Automatic Estimation of Diagnostic Biomarkers for Myocardial Infarction of Left Ventricular Tissue

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Introduction

- Cardiovascular disease is the leading cause of death worldwide
- Coronary heart disease is responsible for 43.8% of these deaths, extreme cases lead to myocardial infarction (MI)
- MI obstructs blood supply resulting in local tissue death
- Pathophysiological changes occur turning the dead tissue into scar
- Scar is thinner and stiffer than healthy myocardium
- Results in less deformation and blood pumping throughout the cardiac cycle

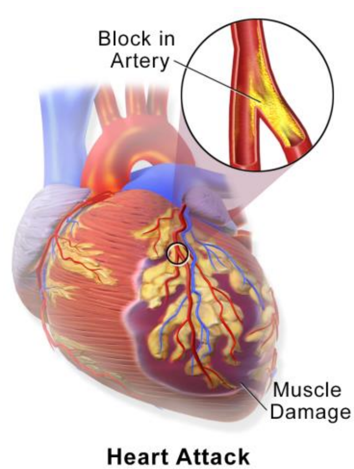


Figure 1. Example of Myocardial Infarction

Introduction

What is a Biomarker?

- Are a broad range of quantitative measurements
- Are objective medical signs that measures the state and progress of disease or the effects of therapeutic intervention
- Examples: blood pressure, presence of certain molecules or proteins, heart rate, etc.

Objective

- Development of an algorithm that automatically calculates three predictive biomarkers for Left Ventricle Infarction
    1. LV Wall Thickness
    2. Ejection Fraction
    3. LV Wall Deformation
- Investigate the use Laplace's Equation to capture left ventricle thickness
- Robustly calculate Ejection Fraction and LV Wall Deformation
- Use to diagnose the extent of infarction and determine the correct treatment/prognosis of patient without the need of contrast enhanced imaging

Methods and Procedure

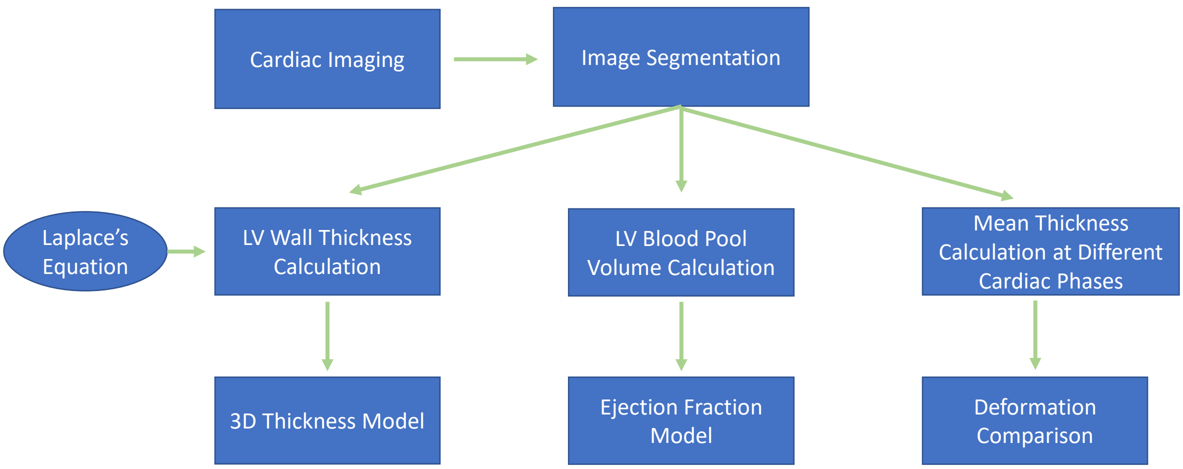


Figure 2. Methods and Procedure Flow Chart

Cardiac Imaging and Segmentation

- CT images of a Pig's heart eight weeks post infarction were taken at end diastole and end systole
- The heart at two different phases in the cardiac cycle were segmented using 3D Slicer
- Segmented LVs were transferred to MATLAB for calculating myocardial thickness

