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- *Original Contribution*

AN ULTRASOUND-DRIVEN KINEMATIC MODEL FOR DEFORMATION OF THE INFARCTED MOUSE LEFT VENTRICLE INCORPORATING A NEAR-INCOMPRESSIBILITY CONSTRAINT

DAN LIN,[*] BRENT A. FRENCH,[*†§] YAQIN XU,[*] JOHN A. HOSSACK,[*‡§] and JEFFREY W. HOLMES[*†§]

[*] Department of Biomedical Engineering, University of Virginia, Charlottesville, VA, USA; [†] Department of Medicine, University of Virginia, Charlottesville, VA, USA; [‡] Electrical and Computer Engineering, University of Virginia, Charlottesville, VA, USA; and [§] Robert M. Berne Cardiovascular Research Center, Charlottesville, VA, USA

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Abstract—Mathematical models of varying complexity have proved useful in fitting and interpreting regional cardiac displacements obtained from imaging methods such as ultrasound speckle tracking or MRI tagging. Simpler models, such as the classic thick-walled cylinder model of the left ventricle (LV), can be solved quickly and are easy to implement, but they ignore regional geometric variations and are difficult to adapt to the study of regional pathologies like myocardial infarctions. Complex, anatomically accurate finite-element models work well, but are computationally intensive and require specialized expertise to implement. We developed a kinematic model that offers a compromise between these two traditional approaches, assuming only that displacements in the left ventricle are polynomial functions of initial position and that the myocardium is nearly incompressible, while allowing myocardial motion to vary spatially as would be expected in an ischemic or dyssynchronous LV. Model parameters were determined using an objective function with adjustable weights to account for confidence in individual displacement components and desired strength of the incompressibility constraint. The model accurately represented the motion of both normal and infarcted mouse LVs during the cardiac cycle, with normalized root mean square errors in predicted deformed positions of 8.2 ± 2.3% and 7.4 ± 2.1% for normal and infarcted hearts, respectively. (E-mail: holmes@virginia.edu) © 2015 World Federation for Ultrasound in Medicine & Biology.

Key Words: **Kinematic model, Myocardial infarction, Incompressibility, Polynomial function, High frequency ultrasound.**

INTRODUCTION

Despite significant achievements in diagnosing and treating cardiovascular disease (CVD), it remains a major global health concern. In the United States, heart disease is the leading cause of death, accounting for 32.3% of all deaths in 2009 (Roger et al. 2013). Ultrasounds are routinely used to diagnose patients with suspected heart disease, including Doppler-based ultrasound such as Tissue Doppler Imaging to assess cardiac function based on myocardial velocities (Sutherland et al. 1994; Sebag et al. 2005), and M-mode echocardiography to analyze the time delay between septal and posterior wall motion (Pitzalis et al. 2005). Post-image formation techniques, using B-mode ultrasound images, such as speckle tracking, can assess myocardial mechanics by tracking tissue motion (Li et al. 2007; Nesser et al. 2009). These measurements are important to the understanding of normal heart function and CVD. Recent advances in high-frequency ultrasound have made it possible to study myocardial mechanics in transgenic mouse models by capturing high-frame-rate cines with spatial resolutions of approximately 50 μm axially and 110 μm laterally (Foster et al. 2009). However, motion estimates using speckle-tracking techniques are often noisy (Bansal et al. 2008; Hjertaas et al. 2013). For example, in mouse heart imaging, high heart rates (400–600 beats per min), consequent limited number of image frames per cardiac cycle and out-of-plane motion can result in significant decorrelation between frames. Additionally, signal dropout, attenuation and anatomic related artifacts (*e.g.,* sternum, rib or lung related multipath reverberation or shadowing) can degrade image quality. To partially compensate for these artifacts, several groups have developed image processing techniques that include clutter and artifact reduction using finite impulse response (FIR)

Address correspondence to: Jeffrey W. Holmes, MD/PhD, Department of Biomedical Engineering, University of Virginia Box 800759, Charlottesville, VA 22908, USA. E-mail: holmes@virginia.edu

filters (Lediju et al. 2009) and principal component analysis (Gallippi and Trahey 2002; Mauldin et al. 2011).

