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Tissue Engineering: A computer simulation model for analysis of the capillary vessel model in diabetic patients with PAD

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Abstract: This study aims to develop a comparative analysis between a-pathological and pathological capillary vessels, in this work we will simulate how vascularization occurs, firstly for non-pathological human cases, and, with diabetes pathology, where it will be possible to graphically analyze the studies of the capillary vessel, with the aid of SolidWorks, COMSOL and Matlab software. It is possible to visualize the viscosity, density and pressure of the vessels, and showing how the technology can benefit health, in an attempt to obtain the prediction of clinical outcomes, and greater understanding of the pathophysiology of diseases such as Diabetes Mellitus.

Keywords: mathematical model; diabetes; capillary vessel; comparative analysis; tissue engineering

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1. Introduction

Diabetes Mellitus (DM) is a metabolic syndrome of multiple origin, it refers to the poor production or difficulty of absorption by the body of insulin and/or the inability to properly exert its effects, characterizing high blood sugar levels (hyperglycemia) of permanently. [1] The most common diabetes is type 1 or type 2, the incidence of type 1 cases is usually controlled in children and adolescents, however, during the last 30 years, type 2 diabetes has manifested itself more frequently and to determine its incidence , a controlled study is needed for the range. [2]

In general, in adults, the incidence of diabetes mellitus is measured from prevalence studies and these are infrequent and currently limited to developed countries.[2] In 2004, due to the availability of data in regions of Africa and the Middle East and India, the WHO revised the prevalence estimates. A study of the year 2000 and a projection for 2030 were carried out.[3]

The study says that at least 171 million people in the world, or 2.8% of the population, suffered from diabetes in 2000. The prevalence of diabetes is similar in men and women, being slightly higher in men <60 years of age and in women at older ages. And by 2030 the number is estimated to double, confirming that the prevalence by age will remain constant.[3]

The number of deaths in Brazil between 2001 and 2012 was 1,076,434 (women: 603,686 – 56.1%; men: 472,748 – 43.9%), for cases of diabetes mellitus as the underlying or associated cause, which is 95, 2% more compared only to the underlying cause of death in this period.[4]

Peripheral arterial disease (PAD), which reduces blood flow to the feet, causes decreased sensation due to the damage that uncontrolled glucose does to the nerves. These

two conditions facilitate the appearance of ulcers and infections, which can lead to amputation. Often, the skin gives the first signs that you may have diabetes. At the same time, associated complications can be traced. People with diabetes are more likely to have dry skin, itchiness, and fungal and/or bacterial infections, as hyperglycemia favors dehydration as excess glucose robs the body of water. [1]

PAD can bring complications when the body's compensatory mechanisms are not sufficient to meet the demand of the lesion, and ischemia or even tissue death may occur. [5] For this work, we are analyzing the rupture of the capillary vessel, which, when it occurs, may be associated with DAP and may lead to tissue death due to lack of nutrients. [5]

The precise mechanisms of vascular damage related to prolonged hyperglycemia have not yet been fully elucidated. Evidences indicate that high levels of intracellular glucose provide increased production of reactive oxygen species (ROS), altering several cellular processes, which cause deterioration in blood vessels. Endothelial dysfunction in DM involves increased oxidative stress, reduced endothelial progenitor cells, decreased proliferation of circulating endothelial cells, reduced vasculogenesis, and increased inflammation in vascular cells. [6]

It is common knowledge that in silico assays can boost the field of research, reducing in vivo tests, which in turn have low efficacy and should be aimed at new discoveries [7], in vivo tests also have more ethical limitations and are being less stimulated. Another alternative is the in vitro tests, which are constantly taking up more space, but they are still expensive mechanisms and the proposal is to reduce this cost with the possibility of starting with the in silico test through the COMSOL software.

The study that will be addressed below is of paramount importance, since in addition to benefiting patients with diabetic pathology, it has its sociais and economic impact. Social by approaching technology and through mathematical models representing the highest percentage of efficiency and efficiency of the system, and economic, since about 90 percent of studies carried out in animals are not replicable to humans, for several reasons. [8]

The purpose of this work is to carry out the computational simulation and mathematical modeling of a blood capillary vessel, in the scenario of Diabetes Mellitus.

1.1. Capillary Vessel

The circulatory system has two stages the first is the transport of blood through the body and the second is the movement of liquid that occurs between capillaries or intercellular spaces, this exchange is continuous and circulation for an active individual occurs once every minute. [9]

In this microvascular scenario, a shear stress analysis is necessary to understand how vessels dilate by controlling pressure without damaging endothelial cells. [9] It is also necessary to study the parameters of the blood vessel for mathematical and computational analyses.

2. Materials and Methods

With the objective of drawing a comparison between the healthy capillary vessel and the diabetic capillary vessel, a procedure with six phases was elaborated: initiation, theoretical foundation, search for parameters, model design, simulation and textual production; according to the image 1.