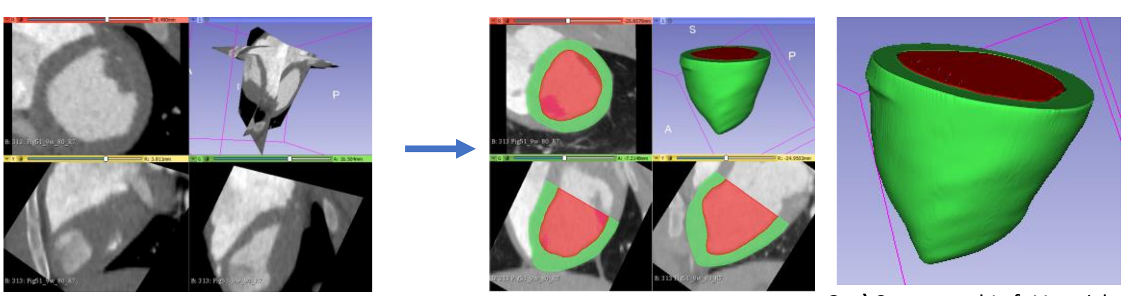


Figure 3. a) Pig Heart (LV) CT Images

3. b) Segmented Pig's Heart (LV)

3. c) Segmented Left Ventricle Wall and Blood Pool Model

LV Thickness Calculation

- Outer LV wall set to a fixed value of 1 and inner LV wall set to a fixed value of 0
- Laplace's Equation (Computational Method) is solved iteratively:

$$\psi_{i+1}(x,y) = [\psi_i(x+1,y) + \psi_i(x-1,y) + \psi_i(x,y+1) + \psi_i(x,y-1)]$$

- The resulting ψ is a smooth transition from $\psi = 1$ to $\psi = 0$

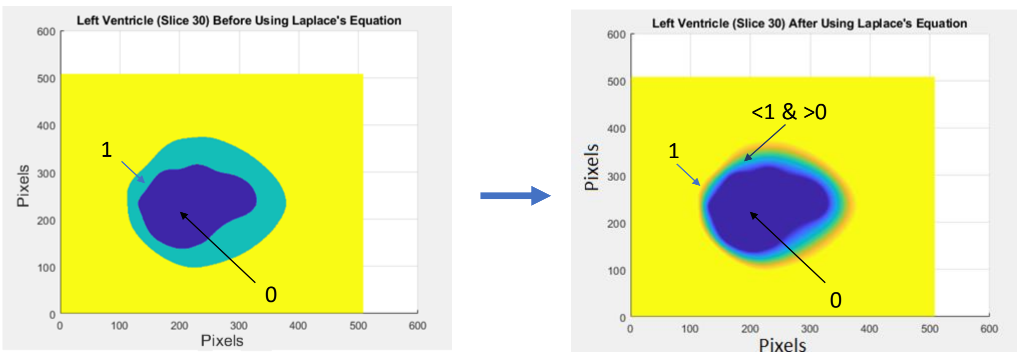


Figure 4. a) LV Slice 30 Before Laplace's Equation

4. b) LV Slice 30 After Laplace's Equation

LV Thickness Calculation

- Iterations continue until the percent difference of the elements is less than a set threshold of 1×10^{-5}
- Percent Difference Formula:

$$(\epsilon_i - \epsilon_{i+1}) / \epsilon_{i+1}$$

- Convergence is reached after a few hundred iterations

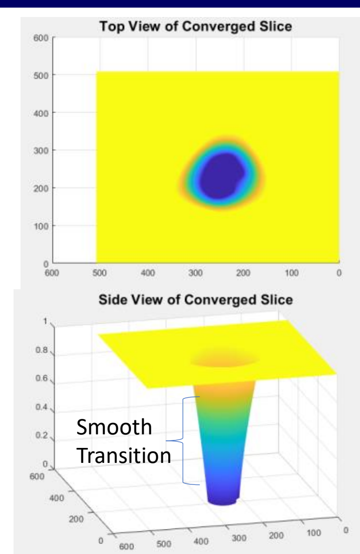


Figure 5. Converged Top and Side Slice View

LV Thickness Calculation

- Once the solution of ψ is obtained, streamlines are calculated with the forward difference of the rows and columns of the scalar field (e.g. dx ψ(x,y) = -[ψ(x,y + 1) - ψ(x,y)])
- Which is normalized by dividing the vectors by its magnitude (e.g. dx ψ(x,y) = dx ψ(x,y) / magnitude)
- Creates unit vectors pointing from the outer LV wall in the shortest path to the inner LV wall