Another approach to compensate for artifacts in cardiac motion estimation is the use of mathematical models. Using this approach, mathematical models can operate as filters by imposing geometric constraints on allowed myocardial motion, to discard and correct improbable motion estimates derived from motion tracking techniques. These constraints might include requiring strains or displacements to be locally smooth or to vary spatially in ways determined by the geometry of the heart. One particularly useful constraint arises from the fact that myocardium is composed primarily of water, and movement of blood in and out of the coronary vessels over a cardiac cycle produces volume changes of less than 4% (Judd and Levy 1991). As a result, myocardium is nearly incompressible; that is, the total volume of any region is nearly constant throughout the cardiac cycle. This is a particularly attractive constraint because it holds locally and requires no assumptions about heart geometry, material properties, or loading. For example, models using tissue incompressibility as a constraint have been used to improve both automated segmentation (Hansegard et al. 2007; Garson et al. 2008; Zhu et al. 2007a; Zhu et al. 2007b; Zhu et al, 2010) and motion estimation (Bistoquet et al. 2008; Mansi et al. 2010; Touil et al. 2010; Wang et al. 2010).

Models using simple geometric shapes appropriate to the LV have been influential in studying cardiac mechanics. Cylindrical models have been used to predict distributions of stress and strain around the myocardium (Humphrey and Yin 1989; Costa et al. 1996), and to estimate material properties of the myocardium (Guccione et al. 1991). While these models have been instrumental in understanding ventricular mechanics, they are generally taken to represent only a mid-ventricular section of the LV and are inadequate in modeling regions near the apex. In addition, they frequently assume that deformation is axisymmetric, limiting their application in settings such as myocardial infarction (MI), where ventricular remodeling and dyssynchrony give rise to substantial regional variation in cardiac deformation. Other models using prolate spheroidal and realistic heart geometries have had better success in describing motion near the apex, as well as regional ischemia and dyssynchrony (Arts et al. 1992; Kerckhoffs et al. 2009). However, increasing anatomic fidelity in such models comes at the cost of steeply increasing computation time and the need to utilize highly specialized modeling software, limiting their routine use in fitting and interpreting imaging data. In this paper, we derive a kinematic model in cylindrical polar coordinates. The model allows radial (r), circumferential (θ) and longitudinal (z) displacements to vary as polynomial functions of initial position R, Θ, and Z within a realistic initial geometry, incorporating the additional constraint of near incompressibility within the myocardium. This formulation allows more freedom in describing cardiac motion while retaining the advantages of enforcing incompressibility in enhancing physical consistency of the reported displacements.

MATERIALS AND METHODS

Mouse heart imaging and motion estimates

Our mathematical heart model was validated using *in vivo* ultrasound mouse data. The animal experiments in this study followed a protocol approved by the University of Virginia Animal Care and Use Committee. Short-axis (SA) and long-axis (LA) cine B-mode images of six healthy male C57 BL/6 mice (10- to 12-wk old, 24 to 26 g) were acquired using a VisualSonics Vevo 2100 scanner (Toronto, Ontario, Canada) with a MS400 transducer operating at 30 MHz, with 50 μm axial and 110 μm lateral resolutions (Foster et al. 2009). Imaging frame rate was approximately 350 frames per second (fps), and the average heart rate of mice under anesthesia was 462 ± 14 bpm (beats per minute). To achieve this frame rate, the field of view (FOV) was approximately 7 mm × 7 mm with standard line density and a single focal zone centered at the mouse left ventricle (LV). During scanning, the mouse was carefully maintained under anesthesia using isoflurane at approximately 1.5–1.8%, mixed with atmospheric air. Body temperature was maintained at 37 ± 0.2°C by a heated platform under the animal and an incandescent lamp, and body temperature was monitored with the aid of a digital thermometer. ECG signals were obtained using ECG electrodes integrated into the heating platform. A constant body temperature was important in maintaining a consistent heart rate. A stack of serial SA images was acquired at 0.5 mm intervals, with 10 to 12 slices from base to apex. An orthogonal stack of six to eight LA images, also using 0.5 mm intervals, was acquired across the LV of each mouse. All mice underwent MI *via* 1-h occlusion of the left anterior descending (LAD) coronary artery followed by reperfusion (Yang et al. 2002). Post-infarct mice were assessed using ultrasound 28 d after MI with the same acquisition parameters (one mouse died after surgery, and another mouse was excluded due to poor ultrasound data). Average heart rate for MI mice was 561 ± 54 bpm. Displacement fields across the myocardium were determined by speckle tracking with approximately 0.2 mm × 0.2 mm pixel block size using a minimum sum absolute difference (MSAD) algorithm and parabolic fit derived sub-pixel resolution (Li et al. 2007). The MSAD algorithm provides approximately equivalent performance to more computationally intensive tracking