Communications

Simulated Characterization of Atherosclerotic Lesions in the Coronary Arteries by Measurement of Bioimpedance

David K. Stiles and Barbara Oakley

Abstract—FEM software was used to determine the feasibility of characterizing various types of atherosclerotic lesions in vivo. This was accomplished by simulating two electrodes as being attached to an angioplasty balloon in the coronary artery. The electrodes on the “balloon” touched and measured the simulated complex impedance of type III, -IV, and -Va and -Vb lesions, as defined by the American Heart Association (AHA). Additionally, the effect of changes in morphology on the complex impedance was determined for type Va and -Vb lesions. The simulations showed that the layer closest to the electrodes had the most significant effect on the measured complex impedance. As a consequence of these simulations, it appears plausible that electrodes could be placed in vivo to determine the characteristics and type of a given atherosclerotic lesion.

Index Terms—Atherosclerosis, bioimpedance, conductivity, finite-element, permittivity.

I. INTRODUCTION

Atherosclerotic lesions have been shown to be present in the coronary arteries from a very young age, particularly in western countries. These lesions contribute to one in every five deaths in the United States [1]. As such, there are numerous interventional techniques that have been developed to reduce the effects of the lesions. Perhaps one of the most common technologies is Percutaneous Transluminal Coronary Angioplasty (PTCA). This technique requires a balloon, attached to a catheter, be placed proximate to the coronary lesion that is constricting the flow of blood to the myocardial tissue. The balloon is then inflated to widen the stenosis to approximately the undiseased lumen diameter. A stent may be placed to maintain the lumen diameter after the procedure.

This paper proposes a technique that would provide more information than either intravascular ultrasound (IVUS) or angiography about the type of lesion that is located on the wall of an artery. The technique involves impedance measurements of a lesion by means of an angioplasty balloon with electrodes placed on it.

To test the proposed technique, we used a finite-element method to calculate the simulated impedance of the lesion as well as characteristics such as composition and thickness of the tissue layers. The finite element model (FEM) software package used for this simulation was MESH3 (FEM Mesher) and PAC3, by Field Precision Software.1

II. METHODOLOGY

A. Atherosclerotic Lesions

The lesions that will be discussed are complex lesions of type III, IV, Va, and Vb, as defined by the American Heart Association (AHA) [2], [3]. A type III lesion, or preatheroma, [4] in the coronary arteries is characterized by a muscular outer cap, intimal thickening, and small lipid inclusions. Type IV lesions exhibit further development with a larger lipid core, and are visible to the naked eye. As the lesion progresses to type Va, the lipid core grows, and more collagen and other fibrous materials develop in the muscular outer cap. The type Va lesion has the potential of severely constricting coronary flow, as well as rupturing and creating a thrombus that completely occludes the artery [5]. The type Vb lesion is the largest and most complex stable lesion that can form, and is characterized by the formation of calcium on the outer cap.

The lesions considered for this study are shown in Fig. 1. They range from type III to type Vb lesions. (Highly progressed type VI lesions were not considered due to their complex geometry.) The electrodes were simulated as mounted on a balloon catheter (Fig. 2), which was placed proximate to the lesion. The ac voltage on both electrodes was modeled at five different frequencies: 1 kHz, 100 kHz, 1 MHz, 10 MHz, and 100 MHz. The top electrode was placed at 1 V and the bottom electrode at −1 V (or 1 V at 180° phase). The electrodes were 100 μm in length and spaced 2.5 mm apart.

Each of these lesions is idealized, since there are differences in histology from lesion to lesion. In the case of the type III lesion, the isolated lipid pools and macrophage foam cells are modeled as a thin continuous layer of fat, which may have resulted in an overestimation of their effect on the impedance. Additionally, the boundaries between the various layers will probably not be so clearly delineated in real lesion morphologies. The lesions also were considered to be not so far developed as to be nearly concentric. Most lesions that have not progressed to a highly advanced state are usually eccentric. (A possible reason for this is that the lesion starts at an injury site, and continues growing until it reaches the other side of the artery.) Mintz et al. found that nearly 70% of all lesions measured using IVUS had an eccentricity greater than two, where the eccentricity is measured as the ratio of the maximum and minimum plaque plus media thickness [6].

