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ANALYSES OF THE DEVICE-TISSUE INTERFACES OF PREVIOUSLY IMPLANTED STENTS WITHIN PERFUSION-FIXED HUMAN HEARTS UTIILIZING MICRO COMPUTED TOMOGRAPHY

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ABSTRACT

Coronary artery disease can be caused by partial or total occlusions of the coronaries, leading to cardiac ischemia. Today, the percutaneous implantation of stents is the most common treatment to open such blockages and thus restore oxygen delivery to the myocardium. Subsequent stent calcification or restenosis may hinder the effectiveness of these stents over time. The Visible Heart® Laboratories have a collection of 30 perfusion-fixed human hearts that had a total of 35 such intervention prior to organ donation. Micro computed tomography (micro CT) can be used to study the device-tissue interfaces of stents implanted up to decades prior to recovery. These procedures were scanned with approximately 40-micron resolution. Computational models were generated such that calcification and restenosis could be visualized and quantified. Within this unique data-set, there was a wide variety of stent length, location, and volume of calcification present. Although 90% of the cases had varying degree of calcification present outside the stent only 11% showed any degree of restenosis. This is a unique research opportunity to micro CT scan 35 cases of therapeutically implanted stents in perfusion-fixed specimens. Extensive visualizations and analyses can be performed on generated computational 3D models, so to provide for better understanding of the variations within the device-tissue interfaces of therapeutically implanted stents.

Keywords: stenting, calcification, percutaneous intervention, micro CT

1. INTRODUCTION

The coronary arteries are responsible for oxygenating all cardiac tissues, including myocardium. Oxygenated blood enters the coronary arteries mainly during diastole through both the left and right coronary ostia. The left coronary ostium leads to the left main coronary artery (LCA) that branches into the left anterior descending (LAD) artery and the circumflex artery to oxygenate the left anterior and posterior regions of the heart respectively [1]. The right coronary ostium leads to the right coronary artery (RCA) with branches that provide oxygen primarily to the right, posterior region of the heart.

Coronary artery disease (CAD) remains as the most prevalent form of heart disease in the United States, affecting 7.2% of adults over the age of twenty and resulting in approximately 361,000 fatalities annually [2]. CAD can be caused by partial or total calcium occlusions of the coronaries, blocking the flow of oxygenated blood to the heart, thus leading to cardiac ischemia. Additionally, the lack of oxygen may ultimately lead to a cardiac infarction or a “heart attack”. Percutaneous coronary intervention (PCI) using stents is the most common treatment to open such blockages which aids to restore oxygen delivery to the myocardium. Subsequent stent calcification or restenosis may hinder the effectiveness of a given stent over time and even require further treatment. Restenosis occurs in approximately 10% of PCI procedures, and is more likely to occur in complex cases such as bifurcation procedures [3].

Micro computed tomography systems (μCT) utilize high field X-rays to scan an object and then reconstruct 3D models. By employing high resolution and gray scale differentiation, micro CT allows for detailed imaging and segmentation of complex anatomies including cardiac tissue, devices, and/or calcification [4]. Additionally, quantitative measurements can be done on the resulting computational models to obtain additional insights [4].

The Visible Heart® Laboratories have a collection of over 30 perfusion-fixed human hearts that had a total of 35 PCI procedures prior to organ donation. Micro computed tomography (micro CT) can be used to study the size, shape, and device-tissue interfaces of stents implanted decades prior to recovery.

2. MATERIALS AND METHODS

The lab was privileged to obtained fresh human hearts for research; these unique specimens had clinically implanted stents in various locations and then were perfusion fixed. Subsequently, for each the device-tissue interfaces were micro CT scanned. 3D models of the stent deployments and present occurrences of calcification were visualized and measured for analysis. Thirty-seven PCI procedures were modeled and analyzed, including: 12 in the RCA, 5 in the LCA, 13 in the LAD, and 5 in the circumflex arteries.

2.1 Sample Preparation

Via a collaboration with Lifesource, the Visible Heart® Laboratories receives fresh human heart donations when they are not deemed viable for transplant. To date, we have obtained approximately 30 hearts with stents clinically implanted prior to donation; as indicated by the included medical histories. Each heart was cannulated and formalin-fixed in an end-diastolic state using a perfusion-fixation apparatus and 10% formalin [5]. Using this system, the coronary vessels were perfused and remained patent during fixation.

2.2 Computational Modeling

The implanted stents, as well as the entire hearts were imaged using the X3000 micro computed tomography (CT) scanner (North Star Imaging, Rogers, MN). The scan parameters were optimized such that a wide range of densities could be visualized so that the metal, calcification, and cardiac tissue could be identified and differentiated. The resulting parameters were approximately 1200 radiographs, 170 kV, 400 mA, and 10 frames per second. The whole hearts were scanned at approximately 90-micron resolution to determine the stent locations (Figure 1A). An additional detailed scan of each procedure was done at approximately 40-micron resolution (Figure 1B). The obtained 2D radiographs were then reconstructed into 3D representations that were exported for further analyses.