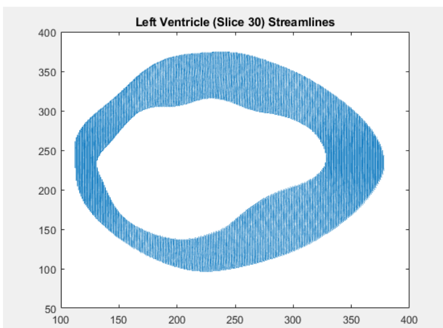
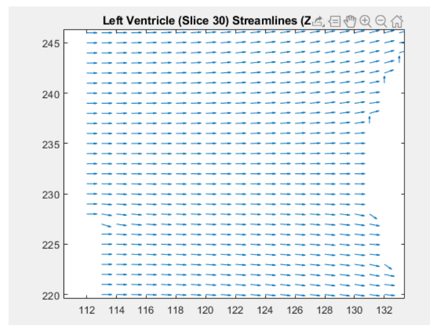


Figure 6. a) LV Slice 30 Streamlines



6. b) LV Slice 30 Streamlines (Zoomed In)

LV Thickness Calculation

- Euler's method is used to calculate thickness by following the unit vectors from one border to the other
- Each thickness value is stored and assigned a colour
- Larger Thickness = Lighter Colour
- Smaller Thickness = Darker Colour

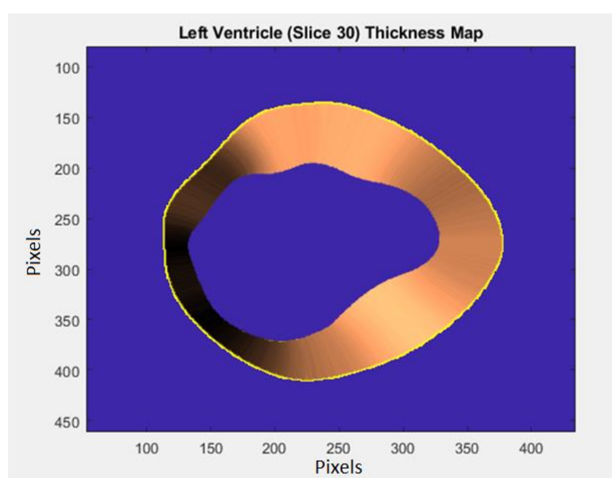


Figure 7. LV Slice 30 Thickness Map

3D Left Ventricle Thickness Model

- Thickness map of each slice of the left ventricle is stacked on top of each other
- Creates a 3D thickness model of the left ventricle

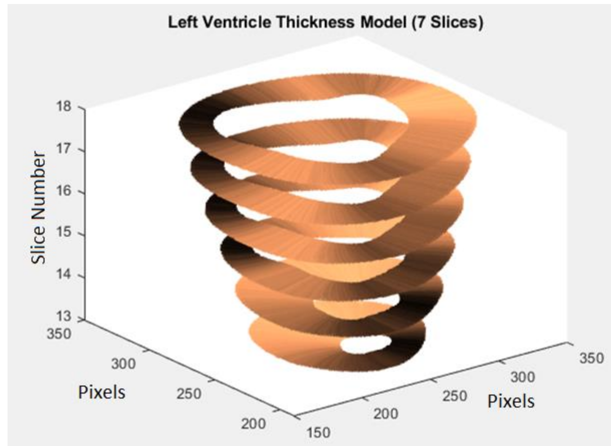


Figure 8. LV Thickness Model (7 Slices)