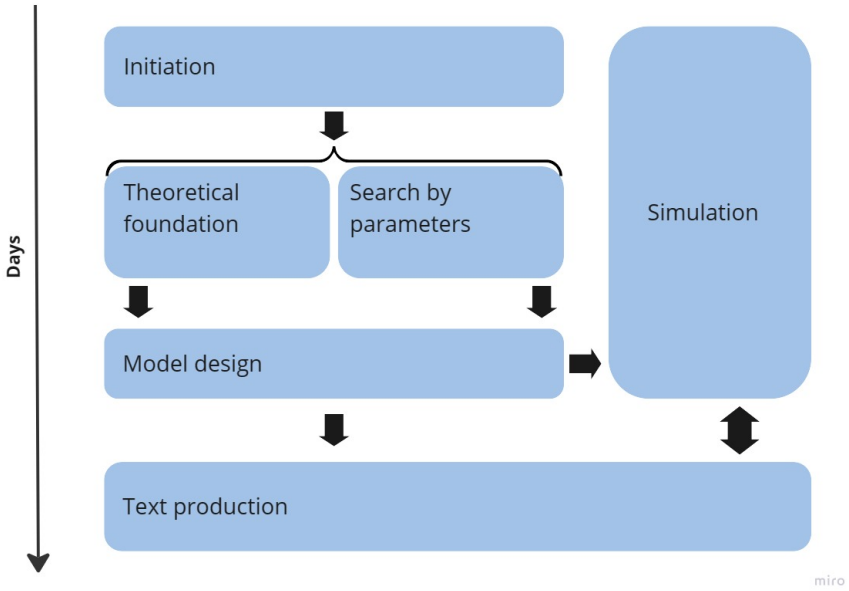

Figure 1. The methodology was carried out through 06 main goals, where specific activities were developed in each of them, in order to reach the results found. Phase 1 was initiation. Phase 2 was theoretical foundation. The 3 was search for parameters. The 4 was model design. Phase 5 was simulation. And phase 6 was textual production.

In the initiation, the aspects of this research were defined, such as the objective and the search criteria, in which the research was idealized and had its beginning demarcated.

After initiation, it was divided into two phases, both with a literature bias, the first, theoretical foundation, aimed at establishing an understanding of each definition that would be necessary for the development of the research. And the second search for parameters where a more specific search was made in order to define the healthy vessel, the diabetic vessel and the blood flow of the cases.

Then, the design of the model was established, in SolidWorks, with input of the structural parameters. Parallel to the previous steps, a study was made on how to use the COMSOL tool to carry out the simulations and these were executed.

Finally, after the simulations, this work was elaborated, containing the main points developed and analyzed.

2.1. Main definitions

The development of the project starts from the hypothesis contained in figure 2 where it identifies that the capillary vessel when subjected to diabetes can be simulated in a computationally and generate input for other approaches.

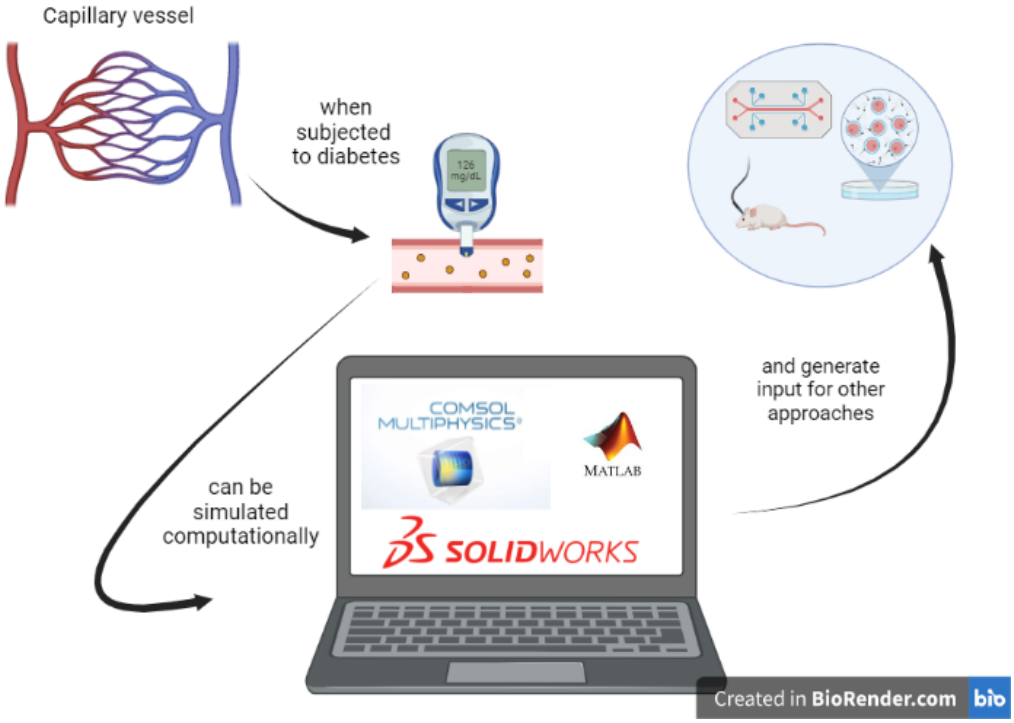

Figure 2. The project is relying on the hypothesis that the capillary vessel when subjected to diabetes can be simulated computationally and generate input for other approaches, this states that from the parameters of the vessel it will be possible to simulate through the COMSOL software and with the help of SolidWorks and the Matlab and that its application may be related to different approaches.

In order to obtain a comparison between the two vessels available in table 1, after reviewing the literature, a gap was noticed with the mechanical definition of what would be a healthy vessel and what would characterize diabetes in that vessel, so it was decided to use the same vessel structure and change the blood flow parameters, and would also result in a more faithful comparison, where both parts have the same wall.

Understanding the principles of biology is a requirement to continue the research to be worked on, mainly reconciling engineering knowledge and taking into account the dynamics of fluids for blood analysis and mechanics of solids for the vessel. [10]

Blood is a non-homogeneous fluid due to the presence of red blood cells, making it a non-Newtonian fluid, which makes it difficult to analyze the shear stress, because in this case the viscosity will depend on the amount of blood analyzed.[11] In this study, the common flow of blood in the capillary vessel for a healthy person and a person developing diabetes mellitus will be analyzed.

In addition, in understanding the vessel, we have that arteries and veins are considered non-homogeneous and non-isotropic because they have several layers with different materials. [11] However, we are working with the capillary vessel that has only one layer of endothelial tissue, so we will use the isotropic definition, using the Lamé parameters and the density for mechanical calculations. [9] [12]

Finally, it was defined that, for a better visualization side by side of the two cases, the parameters that suffered alteration with the influence of diabetes would be evolved by a function, a function that was approximated via Matlab to a polynomial.