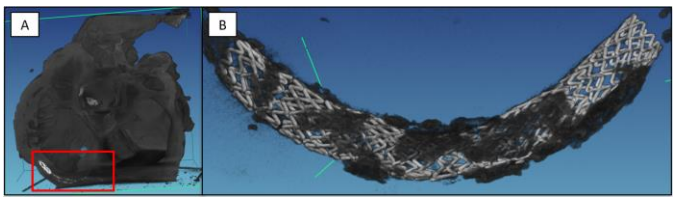

FIGURE 1: (A) A micro CT reconstruction from a formalin fixed human heart with a previously, clinically implanted stent (red box) and (B) detailed micro CT reconstruction of the stent procedure

The 2D slices exported from the micro CT reconstruction were then imported into Mimics Software (Materialise, Belgium) for detailed segmentation. The image slices were viewed in the coronal, sagittal, and axial planes (Figure 2), and the stent and associated calcium were segmented based on the relative brightness within the image. As shone, the high-density metal of the stent appeared the brightest, followed by the calcification, and the lowest density myocardium, appearing as a darker grey.

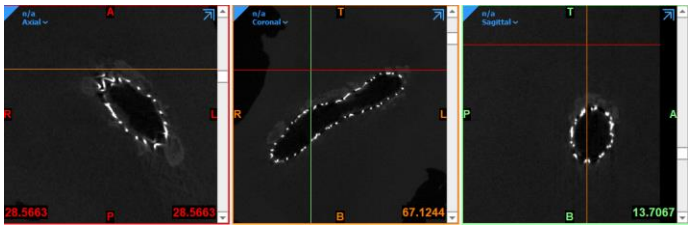

FIGURE 2: Micro CT slices imported into Mimics allowing for axial, coronal, and sagittal views

Using these differences, masks of the stents and calcification and corresponding 3D parts were generated as shown in Figures 3 and 4.

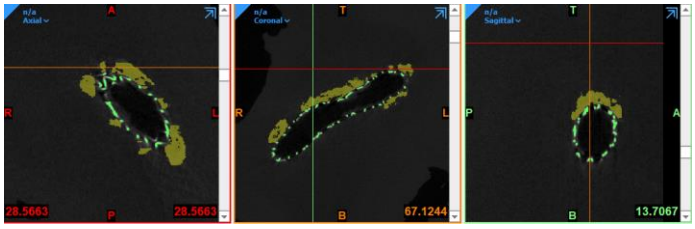

FIGURE 3: Masks of the stent (green) and calcification (yellow)

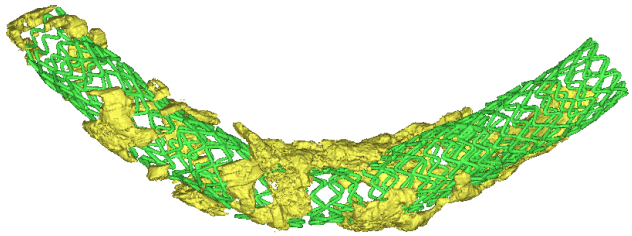

FIGURE 4: 3D parts generated by the masks of the stent and calcification

2.3 Model Analyses

Once the 3D parts were developed, additional analyses and measurements were performed. The sizes of the procedures were characterized using length of a centerline. The 3D part was wrapped using a 3 mm closing distance (Figure 5) so that a centerline could be calculated as shown in Figure 6. The length of the generated centerline was then determined (Figure 6).

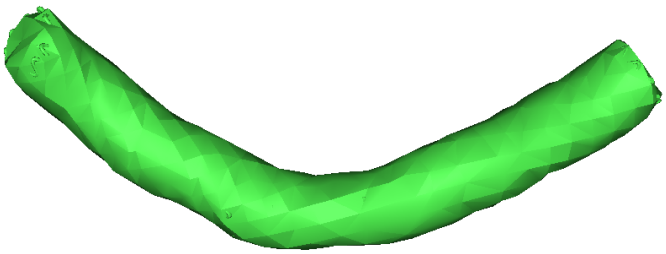

FIGURE 5: Shown is a 3D reconstruction of the wrapped stent used to generate the centerline

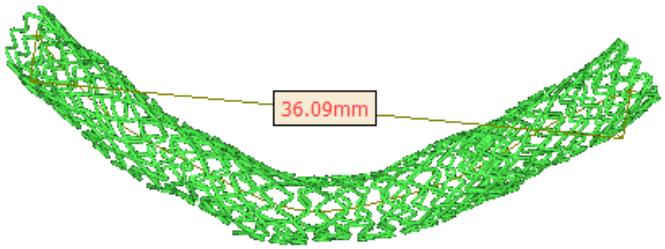

FIGURE 6: The stent with the centerline and the distance measurement indicated

Additionally, the device-tissue interfaces and associated calcification were visualized and quantified. The volumes of calcium present outside the stents were calculated from each calcification model. Relative restenosis was also quantified as the volume of calcification located within the stent structure.

