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Imaging Cardiac Mechanics: What Information Do We Need to Extract from Cardiac Images?

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Abstract — **Cardiac mechanics attempts to relate loading (stress), deformation (strain), and material properties (stress-strain relationships) in the normal and diseased heart. Currently, imaging is employed in cardiac mechanics almost exclusively to track myocardial strains; a number of available methods and their relative strengths and weaknesses are discussed. Looking forward, reliable techniques to image stress or material properties (stiffness) would be immensely valuable contributions to cardiac mechanics, and better noninvasive techniques for imaging electrical activation patterns and ventricular synchrony could make important clinical contributions.**

The overall goal of any mechanics analysis is to relate loading (stress), deformation (strain), and material properties (stress-strain relationships) to completely understand the response of a material or structure under expected real-world loading conditions. In a simple structure such as a metal beam, local stresses everywhere in the structure are easily computed from applied loads, and simple linear equations relate those local stresses to local strains. In the heart, the geometry is much more complex, the material is reinforced by muscle fibers that impart different stress-strain behavior in different directions (anisotropy) and at different times, and the orientation of the muscle fibers varies throughout the structure. Techniques for directly measuring the local stresses acting *in vivo* are not available; rather, these stresses must be estimated from measured deformation and known global loading parameters (such as pressure) using models that take the geometric, structural, and material complexity into account. Cardiac mechanics applications of *in vivo* imaging have therefore focused exclusively on measuring regional and global deformation.

I. IMAGING DEFORMATION

The majority of analyses of regional deformation in solid tissues employ a Lagrangian approach, in which individual points are tracked from some reference state through a deformation. Many early cardiac mechanics studies tracked implanted radiopaque beads using biplane cineradiography and used the positions of the beads to compute strains at various times during the cardiac cycle relative to end diastole.[1] Even without detailed information on local stresses, these deformations often provided useful information. For example, during systole normal myocardium contracts locally (negative strain) in the circumferential and longitudinal directions, and thickens (positive strain) in the radial direction; during myocardial ischemia this pattern reverses, with systolic stretching (positive strain) in the circumferential and longitudinal directions accompanied by wall thinning.[2]

From a mechanics perspective, the critical imaging requirement for any study of this type is that it must be possible to track an individual piece of myocardium; in the language of continuum mechanics, the tracked region must behave as a 'material' point. For example, in order to use implanted markers to track deformation as discussed above, it was necessary to prove that the markers do not move relative to the surrounding tissue. As more modern imaging methods have become available, some have fulfilled this requirement and allowed the same type of analysis familiar from the original implanted-marker studies, while others have not. MRI tagging, which labels a particular small volume of myocardium, then identifies that same volume in subsequent images, provides information on one or more tagged planes rather than single points. As a result, the computation of Lagrangian strains from MRI tagging data is not straightforward. Motion of the tagged plane through any chosen imaging plane means that material points cannot be tracked in single imaging planes. However, when information from multiple imaging planes is appropriately combined, for example using a three-dimensional continuum model,[3] Lagrangian strain analysis can be performed.

In a standard continuum mechanics analysis, strains can be computed either from marker positions at two different times or from marker displacements, the difference between those positions. More recently, both MRI[4] and ultrasound-based[5] methods have been introduced that take advantage of this fact, providing instantaneous 'snapshots' of displacement fields at a particular time rather than tracking individual pieces of myocardium over a longer time. Analysis of these data requires a system for accumulating the displacement information over a series of images to provide the type of information typically of interest, such as strains occurring between end diastole and end systole, and accurate accumulation may require higher frame rates than marker-tracking methods. However, displacement-based methods offer a nice compromise in that they are noninvasive, and therefore more clinically applicable than implanted-marker methods, while still providing data that are less difficult to analyze correctly than MRI tagging data.

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One approach that has been employed in the imaging literature but is fundamentally flawed from a mechanics perspective is using endocardial and epicardial surfaces visualized with echocardiography, angiography, or MRI to try to derive Lagrangian strains. As with MRI tag planes, these surfaces represent a set of points free to translate and rotate through any chosen imaging plane; images of these surfaces do not provide information on the motion of individual material points. Attempts to interpolate between the endocardial and epicardial surfaces are equally problematic, as they require making assumptions about transmural displacement gradients that have a greater influence on the resulting strains than the information actually contained in the images. We have found analysis of the motion of endocardial and epicardial surfaces can still provide clinically useful information on regional mechanics, but this work has required a willingness to abandon strain as the deformation measure of choice and develop alternate parametric measures of surface motion.[6]

II. IMAGING STRUCTURE

Because the relationship between global descriptors of loading, such as ventricular pressure, and the local stresses acting on a particular segment of myocardium is complex, local stresses must be estimated from mathematical or computational models. Current computational models usually incorporate measured anatomy and geometry, then iteratively estimate the stress-strain relationship of the myocardium until strains in the appropriately loaded model match strains measured *in vivo* under the same loading conditions. While other approaches are possible in the laboratory, such as incorporating stress-strain relationships determined directly through mechanical testing of excised tissue, for clinical use any computational model must necessarily rely only on parameters that can be measured noninvasively.