2.2. Parametes

With a search in the literature, two models were defined, a first to represent a non-diabetic vessel and a second containing the diabetic parameters. However, for comparison purposes, it was decided to maintain the same structure and vary blood attributes, this decision is due to the complexity of finding specific parameters of solid mechanics for a

capillary vessel in the literature and, at first, obtaining a close comparison maintaining data and visualizing how changes in diabetic blood inflicted on an ordinary capillary vessel.

For the parameters, the following table was set up, where we obtained data by data to compose the definition of a diabetic case and in this way we define the two cases in the table 1.

Scope	Parameter	Symbol	Non-diabetic	Diabetic	Reference
Vessel	Diameter	$\varnothing$	$8\mu m$	$8\mu m$	[13]
	Wall thickness	$\circ$	$1\mu m$	$1\mu m$	[13]
	Density	**D**	960 g/l	960 g/l	[12]
	Compressibility modulus (Lamé parameter)	λ	$20 \cdot \mu$ N/m²	$20 \cdot \mu$ N/m²	[12]
	Shear modulus (Lamé parameter)	μ	$6.20 \cdot 10^6$ N/m²	$6.20 \cdot 10^6$ N/m²	[12]
Blood	Diastolic pressure	p_{outlet}	12.8 mmHg	13.6 mmHg	[14]
	Systolic pressure	p_{inlet}	22.8 mmHg	25.3 mmHg	[14]
	Density	**D**	1040 g/l	1100 g/l	[15]
	Plastic viscosity	η	0.00142 $Pa \cdot s$	0.00231 $Pa \cdot s$	[16]
	Yield stress	σ	14.4 mPa	14.4 mPa	[17]
	Temperature	T	37ºC	44ºC	[18]

Table 1. Parameters used in the simulation

With the parameters defined, it was possible to define the equations that would be used in the model.

2.3. Formulas

To create a blood flow model in COMSOL, it is important to define the heart rate variation that is delimited by the equation: [12]

- In the time interval of 0 to 0.5 seconds;

$f(t) = (1 - \alpha) \cdot \sin(\pi \cdot t)$

- In the time interval of 0.5 to 1.5 seconds;

$f(t) = 1 - \alpha \cdot \cos(2 \cdot \pi \cdot (t - 0.5))$

Where t is time in seconds and α is the relative pressure amplitude during the beat.

So, with the parameters in Table 1 and with the help of Matlab, it was possible to evolve to functions that would transform the non-diabetic case into a diabetic case and thus observe how the vessel behaves with changes in these parameters.

- Diastolic pressure generated the function:

$diastolic = 0.0000 \cdot x^2 + 0.5333 \cdot x^1 + 12.8000 \cdot x^0$

- Systolic pressure generated the function:

$systolic = 0.0000 \cdot x^2 + 1.6667 \cdot x^1 + 22.8000 \cdot x^0$

- Density of blood generetad the function:

$density = 0.0000 \cdot x^2 + 40.0000 \cdot x^1 + 1040.0000 \cdot x^0$

- Plastic viscosity genereted the function:

$plastic = 0.0000 \cdot x^2 + 0.0006 \cdot x^1 + 0.0014 \cdot x^0$

Where x is is time too. It is possible to observe that when visualizing the equations we have two values that match our x, the first one that refers to the evolution factor and the second one that is the minimum value, obtained by the initial state of the vessel (non-diabetic), remembering that these values were obtained through the approximation performed in Matlab.

In addition to these equations, we have those that were used in the definition of the project, from defining the type of fluid and the type of solid, COMSOL presents equations for physical and mathematical calculations, these equations can be visualized in the project.

2.4. SolidWorks.

To simulate in COMSOL Multiphysics, it was decided to draw the figure in SolidWorks and use the parameters to be studied following the step by step below:

1. Draw lines for reference, these will be the shape of the blood vessel;
2. Defining arbitrary points along the line, it is important to define a minimum value, depending on the number of curves, so that the blood vessel does not deviate from the initial shape;
3. Delimit planes perpendicular to the line at each point;
4. In the foreground draw the circumference of the vessel, in this step the outside diameter of the vessel will be used;
5. Create a block with the circumference and the referenced radius value;
6. Insert the block in the other planes, so it will be replicated keeping the values;
7. Using the circles, create a lofted surface;
8. Define vessel thickness with the internal diameter that was surveyed;
9. Save the vessel and use the project to create the another parts;
10. So, using the vessel created, create a offset surface in the internal surface with the distance in 1 mm;
11. Create a plannar surface closing the parts and knite all surfaces into a solid;
12. Display off the vessel and save as blood;
13. Create an assembly with the two parts and clip them.

2.5. COMSOL Multiphysics.

Now, with the figure defined, we can do the simulation, the following procedures were performed in COMSOL:

1. Create a Blank Model;
2. Define t and α parametes;
3. Define a piecewise functions with formulas of the section 2.3;
4. Add the component and import the assembly of SolidWorks;
5. Define union type and scale the geometry to ajust in a micrometer size;
6. Create a custom material for blood and vessel;
7. In blood add the density, yield stress and plastic viscosity;
8. Already in the capillary add the density and Lamé parameters;
9. Associate each material with its respective part;
10. Add physics like laminar flow and mechanical solid;
11. In laminar flow associate to the blood part and add inlet and outlet for the extremities;
12. Change the fluid properties in laminar flow and define to non-Newtonian fluid and Bingham-Papanastasiou inelatic model;
13. In inlet change the boundary condition to pressure and add the systolic pressure;
14. In outlet change the boundary condition to pressure and add the diastolic pressure;
15. In mechanical solid associate to the vessel part and create a roller with the outside surfaces;
16. Change the linear elastic material in solid mechanical changing to ansiotropic solid model;
17. Add the multiphysics fluid across solid;
18. Set the mesh to physics controlled because the figure does not have many irregularities to calculate in certain parts, fine size;
19. Set study varying as a function of time using the picerwise function;
20. See results in boundary loads, pressure variation, velocity and deformation;
21. You can see the non-diabetic and the diabetic varying the time in results.