Results

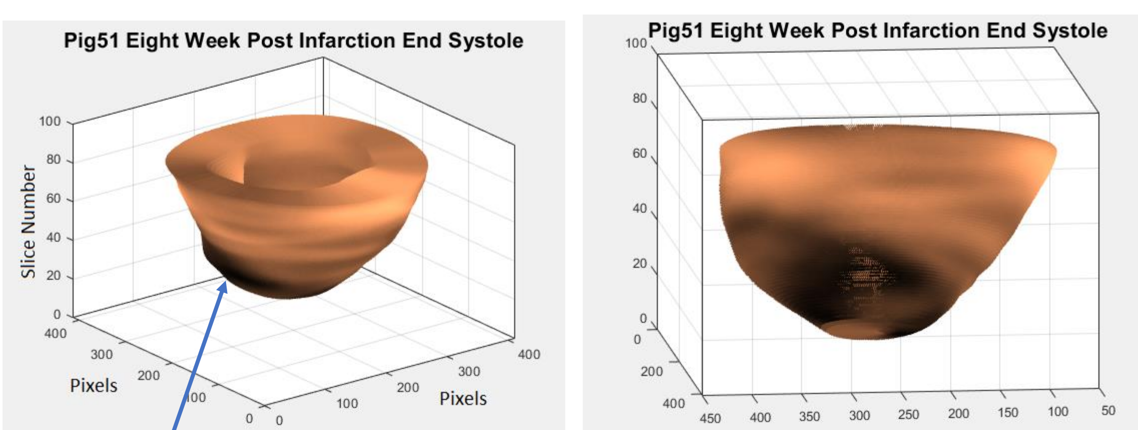


Figure 9. Full LV Thickness Model at End Systole

Results

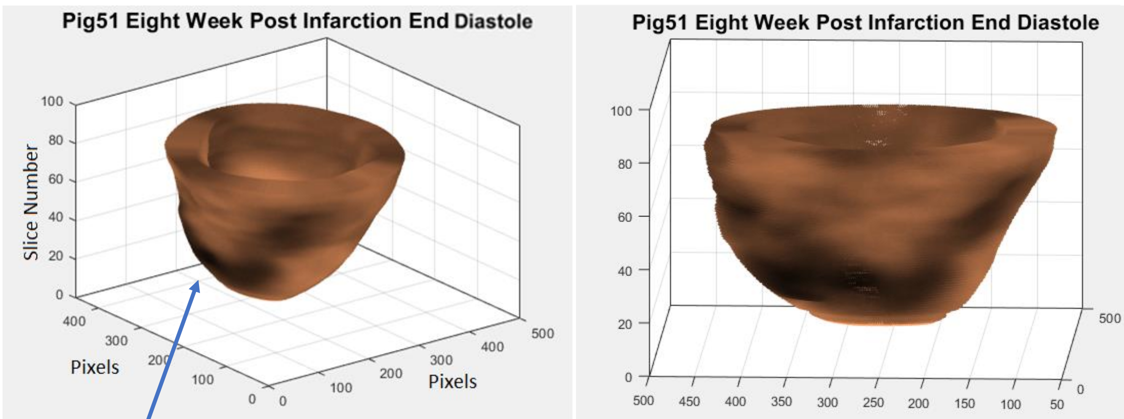


Figure 10. Full LV Thickness Model at End Diastole

Ejection Fraction Calculation

- **Ejection fraction** (EF) is a measurement of the amount of blood the left ventricle pumps out with each contraction, expressed as a percentage
- EF Formula: $EF(\%) = \frac{SV}{EDV} \times 100$
- SV = Stroke Volume

  SV Formula: $SV = EDV - ESV$
- EDV = End Diastolic Volume
- ESV = End Systolic Volume

Healthy Ejection Fraction is between 50% to 70%

Ejection Fraction Calculation

Procedure

1. Load Blood Pool Segmentations into MATLAB
2. Determine Voxel Dimensions
3. Find Volume of one Voxel
4. Compute Blood Volume at Each Phase with Total Voxel Volume
5. Calculate Stroke Volume using newly calculated EDV and ESV
6. Solve for Ejection Fraction

