humans has a problem in that the control group also received antenatal ultrasound.11 The mouse locomotor study indicates that any exposure in utero may be significant, suggesting that only a control group with no history of ultrasound exposure would be suitable—a very difficult study to arrange today.

I appreciate the observations of Drs. Gray and Drasner regarding the bioeffects of ultrasound, including the ability of high-intensity ultrasound to promote nerve regeneration. I remain unsure how to relate the Food and Drug Administration high-intensity ultrasound to promote nerve regeneration. It would be suitable—a very difficult study to arrange today. I am pleased that Drs. Gray and Drasner agree that more work is needed to address the interactions between ultrasound and local anesthetics. In referencing Orebaugh work is needed to address the interactions between ultrasound and local anesthetics. In referencing Orebaugh et al.13 regarding complication rates, I am reminded of the question of who was performing the block. I suspect these data come from resident-performed regional anesthesia, and if so, likely reflect the steep learning curve for safely performing blocks with anatomic landmarks and nerve stimulation as the only guide. It is very clear that ultrasound shortens the steep learning curve substantially but at the steep price of making practitioners ultrasound dependent.

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References
8. Ang ESBC, Glucic V, Dugue A, Schafer ME, Rakic P: Prenatal exposure to ultrasound waves impacts neuronal migration in mice. PNAS 2006; 103:12903–10

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Transpulmonary Determination of Extravascular Lung Water: What You See Is What You Get and It’s Useful

To the Editor:
We read with interest the study by Easley et al.1 comparing changes in the extravascular lung water (EVLW), as measured by transpulmonary thermodilution (TPT), with changes in the tissue density by computed tomography (CT) in an acute lung injury model before and after endotoxin (lipopolysaccharide) administration and the accompanying editorial by Costa and Vidal Melo.2 Although the authors used a reasonable animal model in a well-conducted study, we find significant limitations in data interpretation and a major fault with their conclusions. The study suffers from a small sample size (n = 5), making comparisons between CT-tissue quantification of lung edema and EVLW by TPT (EVLWTPT) difficult. A single EVLWTPT outlier1(fig. 3b, page 1070) seems responsible for most of the differences between the two techniques. However, even when including the outlier, there does not seem to be significant differences in EVLW values as measured by the two methods either after lung lavage or after intravenous lipopolysaccharide. After lung lavage, EVLW by CT was approximately 24 ml/kg versus 23 ml/kg for EVLWTPT (P = 0.1), and after lipopolysaccharide, EVLW by CT was 26 ml/kg versus 29 ml/kg for EVLWTPT (P = 0.2). Furthermore, CT methods for determining EVLW in acute lung injury are very complex and have not been substantiated enough to be considered an accepted standard, as has been pointed out in the editorial.2 Moreover, the authors have obtained perfusion images at a single location in the lung base, excluding the upper lung regions where increased perfusion may have resulted in an increase in the microvascular surface area for fluid exchange and could have increased EVLW significantly. Clearly, the study would have been strengthened had gravimetric determination of EVLW been done instead of relying on the CT.

It is well established that lipopolysaccharide causes a rapid increase in capillary permeability and pulmonary recruitment of inflammatory cells, and its administration has been shown to increase

Drs. Phillips and Perel have served on the Medical Advisory Board for Pulsion Medical Systems, Munich, Germany, makers of the PiCCO device. Neither has any further direct financial interests in the subject matter, materials, or equipment discussed or in competing materials.
EVLW in several animal models. Such an increase was seen by the TPT method but not by the CT. Had the authors controlled for the effects of lipopolysaccharide on EVLW alone, we may have been better able to determine the sensitivity of the two methods for detecting changes in EVLW with changes in V/Q matching and perfusion after lipopolysaccharide administration. As the authors have so eloquently pointed out, understanding the limitations of any device and having as thorough an understanding as possible of the effects changes in physiology have on its accuracy and interpretation are vital for meaningful clinical application. We cannot agree more, and yet, it is doubtful that this study defines the limitations of TPT determinations of EVLW in acute lung injury when pulmonary perfusion is changed. In fact, another equally valid conclusion would be that the TPT method is at least equivalent if not superior to the CT method in this model.

The accompanying editorial appropriately calls into question our current method of introducing medical devices to the market without rigorous scrutiny of efficacy. But TPT has been compared with both the accepted standard gravimetric and dual dilution techniques in a variety of disease states and has performed well.3–5 Furthermore, EVLWTPT is the best pulmonary-specific indice of disease severity and predictor of outcome available to us.6–7 Very importantly, EVLWTPT-guided management of hemodynamics has been shown to decrease mortality in acute lung injury.8 We believe that the foundation for clinical use of EVLWTPT has been established by these studies. We would, therefore, like to join with the authors of the current study and the accompanying editorial and now call for large prospective interventional investigations to examine the benefit.

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References

2. Costa EL, Vidal Melo MF: Lung water: What you see (with computed tomography) and what you get (with a bedside device). Anesthesiology 2009; 111:933–5

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In Reply:

We appreciate the interest of Drs. Phillips and Perel in our recent article.1 However, they seem to have focused on whether there exists a numeric equivalence between extravascular lung water (EVLW) measured by computed tomography tissue volume and the transpulmonary thermodilution method (EVLW TPT). Any such equivalence between these values is as much coincidence as anything else, because it has been shown by Kirov et al.2 that a species-specific correction is required to calibrate the EVLWTPT measurement to accurately reflect gravimetric EVLW. We used the unmodified values from the PiCCO® device (Pulsion Medical Systems, Munich, Germany) because no validated canine correction factors are available. However, because this correction is linear, we believed that the changes in EVLWTPT would be reasonable to follow, and, as we described, the changes in each of these measures after lipopolysaccharide administration were very different. Our goal, however, was not to perform yet another validation of EVLWTPT but to gain insight into the pathophysiologic mechanisms that might impact the reliability of the measured EVLWTPT. Phillips and Perel apparently agree that the EVLWTPT increased after lipopolysaccharide while EVLW measured by computed tomography did not. Even if lipopolysaccharide administration caused an increase in the actual EVLW in the short time between administration and imaging, they offer no explanation as to why this was not evident on whole lung computed tomography imaging, which despite their objections is widely accepted as a sensitive and specific measure of lung mass.3,4 On the basis of the changing perfusion distribution observed, we interpreted this divergence of the two measurements to reflect an acute change in the perfused thermal mass, resulting in an artificial increase in the EVLWTPT.

Nonetheless, we share the enthusiasm of Phillips and Perel in the value of a bedside measurement of lung edema and look forward to careful studies examining its optimal use and effect on outcomes. We hope, however, that the data we

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