2.6. MatLab.

To obtain the functions presented in the section 2.3, the following code was used:

```
% Input data
```

```
x = linspace(0, 1.5, 31);
y = linspace(12.8, 13.6, 31);

% Finding Coefficients of the Fit Polynomial
coefs = polyfit(x, y, 2);

% Creating the polynomial string
diastolic = "";
for i = 1:length(coefs)
    diastolic = sprintf("%s%.4f*x^%d",
        diastolic, coefs(i), length(coefs)-i);
    if i < length(coefs)
        diastolic = sprintf("%s + ", diastolic);
    end
end

% Displaying the polynomial
disp("diastolic = " + diastolic)
```

Where the value of y is changed according to the parameters and the name of the polynomial also follows the change.

3. Results

The definition of the project generated some results, as in figure 3 which represents the design of the vessel model studied in the article, in the image it is possible to see the blood and the vessel layer, and its dimensioning.

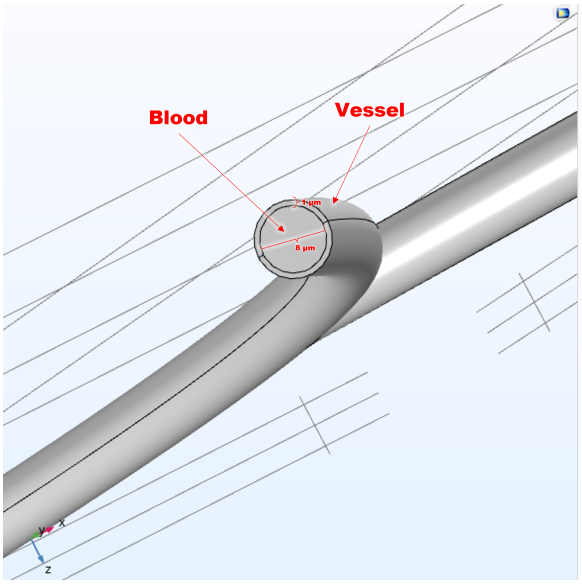

Figure 3. Drawing of the model of the capillary vessel and the blood, both of which have a solid to represent it and then the blood will be assigned as a fluid. As shown in the table 1 the vessel has a wall of 1 μm and an external diameter of 8 μm, that is, 7 μm for the internal diameter and the latter value as well applies to blood.

Figures 4, 5, 6, 7 and 8 are representations of functions and variables, showing, for example, density, pressure, plasticity function, diagnosis, etc. in it, we can observe that on the X axis it is always in second (s) and the variation of the Y axis depends on what we are approaching in the graph.

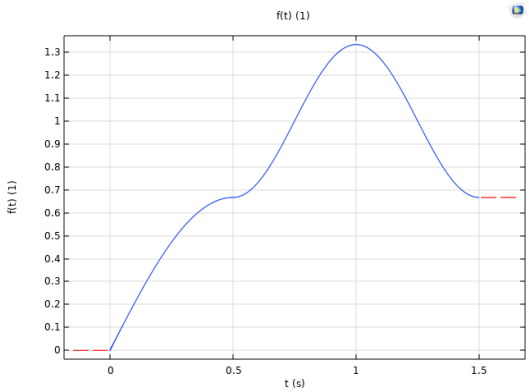

Figure 4. Function presented by COMSOL et al. that has the behavior of the heartbeat, this behavior has a direct influence on the simulation performed in the software.

In the graphs we see a similar behavior for the systolic, diastolic, plastic and density functions, this is due to the method used to approximate the functions where, as there is no clinical follow-up of the evolution of diabetes with gradual measurements, a regular interval between the starting and ending value.

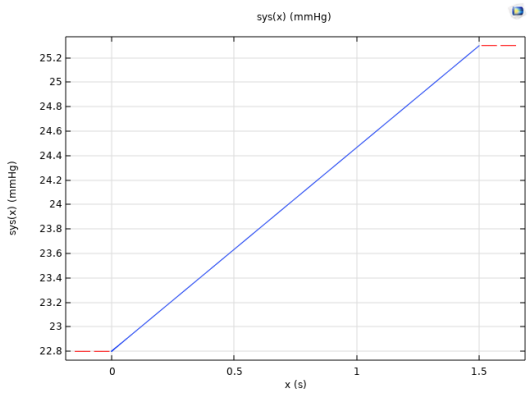

Figure 5. Function designed to approximate the evolution of the systolic pressure parameter in the capillary vessel from a healthy condition to a diabetic condition, through the minimum and maximum values.

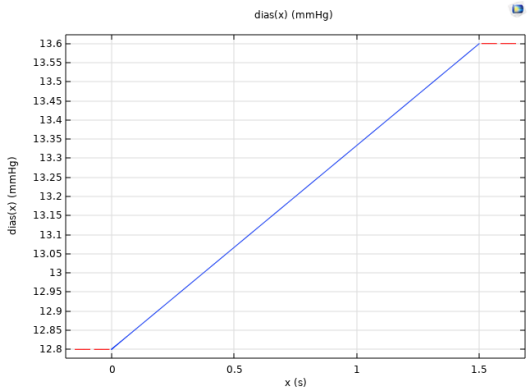

Figure 6. Function designed to approximate the evolution of the diastolic pressure parameter in the capillary vessel from a healthy condition to a diabetic condition, through the minimum and maximum values.