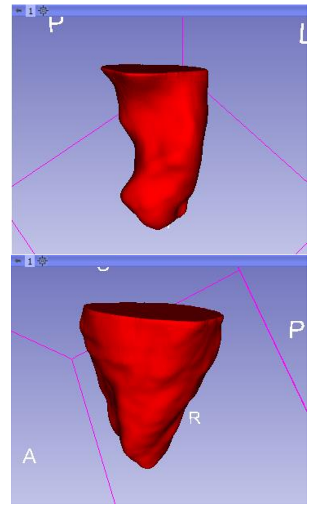


Figure 11. Blood Pool Segmentations at ED and ES

Results

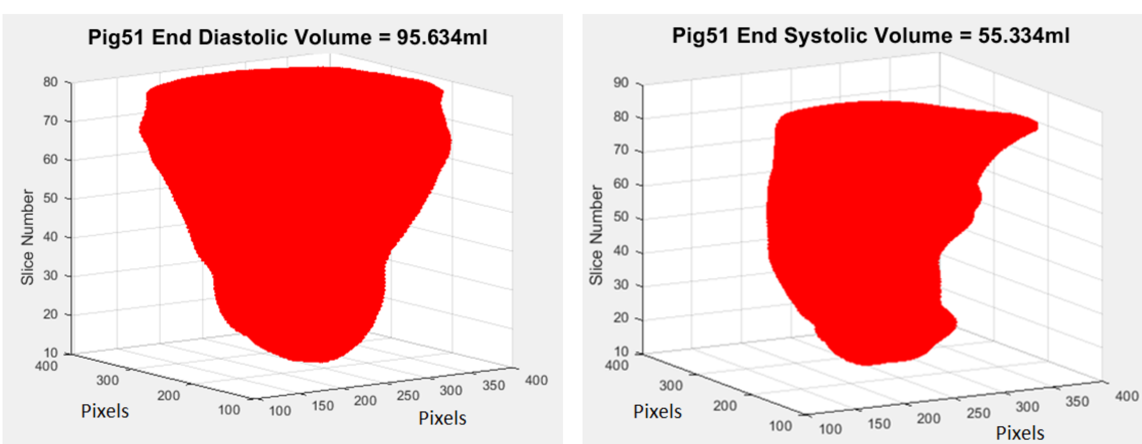


Figure 12. Blood Pool Volumes

Results

$$\text{Pig51 Ejection Fraction} = \frac{SV}{EDV} \times 100$$

$$\text{Pig51 Ejection Fraction} = \frac{EDV - ESV}{EDV} \times 100$$

$$\text{Pig51 Ejection Fraction} = \frac{\text{95.6ml - 55.3ml}}{\text{95.6ml}} \times 100$$

$$\text{Pig51 Ejection Fraction} = 42.2\%$$

LV Wall Deformation Comparison

Procedure

Load Previous LV Thickness Map

↓

Calculate Mean Wall Thickness for Ever Slice of LV

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Mean Thickness Calculation at End Diastole and End Systole

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Plot and Compare Change in Wall Thickness