With respect to using patient-specific computational models to estimate stress-strain relationships and regional stresses, one of the most exciting recent developments in imaging is the ability to measure fiber anatomy in the heart noninvasively using MRI.[7] It should soon be possible to construct patient-specific computational models with individualized geometry and fiber structure. However, recent modeling work from our laboratory suggests that extremely accurate measurements of the fiber structure will be required before patient-specific estimates of myocardial properties will be possible. Standard errors of greater than 10° and 95% confidence intervals of greater than 20° are typical for fiber angles measured using standard histologic techniques. We recently showed that a finite element model of passive inflation of a rat heart was much more sensitive to shifts in the transmural fiber angle distribution than to changes in the fiber-to-crossfiber stiffness ratio.[8] As a result, we predict that uncertainty in measured fiber structure will dominate any attempt to estimate myocardial material properties on a patient-specific basis unless *in vivo* measurements of fiber structure are much more accurate than histologic measurements, something that will be difficult to demonstrate since the goal is to surpass the current gold standard.

III. IMAGING DISEASE

To this point, we have focused on how imaging relates to the typical goals of a solid mechanics analysis of cardiac function. However, the broader goal of cardiac imaging is to detect clinically significant disease. In pursuing this goal, it must be recognized that mechanical parameters are not the only, and not always the best, indicators of disease. The two cardiac diseases that have the greatest clinical impact are coronary artery disease and heart failure. Imaging methods already play a critical role in the diagnosis and management of both diseases, but in each case there remain possibilities for additional contributions from new imaging methods.

Coronary artery disease arises when atherosclerotic narrowing of one or more large coronary arteries becomes severe enough to limit blood flow reserve to some region of the heart. At this point in the disease progression, there is sufficient blood flow available to meet metabolic demands at rest but not at elevated heart rates. The overall detection strategy is therefore to elevate heart rate through exercise or pharmacologic therapy, then look for regions where blood flow is insufficient to meet oxygen demand. These regions may be detected by imaging blood flow directly using tracers or dyes, by imaging aspects of myocardial metabolism, or by detecting changes in mechanics associated with transient ischemia. An alternate approach is to image coronary anatomy directly to identify regions of atherosclerotic plaque or luminal narrowing, using intravascular ultrasound or high-resolution CT or MRI. As a screening tool, this approach should allow detection of disease before it begins to affect flow; this may allow prevention of more heart attacks but will also raise new questions about when and how to treat patients with identified sub-clinical disease.

Our own work on detection of regional myocardial ischemia is based on the fact that cardiologists' qualitative ratings of endocardial wall motion have proven very useful in identifying regional ischemia on cardiac ultrasound images. While imaging the motion of the endocardial surface does not provide the tracking of material points required for Lagrangian strain analysis, the motion can be parameterized and quantified in ways that provide clinically useful information.[6] The fact that this approach provides less direct information about regional mechanics than displacement imaging or tagging approaches is outweighed in our experience by the ready acceptance among clinical cardiologists of measures based on concepts already familiar to them. This project has revealed a mechanism by which cardiac mechanics analysis can feed back on the development of new imaging methods. By utilizing currently available finite element models of the heart to simulate regional ischemia, we can estimate the relative accuracy and

sensitivity of multiple different measures, including regional strain components, wall motion measures, and others, in detecting and quantifying regional ischemia. We can then ask questions such as what would be the most sensitive measure of regional ischemia if any desired parameter could be imaged, what measures provide the best balance between diagnostic accuracy and clinical acceptance among cardiologists, or what measures provide the best balance between accuracy and diagnostic cost.

Until recently, the role of imaging in heart failure has been largely limited to determining the ejection fraction, used to diagnose and classify heart failure patients. However, the recent discovery that heart function can be improved in many heart failure patients by electrical stimulation with a pacemaker at particular locations and intervals (cardiac resynchronization therapy) has raised new therapeutic imaging needs. A method to image three-dimensional electrical activation patterns in vivo, analogous to the optical dyes used to measure electrical activation in the laboratory, would be immensely valuable. A related need is the ability to image and quantify mechanical synchrony throughout the left ventricle in real time. Investigators have begun to apply existing MRI and ultrasound methods to this problem, but the volume of data that must be processed from multiple regions of the ventricle to assess synchrony has so far prevented comprehensive real-time or near-real-time solutions. Overall, ventricular synchrony is one of the most promising areas for future work at the interface of cardiac imaging and biomechanics.

IV. A CARDIAC IMAGING WISH-LIST

As outlined above, much of cardiac mechanics revolves in one way or another around estimates of myocardial stresses than cannot be directly verified. Therefore, the single most exciting imaging development from a mechanics point of view would be a technique to directly image stresses in the myocardium. A related goal would be to directly image myocardial material properties (stiffness). Ultrasound elastography can provide stiffness information in situations where a known force can be applied while displacements are imaged. It should be possible to apply known forces locally to myocardium *in vivo* using ultrasound energy, ferromagnetic particles, or other methods while imaging displacements, and such a method would make an essential contribution to cardiac mechanics. Finally, as mentioned in the previous section, a clinically applicable method for noninvasive imaging of electrical activation patterns would be a very exciting and important contribution.

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