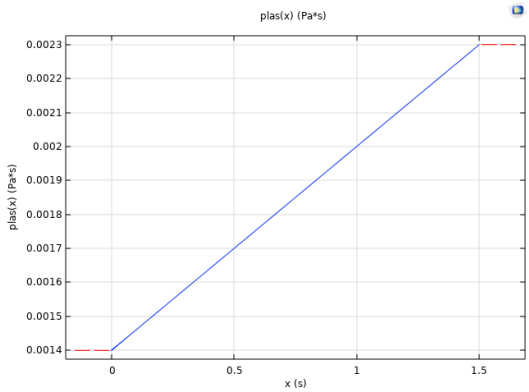

Figure 7. Function designed to approximate the evolution of the plastic viscosity of blood parameter in the capillary vessel from a healthy condition to a diabetic condition, through the minimum and maximum values.

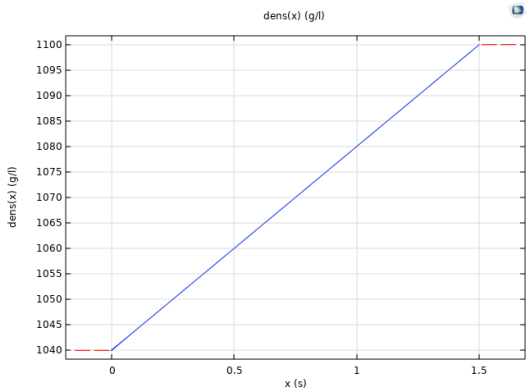

Figure 8. Function designed to approximate the evolution of the density of blood parameter in the capillary vessel from a healthy condition to a diabetic condition, through the minimum and maximum values.

Figure 9 shows in this study the model of the vessel studied, this model above is represented in the 3D image (third dimension), whose unit of measurement is in micrometers.

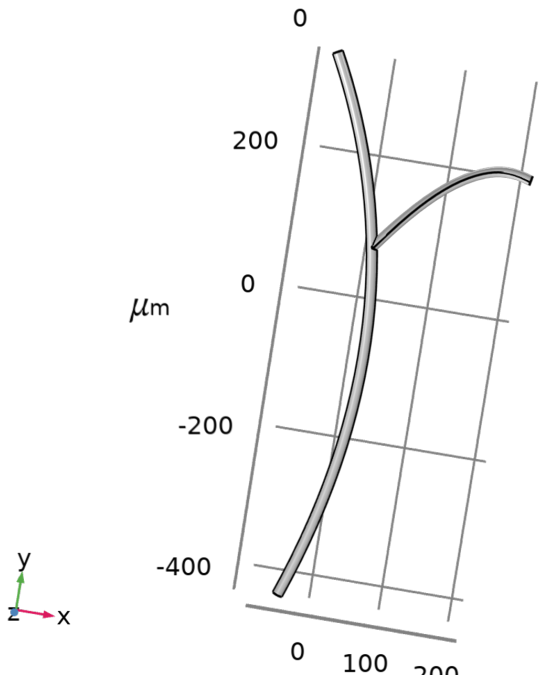

Figure 9. Drawing elaborated to represent the capillary vessel with a branch in the 3D model.

Figure 10 is showing the sections of the vessel model, it is possible to visualize in the following image where the blood fluid flows and where the solid is.

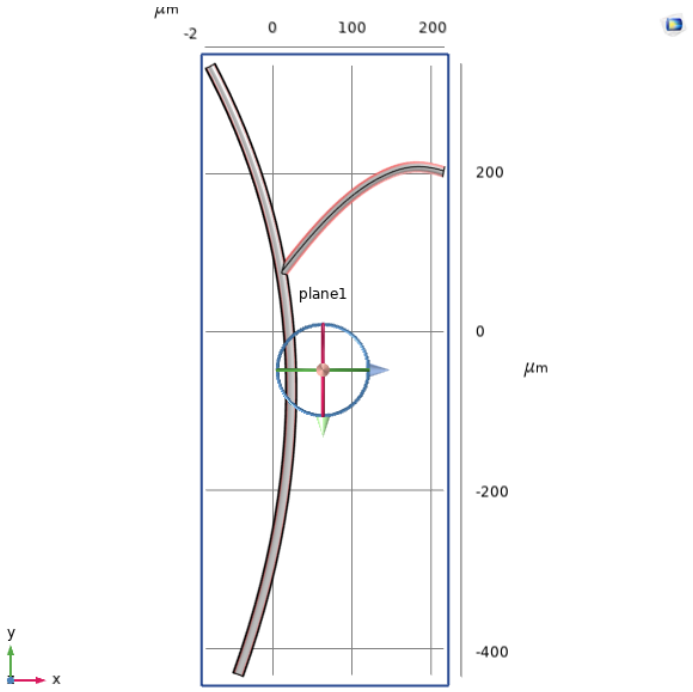

Figure 10. Capillary vessel model with a Z-axis section showing that blood fills the interior of the figure.

3.1. Non-Diabetic Simulation

First, results were highlighted in the non-diabetic vessel, in figures 11, 12, 13, 14, 15, 16.

It is interesting to talk about figure 11, which is represented in several points the limit loads of the vessel, it is seen in several red points the countless points and zones where

the loads are clustered and that may possibly come to have a level of greater tension thus causing a possible rupture of the vessel.

