Myocardium material properties estimation

**Works & Limitations**

Kolawole et al. (2025) – Human data “Characterizing variability in passive myocardial stiffness in healthy human left ventricles using personalized MRI and finite element modeling”

<https://github.com/Fikunwa/LV-passive-myocardial-stiffness/tree/main> (An executable version of the passive material parameter optimization code, along with an example finite element model)

Work summary (abstract)

Altered passive stiffness: important biomarker of maladaptive remodeling + implicated in the etiology of several heart diseases (e.g. heart failure).

Although passive myocardial stiffness can clinically be inferred from the end-diastolic pressure-volume relationship of the left ventricle (LV), this measure reflects an apparent stiffness affected by ventricular geometry, rather than intrinsic myocardial stiffness. For example, a thicker heart wall requires more force to deform compared to a thinner heart wall of the same intrinsic stiffness. This results in higher apparent stiffness, though the intrinsic material stiffness remains constant.

The mechanisms driving changes in passive myocardial stiffness and their effects on heart disease progression are not yet fully understood. This gap has led to the development of cardiac biophysical models aimed at estimating the material parameters governing the mechanical behavior and stiffness of in vivo passive myocardium. The mechanical behavior of a material can be described by a constitutive relation which defines the relationship between stress and strain under various loading conditions, through a set of material parameters.

MRI-based inverse finite element modeling (FEM) has proven effective for identifying subject-specific passive myocardial stiffness, as demonstrated by several research groups **2–4**. Recent contributions to the field of MRI- based cardiac mechanics include validation **5**, uncertainty quantification **6,7**, assessing the impact of boundary conditions **8,9** and residual strains **10**, improvement of the optimization strategy **11**, development of constitutive models of myocardium **12**, and improving the identifiability of passive myocardial stiffness **13**.

When provided with cardiac geometry, microstructural configuration of cardiomyocytes, boundary conditions, kinematics, and end-diastolic (filling) pressure(s), then inverse FEM methods can be used to derive the parameters of the material law that describe the myocardium’s mechanical behavior. End-diastolic pressure(s) can be measured invasively through catheterization or estimated non-invasively (e.g. by mitral flow velocity **14**).

Cardiac surface geometry is best determined from conventional cine balanced steady-state free-precession (bSSFP) MRI as it offers exceptional signal-to-noise ratio and high contrast between myocardium and blood, facilitating excellent delineation of endocardial and epicardial borders **15**. Local kinematics, a measure of the deformation of specific regions of the heart, can be measured using tagged MRI **16** or cine DENSE MRI **17**, and

cardiac microstructure can be assessed non-invasively using in vivo cardiac diffusion tensor imaging (cDTI) **18**.

However, to our knowledge, no study has integrated subject-specific in vivo cDTI, cine bSSFP, and tagged MRI into personalized in silico passive mechanics models. This is partly due to the challenge of acquiring comprehensive, high-fidelity imaging data and the lack of an established framework for combining these benchmark data into a single personalized in silico mechanics model. Additionally, there is a need to better characterize the range of

healthy in vivo myocardial behavior to improve our understanding of cardiac dysfunction.

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Herein, we acquired high fidelity in vivo MRI data-including cine bSSFP, tagged MRI, and cDTI-from healthy adult subjects (N=7) with no cardiovascular disease (male & female, 22-32 years, BMI 22-28). We developed a framework for integrating all the subject-specific MRI data into FEM representations of the left ventricle (LV).

Using this framework, we calibrated the passive myocardial stiffness of each subject’s personalized LV mechanics model based on local kinematics. In addition, we evaluated how variations in cardiomyocyte orientations and loading conditions affect the estimated passive myocardial material parameters. This study not only provides a range of reference values for passive myocardial stiffness in healthy individuals, but also demonstrates the

influence of different factors on variability in these estimates.

