]. We would like to especially address the reservations Hardavella and Navani [1] have regarding our conclusions.

The first issue is whether or not we can terminate EBUS-TBNA based only on a positive result of ROSE. Nowadays, the determination of genotypes has become indispensable for the management decision regarding patients with non-small cell lung cancer (NSCLC) who might potentially benefit from these molecular targets [3, 4]. In addition, the determination of subtype classification even in patients with NSCLC, e.g. squamous or non-squamous cell carcinoma, has become essential for the determination of the chemotherapy regimen [4]. As a consequence, sampling of histologic specimens containing diagnostic materials is very important. In our study, the results of ROSE were the basis for the decision to terminate EBUS-TBNA, but the final decision regarding termination or additional samplings was made by the examiner. If only a cytologic specimen but not visible histologic core specimens was obtained, additional punctures were performed regardless of ROSE results in most cases. In fact, approximately 60% of patients in the ROSE group had a positive ROSE result at the first puncture, but 70% of the patients underwent 2 punctures. Nevertheless, the puncture number was fewer in the ROSE group.

The second issue involves the lower negative predictive value (NPV) in the ROSE group. One reason for the low NPV in the ROSE group is the occurrence of false-positive ROSE results. Although the concordance rate in the diagnosis of malignancy between ROSE and the final pathologic diagnosis was high, 2 patients with a false-positive ROSE result, which decreased the NPV, were

observed. However, the value of ROSE cannot be discussed in terms of the NPV in our study because the number of true- or false-negative patients in the ROSE group was very small (a total of 10 patients), and the difference in the NPV between the ROSE group and non-ROSE group was not statistically significant ($p = 0.4$ using Fisher's exact test). The false-negative ROSE results are less likely to affect the diagnostic accuracy though they may prolong the procedures. In our study, patients with a negative ROSE result underwent a median of 3 (range 2–6) punctures for the main target lesion, which seems similar to the puncture number in the non-ROSE group, but most of the patients underwent additional diagnostic procedures in the same settings.

Although our study is too small to compare the diagnostic yield, the clinical benefit of ROSE during EBUS-TBNA seems limited from our results, so we do not recommend the routine use of ROSE during EBUS-TBNA for the initial diagnosis of lung cancer. As Hardavella and Navani [1] suggest, the cost-benefit ratio should be considered when the use of ROSE is justified. Further larger studies are needed to clarify the cost-benefit or risk-benefit ratio on the use of ROSE during EBUS-TBNA.

References

- 1 Hardavella G, Navani N: EBUS-TBNA with ROSE-tinted spectacles? *Respiration* 2013;86:439.
- 2 Oki M, Saka H, Kitagawa C, Kogure Y, Murata N, Adachi T, Ando M: Rapid on-site cytologic evaluation during endobronchial ultrasound-guided transbronchial needle aspiration for diagnosing lung cancer: a randomized study. *Respiration* 2013;85:486–492.
- 3 Lindeman NI, Cagle PT, Beasley MB, Chitale DA, Dacic S, Giaccone G, Jenkins RB, Kwiatkowski DJ, Saldivar JS, Squire J, Thunnissen E, Ladanyi M: Molecular testing guideline for selection of lung cancer patients for EGFR and ALK tyrosine kinase inhibitors: guideline from the College of American Pathologists, International Association for the Study of Lung Cancer, and Association for Molecular Pathology. *J Thorac Oncol* 2013; 8:823–859.
- 4 Thunnissen E, Kerr KM, Herth FJ, Lantuejoul S, Papotti M, Rintoul RC, Rossi G, Skov BG, Weynand B, Bubendorf L, Katrien G, Johansson L, López-Ríos F, Ninane V, Olszewski W, Popper H, Jaume S, Schnabel P, Thiberville L, Laenger F: The challenge of NSCLC diagnosis and predictive analysis on small samples: practical approach of a working group. *Lung Cancer* 2012;76:1–18.