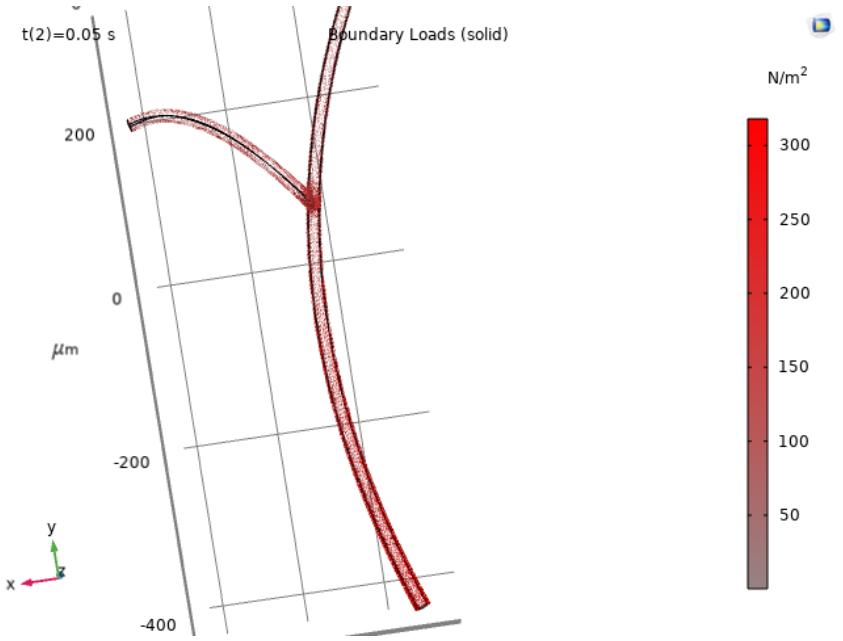

Figure 11. Representation of the vectors that affect the solid with the boundary loads, which intensify in the branching of the vessel, in the healthy case.

Image 12 shows us the level of velocity and magnitude of the vessel, where it is possible to see that through the X axis the blood is coming with a greater velocity and that it has been gradually decreasing along the course, on the side, there is a caption that is very easy to understand, as the tone of the vessel becomes lighter, the less speed the fluid travels along the way.

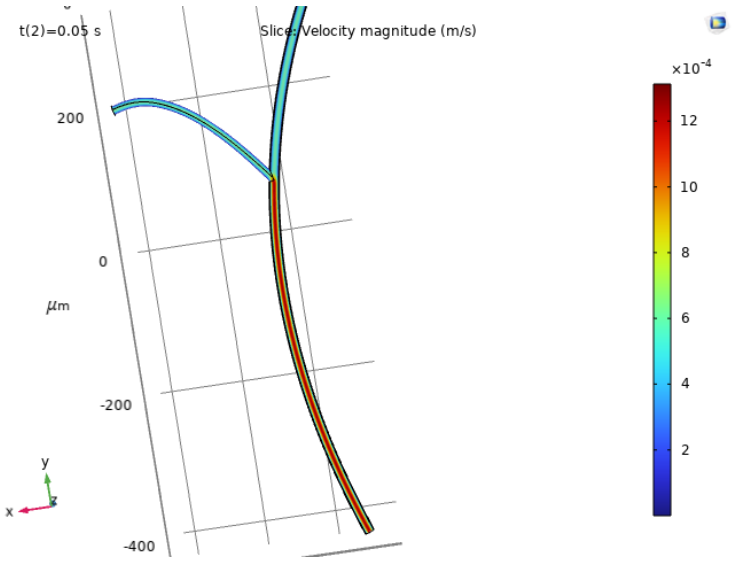

Figure 12. Representation of the velocity that the fluid travels, which intensifies in the center of the vessel and decays as it approaches the wall, in addition to decaying in general when passing through the branch, in the healthy case.

Figure number 13 represents the pressure level of the vessel, we have the caption on the side that shows the layer and what pressure is flowing in the vessel from the fluid inlet to its division at the vessel bifurcation, going towards to other layers of vessels.

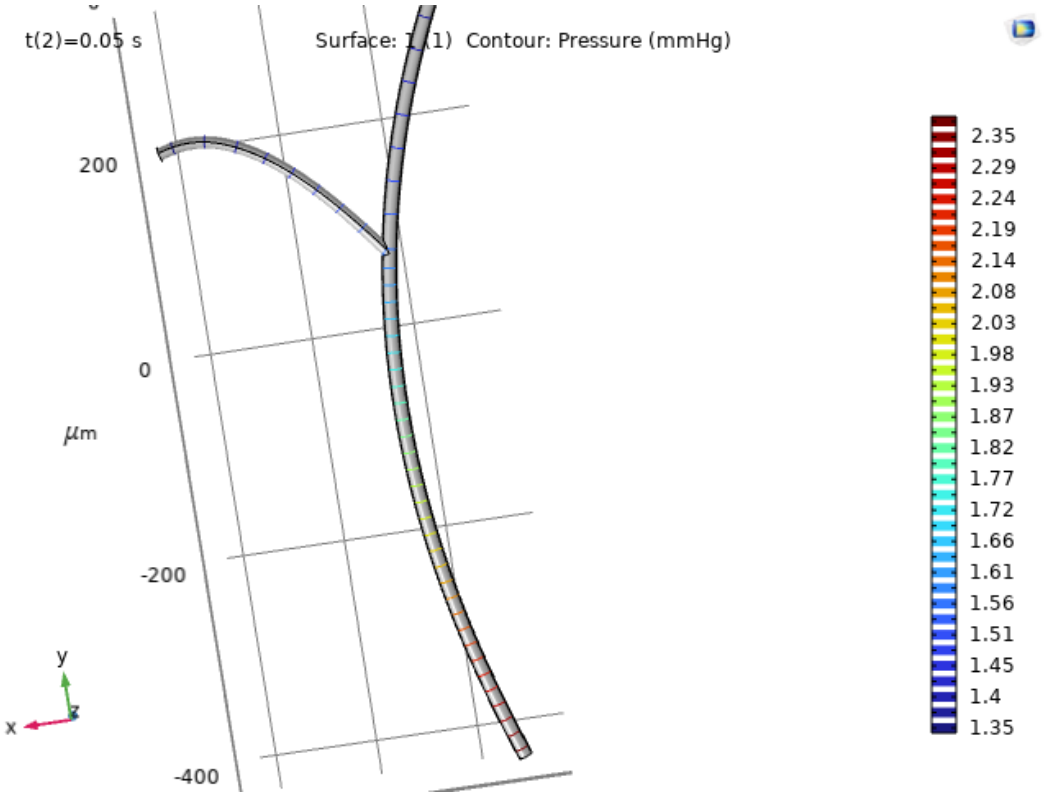

Figure 13. Representation of the pressure along the vessel that has a high input value but decays along the vessel, in the healthy case.