Values for conductivity and permittivity (Table I) were largely obtained from [7] and [8], though some had to be inferred. The values of the calcified outer layer were inferred from cancellous bone values. Slager, et al. [8] measured the conductivity of the thrombus and artery wall for a frequency range of 5–500 kHz and obtained a single value. This is reasonable, as other investigations researching tissue conductivity reveal relatively constant conductivity values up to about 1 MHz. In this paper, the conductivity values for thrombus and artery were assumed constant up to 1 MHz. Beyond 1 MHz, however, it was assumed that the conductivity of thrombus and artery wall increased slightly, and these values were inferred as shown. Additionally, it was assumed that fibrous tissue had relatively low capacitance due to an extracellular matrix of various collagens. Finally, the capacitance of the vessel wall was assumed to be mostly due to the smooth muscle, combined with the effects of fat.


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Fig. 1. Front cross section of the various types of lesions modeled in the simulations. The geometries are approximate. The constituent parts are (A) blood, (B) vessel wall, (C) lipid core, (D) Smooth muscle, (E) vacuum (balloon), (F) fibrous tissue, and (G) calcium.

Fig. 2. Electrodes on a balloon catheter that is expanding to make contact with an artery. Twenty-four four-point electrodes are shown around the balloon. As the balloon expands, the blood is displaced. For simplicity, only one of the electrodes was modeled in situ.

For this analysis, two conditions were considered: the impedance of all four types of lesions, and the impedance due to morphology changes in the type Va and Vb lesions. In the type Va and Vb lesions, the thickness of the layers was changed and analyzed at each frequency. The minimum lumen diameter and maximum layer thicknesses are shown in Tables II and III. The values for the thicknesses are proportionally smaller than the thickness found in the aortic lesions observed by Slager, et al. They have been approximately modeled after the cross sections observed in excised coronary tissue, such as in [9]. The investigation herein shows whether impedance measurement might allow for differentiation between various morphologies, such as those in Tables II and III. Ideally, it would be desirable to determine the amount of fibrous tissue, calcium, and smooth muscle that exists in the lesion. This investigation also shows that this might indeed be attainable in practice.

In an actual in vivo configuration, a conventional four-point electrode would be used to reduce the effects of the impedance of the electrode-electrolyte interface [10]. A four-point electrode consists of two current injection electrodes and two voltage measuring electrodes. The voltage measurement electrodes are assumed to have infinite impedance. The model presented in this paper simulated a four-point electrode by injecting current using the electrodes seen in Fig. 3. The differential voltage was measured at a point 100 μm from the two current electrodes, as might be found in an experimental four-point measurement. A uniform distribution of specific polarization impedance was assumed, such that no net polarization potential existed [11]. The impedance was determined using Ohm’s law, $Z = V/I$, where $V$ is the resultant voltage and $I$ the injected current.

The finite-element method used in the Field Precision software is described in [12]. The software was originally developed to determine the

### TABLE I

VALUES FOR THE CONDUCTIVITY AND PERMITTIVITY OF THE TISSUES MODELED FOR THE TYPE Va AND TYPE Vb LESIONS. VALUES IN GREY ARE INFERRED

<table>
<thead>
<tr>
<th>Material</th>
<th>Conductivity (S/m)</th>
<th>Conductivity (S/m)</th>
<th>Conductivity (S/m)</th>
<th>Conductivity (S/m)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>0.70</td>
<td>0.70</td>
<td>0.70</td>
<td>1.00</td>
</tr>
<tr>
<td>Fat</td>
<td>0.025</td>
<td>0.025</td>
<td>0.030</td>
<td>0.040</td>
</tr>
<tr>
<td>Muscle</td>
<td>0.40</td>
<td>0.40</td>
<td>0.40</td>
<td>0.40</td>
</tr>
<tr>
<td>Fibrous Material</td>
<td>0.24</td>
<td>0.24</td>
<td>0.24</td>
<td>0.29</td>
</tr>
<tr>
<td>Calcium</td>
<td>0.08</td>
<td>0.08</td>
<td>0.10</td>
<td>0.12</td>
</tr>
<tr>
<td>Vessel Wall</td>
<td>0.58</td>
<td>0.58</td>
<td>0.58</td>
<td>0.67</td>
</tr>
</tbody>
</table>