Limitations

* The passive myocardial stiffness estimates obtained in this work were not validated. The patient-specific data used to evaluate in vivo passive myocardial stiffness are unavoidably subject to uncertainty that would propagate into the final stiffness estimates. In our previous work, we addressed elements of this validation challenge by implementing a similar MRI and FEM-based passive myocardial stiffness estimation method in isotropic myocardium-mimicking heart phantoms of known stiffness **5 – EASIER IN A WAY, ISOTROPIC MATERIAL AND A WHOLE PHANTOM, NOT AN ISOLATED REGION AS IT COULD BE THE HYDROGEL AREA**. In that study, we demonstrated that MRI-driven computational constitutive modeling can be used to accurately estimate synthetic heart material stiffnesses in the range of 200-500 kPa. Future work can involve more robust uncertainty quantification and sensitivity analysis for each input used in this study to better understand the precision of our approach.
* Additionally, higher performance MRI scanners than those which we used here would enable better quality cDTI images (i.e. higher resolution, higher SNR), enabling more effective evaluation of cardiac microstructure.
* Although estimated residual stresses in the in vivo heart are well documented **57**, we did not incorporate this effect and assumed the diastasis cardiac phase corresponding to the start of atrial systole as the unstressed configuration. Algorithms for unloading the prestressed geometry exist 58,59, but they require prior knowledge or assumptions about the material properties as the calculated residual stresses are affected by the chosen material parameters. Additionally, there isn’t a universally accepted approach for identifying the residual stresses and current published approaches have yet to be validated using the suite of patient-specific data acquired in our study. Moreover, the lack of an end-diastolic pressure trace meant we did not have the minimum LV pressure, an important piece of information necessary for unloading. Given that the diastasis pressure is generally nonzero and positive, we expect that unloading the models to an unstressed state prior to material parameter calibration would lead to a softening in the estimated passive myocardial stiffness parameters.
* Furthermore, despite evidence of orthotropy in myocardium, we used a transversely isotropic material model. This is because our cDTI acquisition is mostly sensitive to diffusion in the fiber direction, without providing distinct information about sheetlet orientation. When this data becomes available, the passive stiffness estimation framework could easily be extended to incorporate orthotropic material models. Generally, acquisition of myocardial microstructure with cDTI is challenging, as evidenced by the failure to get adequate personalized fiber orientations in Subject-4. In this subject, we used the R60,−60 rule-based description in place of personalized fibers as necessary.
* Lastly, it is important to acknowledge that currently, both the MRI examination and the subsequent image processing, model building, and material parameter optimization are prohibitively complex and time intensive. Hence, there is a need for efforts focused on streamlining or expediting various aspects of the pipeline.

Mojsejenko et al. (2014) – Porcine data “Estimating passive mechanical properties in a myocardial infarction using MRI and finite element simulations”

Work summary (abstract)

The goal of the current study is to quantify the in vivo material properties of infarcted and remote myocardium 1 week after MI, as well as the orientation of collagen fibers in the infarct (**we have 3 days post MI** **data too**). This will be accomplished by using a combination of magnetic resonance imaging (MRI), catheterization, finite element modeling, and numerical optimization to analyze a porcine model (*N*= 4) of posterolateral myocardial infarction (**need to check what type of MI we have and whether this plays a role?**). IT

In spite of the importance of infarct material properties on infarct expansion, little data exist on the time-dependent changes in this critical parameter during the remodeling process [**WE HAVE TWO TIME POINTS AFTER MI TO TRACK THIS VARIATION**]. Such data are crucial to a full understanding of MI-induced LV remodeling as well as for the development of new and more effective therapies to treat and/or prevent the development of heart failure after MI [they report experimental works in literature that have tried to do this].

Techniques have been developed that use a combination of magnetic resonance imaging (MRI), catheterization,and finite element modeling in order to estimate in vivo myocardial material properties in a noninvasive manner. In all of these studies, the finite element models were based on anatomically correct geometry, which was contoured from MRI data [they report works in literature that have tried to do this].

Each of the aforementioned in vivo and isolated heart studies focused on determining properties only in viable myocardium. To our knowledge, no such studies have determined the in vivo passive material properties of a myocardial infarction. The goal of the current study is to **quantify the in vivo material properties of infarcted and remote myocardium in a porcine model 1 week after MI** [we have also another point in time + hydrogel], as well as **the orientation of collagen fibers in the infarcted zone, rather than assigning them a priori** [maybe we can optimize this too?]. This will be accomplished by using a combination of MRI, catheterization, and finite element modeling. Properties will be determined by using an optimization scheme to minimize the difference between in vivo strains and volume calculated from MRI and finite element model predicted strains and volume. This investigation will ultimately provide a means of predicting remote and infarct mechanical properties at any time point post-MI.

GENETIC ALGORITHMS USED? PROBABLY THAT IS WHAT IS NEEDED IN MY CASE TOO

Limitations

There are several limitations associated with the approach presented in this work. In the current study, and the study by Xi et al. (2013), average myofiber angles were assigned to the myocardium, which does not fully represent the spatially varying fiber architecture. In the future, fiber angles will be based on DTMRI data, similar to the study by Wang et al. (2009), in order to incorporate more accurate spatial variation.