Results

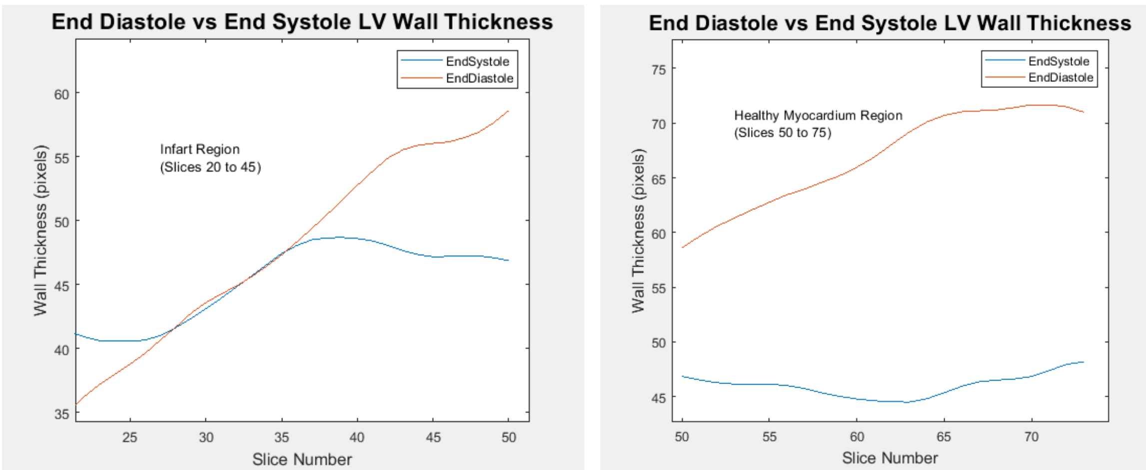

Figure 13. Wall Deformation Comparison (Slices 20 to 45 vs Slices 50 to 75)

Results

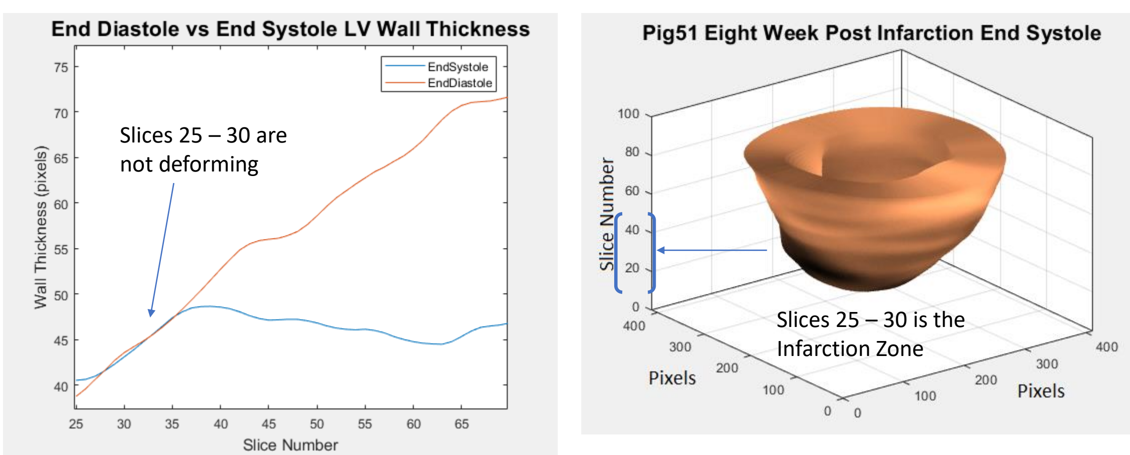

Figure 14. Wall Deformation Comparison (Slices 20 to 75)

Conclusion

- An algorithm is presented that can accurately and automatically determine three predictive biomarkers for LV Myocardial Infarction
- It effectively identified the wall thickness to localize infarction zones of the LV in different phases of the cardiac cycle (End systole and End Diastole)
- Robustly determines ejection fraction
- Accurately compares wall deformation to determine tissue health and functionality
- Algorithm provides useful diagnostic and prognostic information useful in the clinic

Further Work and Improvement

- Use of more accurate methods of thickness calculation like Runge-Kutta of Euler's method
- Extend the algorithm to 3D where the entire segmentation can be used at once instead of solving for each slice
- Create Finite Element Model of the Left Ventricle and use Stiffness Matrix to more accurately calculate wall deformation

References

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Jones, S. E., Buchbinder, B. R., & Aharon, I. (2000, August 7). Three-dimensional mapping of cortical thickness using Laplace's Equation. https://onlinelibrary.wiley.com/doi/pdf/10.1 002/1097-0193(200009)11 :1<12::AID-HBM20>3.0.CO;2-K

References

Wisneski, J. A., Pfeil, C. N., Wyse, D. G., Mitchell, R., Rahimtoola, S. H., & Gertz, E. W. (1981). Left ventricular ejection fraction calculated from volumes and areas: underestimation by area method. *Circulation*, *63*(1), 149–151. https://doi.org/10.1161/01.cir.63.1.149