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barrier to standardization of R-EBUS TBB in pediatric populations is the lack of formal training programs in pediatric interventional bronchoscopy. Although further research in larger populations is needed, these findings suggest that adding R-EBUS TBB to standard BAL sampling in immunocompromised children with radiographic opacities considerably improves the microbiologic diagnostic yield. These results represent progress in the emerging field of pediatric interventional pulmonology.

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## Simple Electrical Impedance Tomography Measures for the Assessment of Ventilation Distribution

To the Editor:

Electrical impedance tomography (EIT) is a functional imaging method that allows for continuous assessments of regional ventilation and lung volume changes at the bedside. Two-dimensional functional EIT images of tidal impedance variation (TV) are frequently used to determine the distribution of regional VTs in a transverse section of the chest and its trends. Different measures can be derived from these images (1), ranging from simple parameters (e.g., the sums of TV values in various regions of interest or one-number measures characterizing the degree of heterogeneity of pixel TV values) to more complex ones (e.g., ventilation profiles, regional respiratory compliance, and time constants).

A recent research letter demonstrated that the sum of pixel TV values in the dorsal image half as a fraction of the global sum in the whole image ( $TV_{dorsal}/TV_{global}$ ) reflects the changes in V<sub>T</sub> distribution induced by changes in positive end-expiratory pressure (2). The authors inaccurately termed this EIT measure the "center of ventilation" (CoV). The actual CoV is an established EIT measure that was first introduced in 1998 (3) and since then has often been applied in clinical studies to characterize the ventilation distribution in the ventrodorsal direction (e.g., References 4–6). The CoV describes the weighted geometrical center of the ventilation distribution distribution, which is not identical to the  $TV_{dorsal}/TV_{global}$  used by the authors. (For an exact definition and calculation of the CoV, *see* the unified EIT terminology and the section on EIT measures in the recent consensus statement on chest EIT [1]).

By coincidence, both  $TV_{dorsal}/TV_{global}$  and the ventrodorsal CoV exhibit values higher than 50% when ventilation is preferably distributed in a dorsal image section. However, because the CoV is a function of each pixel layer in the image, it is more sensitive to ventilation shifts than the dorsal fraction of ventilation, which is based on a simple division of the image into ventral and dorsal halves. The differences in information captured by the CoV and  $TV_{dorsal}/TV_{global}$  can be perceived easily in Figure 1A. The EIT images show four hypothetical regions of identical ventilation in each image quadrant. Consequently, both the CoV and  $TV_{dorsal}/TV_{global}$  equal 50% (Figure 1A, left). If one (Figure 1A, middle) or both (Figure 1A, right) dorsal ventilation regions shift further toward the back, only the CoV reflects these changes.

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**Figure 1.** Examples of functional electrical impedance tomography images showing different hypothetical distributions of pixel tidal impedance variation (TV) and their effects on the calculated values of 1) the center of ventilation (CoV) and 2) the proportion of ventilation in the dorsal regions as a fraction of global ventilation detected in the image ( $TV_{dorsal}/TV_{global}$ ). The top images illustrate the effects of a dorsal shift (white arrows) in ventilation (A) and the bottom images show the effects of ventrodorsal asymmetry in the ventilation distribution (B). The ventral side of the chest is shown at the top and the right side of the chest is shown on the left side of each image. The red dashed lines divide all images into two halves. The total sum of all pixel TV values is identical in all six images. The regional sums of these values in the ventral image halves equal those in the dorsal ones in all top images (A) and in the left bottom image (B). The middle image in B has a higher sum of pixel TV values in the dorsal image than in the ventral image half, whereas the opposite is seen in the right image.

When the regional sums of TV values differ between the ventral and dorsal image regions, both the CoV and  $TV_{dorsal}/TV_{global}$  identify this asymmetry (*see* Figure 1B). In contrast to fully symmetrical ventilation distribution (Figure 1B, left), both the CoV and  $TV_{dorsal}/TV_{global}$  are higher than 50% when ventilation is distributed predominantly in the dorsal image half (Figure 1B, middle) and lower than 50% when higher ventilation is noted in the ventral half (Figure 1B, right). However, the values are not comparable because the CoV shows the location on the ventrodorsal thoracic axis in the percentage of chest diameter onto which the center of "ventilation mass" projects, and  $TV_{dorsal}/TV_{global}$  shows the dorsal fraction of ventilation in the percentage of the whole image ventilation.

In addition, we wish to mention that "normal" physiological ventilation distribution need not render  $TV_{dorsal}/TV_{global}$  and the CoV equal to only 50%. Interindividual differences with values slightly higher or lower exist that are related to, for example, different chest anatomy or the EIT electrode interface placement. Nevertheless, the trends in both  $TV_{dorsal}/TV_{global}$  and the CoV that result from changed ventilator settings, other therapy measures, and natural disease history are valuable for clinical decision making, as demonstrated in the current research letter (2).

In conclusion, even simple EIT measures such as the CoV and  $\rm TV_{dorsal}/\rm TV_{global}$  can serve as intuitive measures of ventilation

distribution that can be used for personalized guidance of ventilator therapy. However, standardized use and reporting of EIT measures are needed to ensure comparability among the findings of different studies.

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## Beply to Frerichs et al.

### From the Authors:

We thank Dr. Frerichs and colleagues for their interest in our research letter (1). We used both experimental data and clinical findings in our study to demonstrate that an excessive level of positive end-expiratory pressure (PEEP) could be easily—and almost immediately by visual inspection—identified by detecting a distribution of ventilation being predominantly dorsal as compared with a frequently predominantly ventral ventilation in patients ventilated at lower PEEP. We suggest that decreasing PEEP in such cases to obtain a more equilibrated dorsal-to-ventral distribution can be proposed to patients right away. We also showed from experimental data that using compliance of the respiratory system for this purpose would be misleading.

In our letter, we used the term "center of ventilation," as proposed in a previous study (2). We appreciate Frerichs and colleagues' comment regarding the fact that this does not correspond to the most recent definition of center of ventilation, as indicated in a recent consensus statement (3). We also acknowledge that using the center of ventilation, as proposed in that paper, requires a much more complex calculation than our own use of the distribution of ventilation. We believe that keeping this marker as simple as possible is important for clinical dissemination. We also believe that, based on the examples proposed, the center of ventilation as calculated from the reference value is much less clinically relevant for our purpose. We agree that a new denomination is needed for our index, and we propose the term "dorsal fraction of ventilation" as a better description.

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# More Insights into the Association between RVX-208 and Pulmonary Arterial Hypertension

### To the Editor:

We read with great interest the recent publication by Van der Feen and colleagues (1) highlighting that RVX-208 could normalize the

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