Another limitation that affects the current study, as well as several previous studies, is the absence of a pericardium and a right ventricle (RV) in the FE model. The RV not only affects the pressure loading on the septum, but also the deformation that is induced by the interaction between the LV wall and RV insertion points, as seen in Fig. 8 of the current study. These effects could alter the resulting parameters and will be incorporated in the future studies.

Additionally, the reference configuration of the FE model was based on early diastole, where pressure is at a minimum, but the ventricle is still partially loaded. In the future, techniques for determining the unloaded geometry will be incorporated, similar to Krishnamurthy et al. (2013). It has been shown by Xi et al. (2013) that there may be residual active tension in the myocardium at early diastole, which was not taken into account in the current work. While this is not a concern in the infarct region, since there are no contracting myocytes, this could affect the remote region leading to different mechanical properties.

Alterations to the border-zone properties were not addressed. In terms of the transition in material properties between the remote and infarct, it is difficult to see a gradient in fibrosis in the border zone when viewing the LGE images. The MI boundary appears to be very stark. Therefore, it was assumed that the border-zone gradient was not yet defined. Further experimental work is needed to define the border zone at 1 week post-MI.

Finally, the strain field that was calculated from the 3D SPAMM images contained a small amount noise. This was minimized as much as possible by smoothing the strain at each point of interest with the neighboring values.

McGarvey et al. (2015) – Porcine data “Temporal Changes in Infarct Material Properties: An In Vivo Assessment Using Magnetic Resonance Imaging and Finite Element Simulations”

Work summary (abstract)

Infarct expansion initiates and sustains adverse left ventricular (LV) remodeling after myocardial infarction (MI), resulting in ventricular dilatation, loss of global contractile function, and symptomatic heart failure. Infarct expansion that occurs concomitantly with the onset of ischemia is readily explained by loss of active contraction of the infarct region.

the infarct region ceases to contract and is subjected to the hemodynamic load produced by the remainder of the ventricle. This abnormal loading results in thinning and stretching of the infarct and in increased mechanical stress in the perfused border zone region adjacent to the infarct. These time-dependent changes determine the extent of infarct expansion and, therefore, the fate of the entire LV. In spite of the central role that infarct material properties must play in the remodeling process, few quantitative data exist that describe their temporal changes after MI. We have recently described a technique that uses LV strain measurements based on magnetic resonance imaging (MRI) and finite element (FE) simulations **[2 - Mojsejenko].** We applied this new approach to study a posterolateral infarct in pigs.

Nikou et al. (2015) – Porcine data “Computational Modeling of Healthy Myocardium in Diastole”

NOTES:

VALIDATION IS DEFINITELY A BIG GAP

FIBER ORIENTATION – Maybe lifex-fibers provides more accurate fiber definition rather than R60, -60 rule in absence of personalized fibers

INCLUSION OF PRESTRESS – Maybe I can include/exclude them and see whether this impacts parameter estimation

Do people have so many points in time post-MI? I have day-3, day-7 in which I can track material properties change (if any), same after hydrogel delivery and validation with that

By Thursday when you talk to Martin:

* Try fiber generation (lifex-fiber) and understand whether this is better/more accurate than what people do
* Understand how we could include/exclude prestresses (maybe even with different constitutive models)
* Properly understand available dataset and design the study:

From Midgett et al. (2022)

*Serial in vivo cineCT imaging provided data in hearts from control pigs (n =3) and data from pigs (n =5) under baseline conditions before MI induction, post-MI day 3, post-MI day 7, and one hour after intramyocardial delivery of a hyaluronic acid (HA)-based hydrogel with shear-thinning and self-healing properties to the central infarct area.*

* Understand then how physics-informed NN can be included in a more systematic and robust way – Chen et al. (2025) “**Deep Learning-Based Estimation of Myocardial Material Parameters from Cardiac MRI”**
* Show him tutorial video of AngioIVUS tool, discuss methodologies, how they got from points definition to vessel centerline definition to orientation of planes

LAGRANGIAN AND EULERIAN STRAINS:

Imagine stretching a rubber band:

* **Lagrangian**: You track a specific point on the rubber band and see how far it moves from its original position.
* **Eulerian**: You stand at a fixed spot in space and observe what material (rubber) passes by and how it deforms there.