Now let's talk a little about the magnitude of displacement of the vessel, we can see in Figure 14 that in the middle of the studied capillary vessel is where there is a greater probability of displacement due to the level of pressure that the fluid travels through.

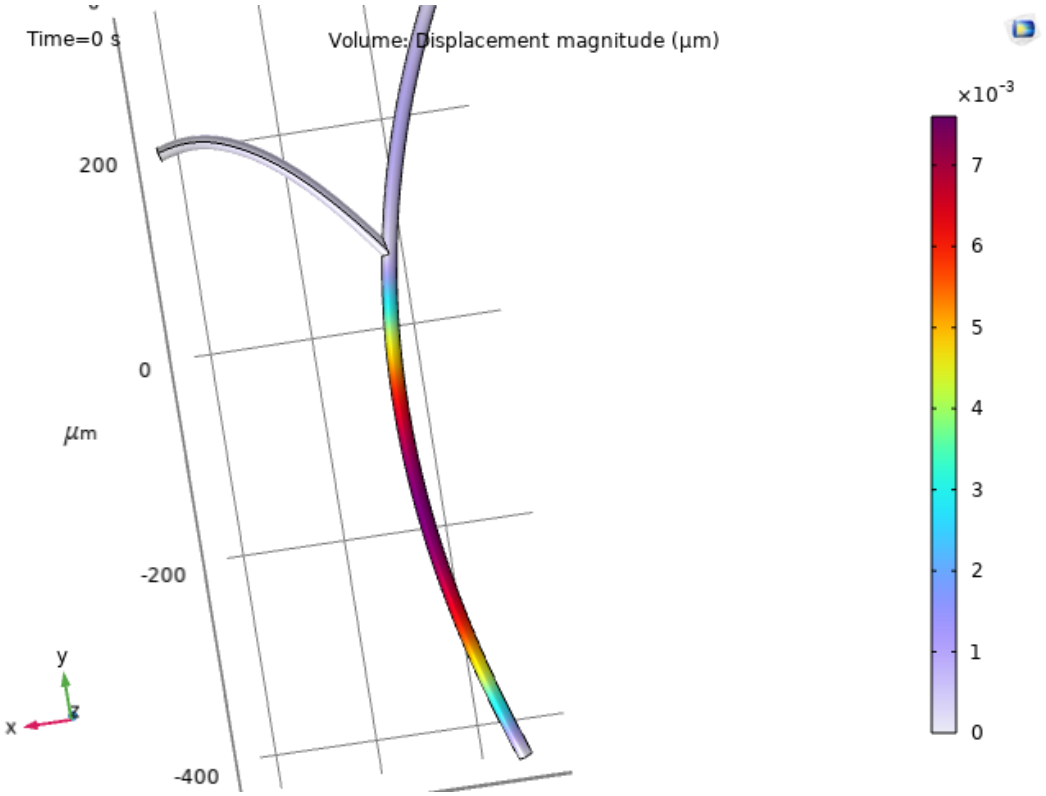

Figure 14. Representation of the magnitude of the displacement that represents how the vessel deforms to avoid rupture, this representation remains constant in the healthy and pathological cases.

The Von Mises Force The maximum von Mises stress criterion is based on the von Mises-Hencky theory, also known as shear energy theory or maximum distortion energy theory. This theory states that a ductile material begins to yield at a location where the von Mises stress becomes equal to the stress limit. In most cases, the yield point is used as the stress limit. However, the software allows you to use maximum traction or define your own voltage limit. Image 15 has even been zoomed into the zone that has the highest probability of fluid shear stress occurring.

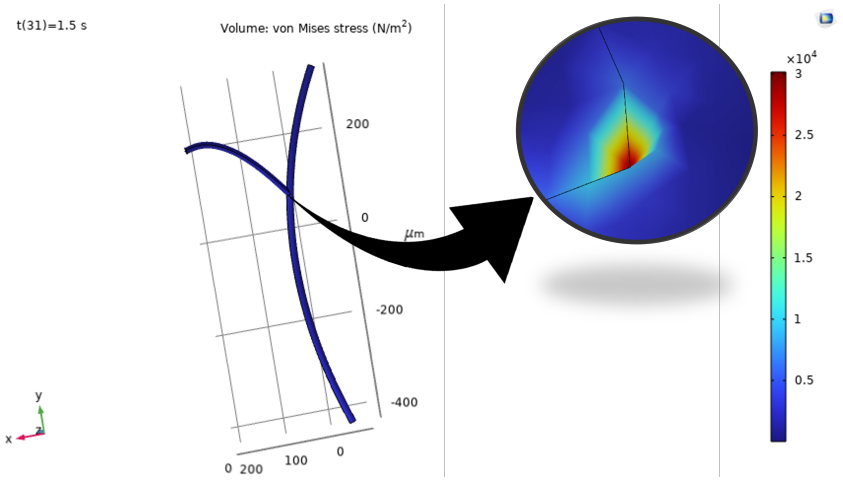

Figure 15. Graphical representation of how Von Mises stress behaves, focusing mainly on the vessel wall at the level of branching, this representation remains constant in the healthy and pathological cases.