### TABLE II

MAXIMUM THICKNESS OF EACH LAYER IN VARIATIONS OF THE TYPE Va LESION. THE MINIMUM LUMEN DIAMETER FOR EVERY CASE IS 2.4 mm

<table>
<thead>
<tr>
<th>Layer Material</th>
<th>Fibrous</th>
<th>SMC</th>
<th>Lipid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>0.3</td>
<td>0.3</td>
<td>0.3</td>
</tr>
<tr>
<td>Var. 1</td>
<td>0.2</td>
<td>0.2</td>
<td>1.1</td>
</tr>
<tr>
<td>Var. 2</td>
<td>0.4</td>
<td>0.3</td>
<td>0.8</td>
</tr>
<tr>
<td>Var. 3</td>
<td>0.4</td>
<td>0.4</td>
<td>0.8</td>
</tr>
<tr>
<td>Var. 4</td>
<td>0.4</td>
<td>0.4</td>
<td>0.7</td>
</tr>
</tbody>
</table>

### TABLE III

MAXIMUM THICKNESS OF EACH LAYER IN VARIATIONS OF THE TYPE Vb LESION. THE MINIMUM LUMEN DIAMETER FOR EVERY CASE IS 1.0 mm

<table>
<thead>
<tr>
<th>Layer Material</th>
<th>Calcium</th>
<th>Fibrous</th>
<th>SMC</th>
<th>Lipid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial</td>
<td>0.1</td>
<td>0.3</td>
<td>0.3</td>
<td>1.0</td>
</tr>
<tr>
<td>Var. 1</td>
<td>0.2</td>
<td>0.2</td>
<td>0.2</td>
<td>1.1</td>
</tr>
<tr>
<td>Var. 2</td>
<td>0.2</td>
<td>0.2</td>
<td>0.5</td>
<td>0.8</td>
</tr>
<tr>
<td>Var. 3</td>
<td>0.5</td>
<td>0.3</td>
<td>0.8</td>
<td></td>
</tr>
<tr>
<td>Var. 4</td>
<td>0.1</td>
<td>0.1</td>
<td>0.7</td>
<td>0.8</td>
</tr>
</tbody>
</table>
The calculated impedance between the densities greater than by a solid, darker grey area. The area in dark grey represents conductive current electrodes is determined for every element using standard solution methods for a and depth are 50, 37.5, and 18.75 mesh consists of approximately 2.5 million hexahedrons. Every ele-
simulated as being delivered to a coronary lesion. The 3-dimensional to account for both the conduction and displacement current that is
during defibrillation. For this application, the software was modified
of conduction current being delivered to myocardial tissue power loss of conduction current during defibrillation. For this application, the software was modified to account for both the conduction and displacement current that is simulated as being delivered to a coronary lesion. The 3-dimensional mesh consists of approximately 2.5 million hexahedrons. Every element is identical in its linear dimensions. The elements’ length, width, and depth are 50, 37.5, and 18.75 μm, respectively. The electric field is determined for every element using standard solution methods for a variation of Poisson’s equation

\[ \nabla \cdot \left( \varepsilon \frac{j\omega}{\varepsilon} \nabla \phi \right) = 0. \quad (1) \]

The computer simulation was validated by modeling a coaxial inner and outer connector with a known analytical solution. The inner conductor and outer conductors were 1 mm and 3 mm in diameter, respectively, and 5 mm in length. Between the two conductors was a conducting dielectric. The geometry was modeled twice, with a coarse mesh of 18,605 hexahedrons and with a fine mesh of 342,015 hexahedrons. In both cases, the simulated results correlated very well with theory. The coarse and fine mesh exhibited an error of approximately 1.8% and 0.76%, respectively.

### III. RESULTS

Fig. 3 shows a typical result from the PAC3 program. The electrodes are in direct contact with the lesion, and the conductive current density is shown. The solid black area to the left of the electrodes contains no current density at all, as it is modeled as a vacuum. This is to simulate the balloon in place. The analysis conducted from these results can be divided into two parts: the impedance per se of each lesion type, and the change in impedance due to geometry changes in the lesion. Figs. 4 and 5 show the variation in the resistance and phase of the calculated impedance due to the different lesion types. Figs. 6 and 7 show the variation in impedance due to different type Va and type Vb lesion geometries, respectively.

