and the uptake of Ca_i^{2+} by the sarcoplasmic reticulum (SR) with the onset of relaxation. For example, it has been shown in isolated canine LV wedge preparations near the LAD (same species and same site as in the in vivo studies of Ashikaga et al.) that whereas the onset of the epicardial and endocardial Ca_i^{2+} transients are almost synchronous, the epicardial decline of the Ca_i^{2+} transient (onset of relaxation) precedes the endocardial decline (3). Furthermore, the rate of Ca_i^{2+} uptake by the SR is faster in the epicardium compared with endocardium (3). These effects mimic the in vivo canine observations made by Ashikaga et al. (1). Because the dynamics of Ca_i^{2+} mirror that of contractility, changes in Ca_i^{2+} are considered to be surrogate of myocardial contractility (4). Consequently, we think that the combined tissue tethering and transmural cellular differences in Ca_i^{2+} handling need to be considered simultaneously as possible mechanisms for the in vivo observation of depth-dependent differences in myocardial mechanics in the canine mid-anterior LV.

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Reply

Our recent article (1) reported a new observation that there is discrepancy between cardiac electrical and mechanical behaviors by detecting relatively large mechanical dispersion with little electrical dispersion during both activation and relaxation in the canine mid-anterior left ventricle (LV). In his letter, Dr. Karagueuzian logically and correctly points out the potential contribution of transmural difference in intracellular calcium handling (2) to the transmural mechanical gradients that we had described in the article. Given a slower decay of intracellular calcium to diastolic levels at the endocardium, due in part to significantly lower levels of sarcoplasmic reticulum Ca^{2+} ATPase (SERCA2a) expression in endocardial cells than epicardial cells, the transmural differences in calcium handling likely contribute to the transmural dispersion of myofiber relaxation and should be added to the list of potential contributing factors, such as transmural dispersion of electrical repolarization, even if it is small at physiological heart rates, and tissue tethering. However, this does not seem to be the case with the transmural dispersion of myofiber shortening. Transmural differences in intracellular calcium during activation, where endocardial cells have a slower time to peak than epicardial cells, result in an earlier onset of myofiber shortening in the epicardium than in the endocardium by approximately 20 ms (3). This delay is close to the transmural conduction delay in the canine LV (1,4), thus allowing the impulse to traverse the LV wall to synchronize contraction across the ventricular myocardium; that is, the transmural differences in calcium handling do not contribute to but rather "negate" the transmural dispersion of myofiber shortening due to the delay in action potential propagation across the wall. Therefore, the transmural dispersion of myofiber shortening should be accounted for by other factors, including tethering.

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Immediate Coronary Imaging for Acute Chest Pain: Are We There Yet?

We read with great interest the elegant study by Goldstein et al. (1) suggesting the value of multislice coronary computed tomography (MSCT) in the evaluation of acute chest pain patients. The investigators should be commended for this landmark trial that constitutes one of the few studies assessing the value of an imaging diagnostic technique using a randomized design. As compared with patients managed in the emergency department with standard of care measures, those assigned to the MSCT arm not only had reduced diagnostic times and costs but also required less frequently repeated evaluations for recurrent chest pain (1). Considering the potential clinical implications of this provocative study, addressing some methodological issues would be appreciated.

First, in a randomized study defining the sample size calculation is critical. This is especially relevant considering the very-low-risk patient population included in the present study (none of the patients suffered an event after discharge). Likewise, the primary outcome measure of the study was not clearly stated. Therefore, the value and implications of the different study findings remain