It’s about numbers, not pictures

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THE ARTICLE IN THE CURRENT issue by Horn and colleagues (4) from Sheffield presents a significant change in the manner in which MRI in the lung using hyperpolarized gas (3He in this case, but also potentially 129Xe) is used. Since its inception, hyperpolarized gas imaging has shown an ability to produce images of gas distribution in the lungs of both animals and humans, sometimes with stunning levels of detail. However despite these high-quality images, the physiological interpretation of the data has been severely hampered by the lack of quantification available from the data. Although quantitative measures of lung structure have been derived from apparent diffusion coefficients (3, 10), often the functional “quantification” that has resulted from these images has been a presentation of the number and/or size of “ventilatory defects” (2, 6, 9).

Although such results are in themselves useful and important in that they show in a very graphic manner the ventilation heterogeneity that results from some lung disease, they are, from a physiological standpoint, unsatisfying. Deciding what to classify as a “defect” inevitably requires some sort of threshold decision to be made, but this is challenging because different studies have different signal-to-noise ratios (5, 8), and there is spatial heterogeneity in coil sensitivity and flip angle, both of which affect signal levels. Furthermore, the result is a rather binary outcome: ventilated or not ventilated. Yet ventilation is a continuum that varies, even in the normal lung, and if we want to make quantitative physiological inferences, then we need to quantify ventilation.

It is exactly in this area where this new publication shines. In this paper the authors used hyperpolarized 3He as their tracer, and it is inspired in the usual fashion from a small bag. In a manner similar to other hyperpolarized gas studies, a postinspiration image is acquired. It is what happens next that is the innovative step. The subject then expires, a breath of air is inspired, and another image taken. This air breath followed by image acquisition is repeated 4 or 5 times. In essence, following the initial “loading” inspiration, a short multiple-breath washout occurs with the initial condition of the washout being the hyperpolarized gas signal in a region of interest obtained from the “breath-0” image. The translation of a multiple breath washout time constant to a measure of specific ventilation (the ratio of fresh gas inspired to resident gas volume) is well established and provides a direct and quantitative measure of ventilation efficiency.

The authors were able to show that adequate signal-to-noise ratio was achieved using only modest amounts of 3He (200 ml diluted into a 1-liter volume), an important consideration given the scarcity of this resource.

The approach taken is similar to the proton based approach developed by Sá et al (7) in that both derive a measure of specific ventilation from a washout (or in the case of the proton technique, a combination of washins and washouts) [It should be noted that the two groups worked independently.] The hyperpolarized technique has the clear advantages of a 3D acquisition and, with a better signal-to-noise ratio, acquires data from only a single washout. Furthermore, the hyperpolarized technique has the potential advantage that it is the washout of gas from the lung that is measured, whereas the proton technique measures a change in the MR signal resulting from the paramagnetic effects of O2 on the T1 relaxation time. Whether this latter difference is important is at present unknown, but there is an obvious intellectual attraction to directly measuring the washout of the gas itself.

There are other issues that also need to be resolved. The hyperpolarized method uses a series of images taken at end-inspiration following the end-inspiration image of the loading breath. Thus the parameter that defines the washout is the regional tidal volume to end-inspiratory volume. The proton-based method presently uses end-expiratory images, and so the washout is defined by regional tidal volume to end-expiratory volume. From a theoretical basis the transformation between the two is straightforward but that needs to be tested in practice. Both techniques have the potential to disturb the underlying physiology: the hyperpolarized method with an initial anoxic breath, the proton method with the repeated administration of 100% O2.

Another open question is the degree to which gross unevenness of ventilation, which will serve to make for a very heterogeneous breath-0 image, affects the washout rates in adjacent regions through the common deadspace. Furthermore, the breath-0 image is potentially affected by poorly ventilated regions, what has in the past been referred to as “slow-space” (1). The authors attempt to address this by including a short breathhold between the inspiration and breath-0 image to allow time for the 3He to reach these regions of the lung. However, how this skews the subsequent washout when these short breathholds are absent is at present unclear. Furthermore, it remains to be demonstrated how well these regions of slow space can be quantified given the relatively few breaths that the washout covers before signal loss from radio frequency-induced loss of polarization and O2 quenching of the polarization eliminates any useful signal.

This is a potentially important first step in moving hyperpolarized gas imaging into the realm of quantitative physiological studies of ventilation. Nonetheless, work remains: comparing the techniques would be useful as would modeling studies of the issues described above. But as our somewhat facetious title suggests, the move toward the extraction of physiologically relevant numbers characterizing ventilation from hyperpolarized gas imaging, as opposed to pictures, is a welcome one.
AUTHOR CONTRIBUTIONS

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REFERENCES