### IV. DISCUSSION

#### A. Comparison of the Various Types of Lesions

1) Type III and IV Lesions: The lowest resistance is seen in the type III lesion. This is primarily due to the high conductivity of the outer muscle layer. Most of the current density remains in this layer. Because the lipid layer between the muscular cap and the vessel wall is so thin, some current can penetrate through this layer into the comparatively conductive vessel wall. All of these regions of high conductivity have the effect of decreasing the impedance seen by the current, thus reducing the total impedance seen by the two electrodes. A decrease of the resistance for the type III and IV lesions is seen at 1 MHz and 100 MHz. This corresponds to a sharp increase in phase shift as a consequence of the increase in imaginary component of the impedance. These increases are due to the displacement current, which has a significant effect at these frequencies. This displacement current decreases the total impedance between the two electrodes, but has the effect of increasing the imaginary component of the impedance relative to the real component.

2) Type Va and Vb Lesions: The resistance of the type Va lesion impedance is much less than that of the type Vb lesion impedance, an effect due almost entirely to the calcium outer layer of the Vb lesion. With the exception of the lipid core, calcium has the lowest conductivity for any frequency range considered. What is noteworthy, however, is that the resistances of the two lesion types are very similar at 100 MHz. It is speculated that this is due to the higher conductivity of calcium at this frequency, which allows more current to pass through to the underlying layers of fibrous and smooth muscle.

The phase is also characteristically low for the type Va lesion for all the frequency ranges considered. It is worth remembering that the collagen contained within fibrous tissue was assumed to have comparatively low relative permittivity; this would provide for the low phase differences observed. (In reality, very little experimental research has been conducted in evaluating the dielectric properties of the various types of collagens, and it would be a fruitful research topic to support the characterization of atherosclerotic lesions.) The same low phase shift is true for the type Vb lesion, for the frequencies of 1 kHz, 100 kHz, and 1 MHz. For the other frequencies, the phase shift is fairly high, due to the relatively high “ωε” term for calcium at these frequencies.

#### B. Variation of the Type Va and Vb Lesions

The resistance and phase for each lesion variation differs less than it does from lesion type to lesion type, but it is informative to observe these changes and their causes. The resistance of the type Va lesions does not vary to a significant degree through all the variations, but there
Fig. 4. Calculated resistance of type III, IV, Va, and Vb lesions.

Fig. 5. Calculated phase impedance of type III, IV, Va, and Vb lesions.

is a noticeable rise in phase shift for variation 1. This corresponds to a thin fibrous outer layer. The thin layer allows more current density to pass through to the underlying smooth muscle layer as the frequency increases. This muscle layer has a higher permittivity than that of fibrous tissue, thereby increasing the capacitance as measured between the two electrodes as compared to the original lesion.

Both resistance and phase of the impedance vary significantly for the type Vb lesion variations. Most noticeable is the rise in the resistance and phase portions of the impedance for variations 1 and 2 as opposed to the other variations. The thicker calcium layer causes an increase in the resistance due to the low conductivity of calcium. Simultaneously, however, the “ωε” term is also very high, causing a thicker layer of calcium to yield a higher phase shift than the thinner layer. For the other lesions with a thinner layer of calcium, variation 4 stands out in particular. This effect is due to the thick underlying layer of smooth muscle cells, which also tends to increase the phase due to its own high “ωε” term.
V. CONCLUSION

These results show that each type of coronary lesion has its own characteristic impedance “signature.” For each case, for various frequencies, the phase components vary for different amounts of lesion.
components. Additionally, the lesion morphology, especially that of the outer layers of material, changes the observed impedance. Using these signatures, it may possible to characterize the lesion type \textit{in vivo}, and to determine the amount of constituent material that exists in each lesion. In previous work [13], it was shown that it can be determined when the electrodes engage the lesion by monitoring the resistance. When the electrodes attached to a balloon catheter are in the blood stream, the resistance is much lower than when engaged to the lesion. Once engaged, the lesion could then be characterized, as has been discussed in this paper. The most useful frequencies to characterize the lesion would be in the range of 100 kHz–100 MHz, primarily since the phase component is much higher at these frequencies, which allows for straightforward differentiation between lesion types. The technique proposed in this paper would also be enhanced by incorporating already existing techniques, such as IVUS and angiography. If the lesion shape were known \textit{a priori}, this technique would be especially effective in further characterizing the lesion.

Fig. 6. Calculated resistance for the original and four variations of the type Va and Vb lesions. Geometry of the variations is listed in Tables II and III.

Fig. 7. Calculated phase of the original and four variations of the type Va and Vb lesions.
REFERENCES