3. RESULTS AND DISCUSSION

Computational models were successfully generated such that the data-set of 35 stents and associated calcification and restenosis could be visualized and quantified. These samples contained a variety of stenting locations, sizes, and procedure types. As shown in Table 1, this particular sample-set elicited a higher prevalence of RCA and LAD procedures compared to the left main and the circumflex arteries. Additionally, four (11%) of the cases analyzed, where 2-stent bifurcation procedures, three of which were located within the LAD. Although there was a wide range of lengths among the analyzed procedures, the RCA and LCA stents tended to be the longest and shortest in length respectively.

Group	Number of Procedures	Number of Bifurcation Procedures	Median Length (mm) (25th-75th Quartiles)
All	35	4	27.19 (16.51-36.84)
RCA	13	1	36.09 (23.41-53.80)
LCA	5	0	16.02 (13.34-29.38)
LAD	12	3	25.41 (17.24-33.17)
Circumflex	5	0	19.06 (15.74-35.56)

TABLE 1: Relative sample sizes of procedures within each region, the numbers of procedures that were bifurcation techniques, and the median lengths of the procedures

The presence of calcification inside a given stent indicates restenosis, as it would have formed after implantation. Although approximately 83% (29) of the analyzed stents elicited some degree of calcification, only 11% (4) had visible plaque within the stent structures (Table 2), which is consistent with the restenosis prevalence observed in previously reported clinical studies. In our studied specimens, the volume of calcification within a given stent procedure ranged from 0.23 to 10.34 mm^3.

Group	Number of Procedures	Number with Calcification Present	Number with Restenosis
All	35	29	4
RCA	13	10	0
LCA	5	4	0
LAD	12	10	2
Circumflex	5	5	2

TABLE 2: Sample size of procedures in each region, and the number of procedures that had calcification and restenosis present

It is expected that stents are placed in locations of a blockage, which was observed in the majority of these cases. The volume of calcification outside the stent structure for each coronary artery is shown in Figure 7. As shown, there is wide variation in plaque for each vessel; however, there were not significant differences between the medians of the various locations.

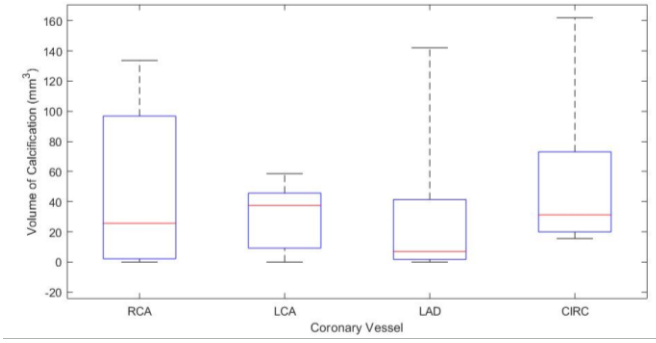

FIGURE 7: Median (red), maximum, (top), minimum (bottom), 25th quartile (top of box), and 75th quartile (bottom of box) for the volumes of calcification located outside of the stent structures, for each artery location

Due to the variation in procedure lengths, the relative volumes of calcification were normalized to the stent length (Figure 8). As shown, in most of the specimens the degrees of stent calcification ranged from one to three mm^3 per mm of stent length.

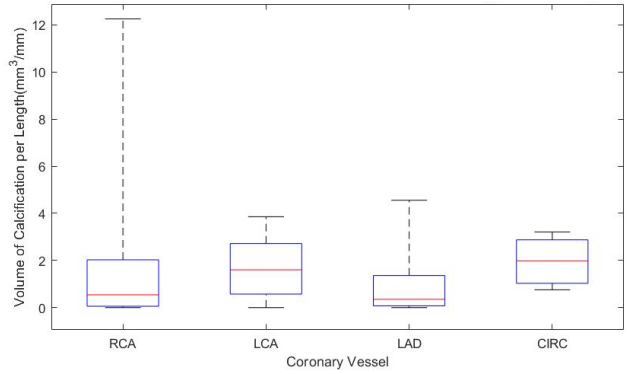

FIGURE 8: Median (red), maximum, (top), minimum (bottom), 25th quartile (top of box), and 75th quartile (bottom of box) for the volumes of calcification located outside of the stent structures, normalized to the stent lengths within each artery location

4. CONCLUSION

Uniquely here, we micro CT scanned human hearts donated for research, with a combined 35 previously, therapeutically implanted stents. Most of these cases elicited calcification between the stent structure and the vessel wall as expected; however, only 11% of the observed procedures presented with any degree of restenosis. Overall, extensive detailed visualizations and analyses were performed from generated computational 3D models, which were also shared on the free access website, the Atlas of Human Cardiac Anatomy. Sharing the models provides an educational resource to physicians and device designers as a means to provide better understanding of the device-tissue interfaces of stents placed in a variety of coronary locations, using varied techniques, and stent types.

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