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Editorial Comment

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Dancing in the Dark

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Peripheral pulmonary lesion (PPL) is a relatively frequent finding on the chest computer tomography scan. Etiologies are different, but lung cancer is by far the most common when the PPL reaches the size of 1 cm or more, especially in smokers. However, a significant proportion of patients have benign causes, and surgical removal without prior cytological/histological verification is no longer acceptable. Numerous minimally invasive diagnostic techniques have evolved in the past decades with accelerated development recently.

Interventional pulmonologist nowadays has an enviable set of different techniques at her/his disposal. They include various imaging techniques, which provide 3D reconstructions and virtual pathways to PPL location; guide the navigation toward PPL, sometimes similar to GPS; confirm the tool in lesion, but also cover a rich selection of biopsy accessories and thinner bronchoscopes with increased range, not to mention the tools for rapid evaluation of the biopsy specimen [1]. Despite substantial and growing body of literature, approaches and techniques used for diagnosing PPLs vary widely among centers, as well as diagnostic yield and complications [2]. But where is the place for evidence-based practice throughout this story?

In this issue of *Respiration*, Dandanell Juul and coworkers published a systematic review to evaluate if addition of radial endobronchial ultrasound (rEBUS) improves the diagnostic yield of electromagnetic navigation bronchoscopy (ENB) [3]. Authors initially aimed to perform a meta-analysis, but the attempt failed in spite of extensive research of available literature, where they were able to identify only five relevant publications. Although both technologies: rEBUS and ENB are available for more than 15 years, only one of these studies was a randomized controlled trial (RCT) with the highest level of scientific evidence [4]! Authors also found significant methodological differences between the five studies, which pose a risk to spurious causality and bias. Not surprisingly, the conclusion emphasizes the concerning lack of evidence from both a patient and organizational perspective and calls for more consistent data.

But the gap is actually bigger than it seems at the first glance. McGuire et al. [5] recently published a systematic review on diagnostic yield of rEBUS and ENB when procedures were performed separately, not in direct comparison or complementary. Forty-one studies were included in the analysis with high amount of heterogeneity and moderate or poor QUADAS score. Only four studies

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were RCT and only one of them directly compared diagnostic yields of rEBUS and ENB [4]. Similar results were obtained by another meta-analysis of sensitivity and safety of ENB for lung cancer diagnosis [6]. Among forty included studies, more than half were retrospective and all but three were performed in a single center. Heterogeneity was high due to a number of factors (lung cancer prevalence, sampling techniques used, additional modes of navigation, etc.). Another three recently published systematic reviews evaluating rEBUS-guided cryobiopsy of PPL, virtual bronchoscopic navigation and comparing rEBUS and computed tomography-guided biopsy ended up with similar results [7–9].

Introduction of new diagnostic tools on the market is less regulated than launching new therapeutic substances or procedures. The latter must prove their efficacy and safety in comparative RCT studies with existing therapeutics, while new diagnostic tools usually get through by efficacy study in one of the expert centers and push of the manufacturer. New methods are not properly evaluated and compared to existing in RCTs, and real-life data are also scarce. AQuIRe registry reveals us completely different picture than designed studies [2]. It seems, that interventional pulmonology did not complete its homework satisfactorily in the past, and field of PPLs urgently needs independent evaluation and standardization which are primarily in the interest of patients.

The task is, however, quite demanding due to its complexity: the diagnostic yield depends on many factors. Basic characteristics of PPLs (size, bronchial access, primary/metastasis), still relevant today, which were described already many decades ago [10], should be evaluated in-depth systematically. Comparative studies between different navigational methods and their synergies should be made. Biopsy accessories should be properly evaluated in the same way. Training, experiences, dexterity, and performance of interventional pulmonologists should be evaluated and graded. Pragmatic protocols, which consider all the characteristics of patient, equipment, and investigator shall be created and evaluated, regarding diagnostic yield, complications, and costs. Clinical registers shall be opened in every interventional pulmonology department to properly implement quality and safety principles. While dancing in the dark is worth taking a step back, before making two forward into the light.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Founding Sources

None.

Author Contributions

Ales Rozman drafted the paper and provided substantial contributions to the concepts expressed in the paper; Lina Zuccatosta and Stefano Gasparini critically revised the draft and provided substantial contributions to the concepts expressed in the paper.

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