From figure 16, the diabetic study of the article began and in it, the comparison of figure 10 was performed, showing the main points of limit load of the vessel, since the

patient with diabetic pathology has some other variables that may come impairing the functionality of the studied vessel system, over time it can even cause a vessel clogging, and this study calculated some variables as such.

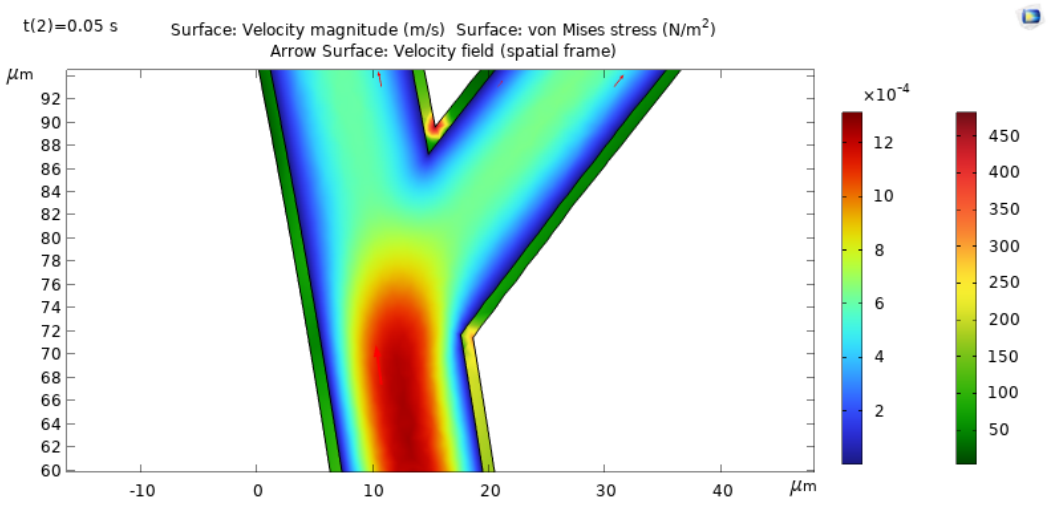

Figure 16. Representation relating Von Mises stress with fluid velocity, containing direction vectors, which shows how the incidence of fluid on the wall weakens it, the values are adequate in the healthy case.

3.2. Diabetic Simulation

Now, for comparison purposes, results of the simulation in the diabetic period will be presented.

In Figure 17, similar to the non-diabetic period, we have the Boundary Loads graph with visible limits, it is possible to notice that, despite appearing to be the same case, we have the caption showing another magnitude as a result, that is, the values increased.

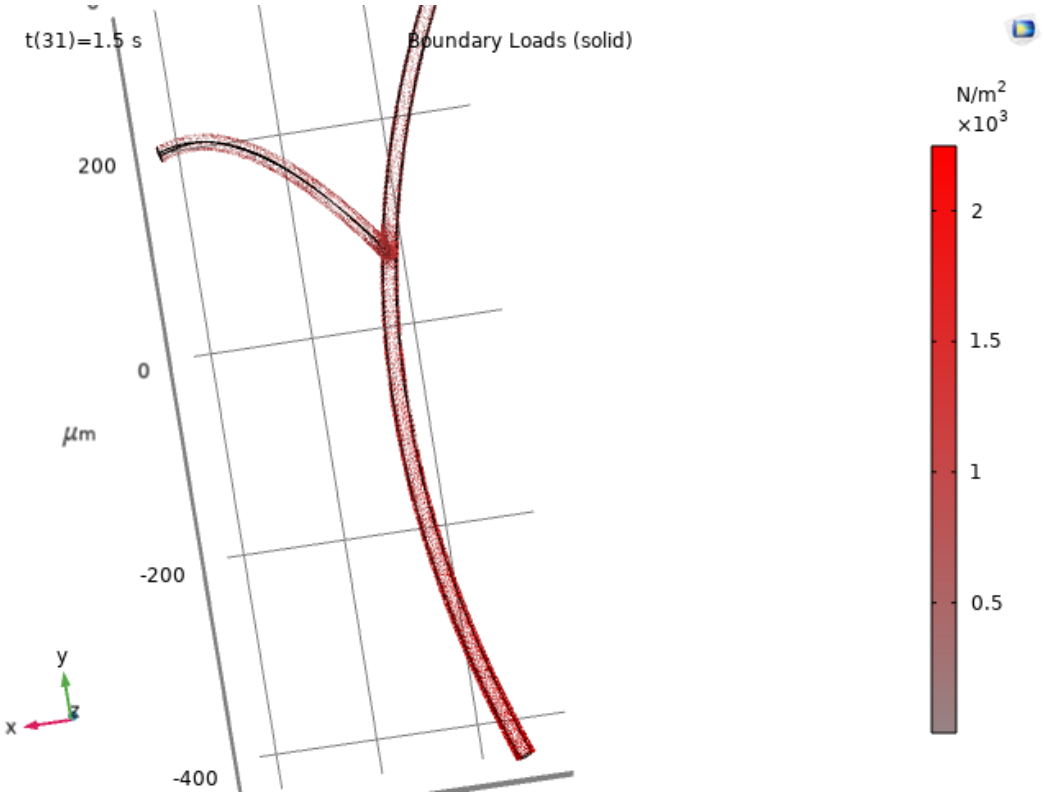

Figure 17. Similar representation in the figure 11, of boundary loads, containing diabetic values, it is important to pay attention to the caption, that even though the figure looks the same, the scale of the results are altered.

As in the previous figure, in the image 18 we have an increase when compared to the non-diabetic moment, where the values represented by 10^{-4} are now represented by 10^{-3}.

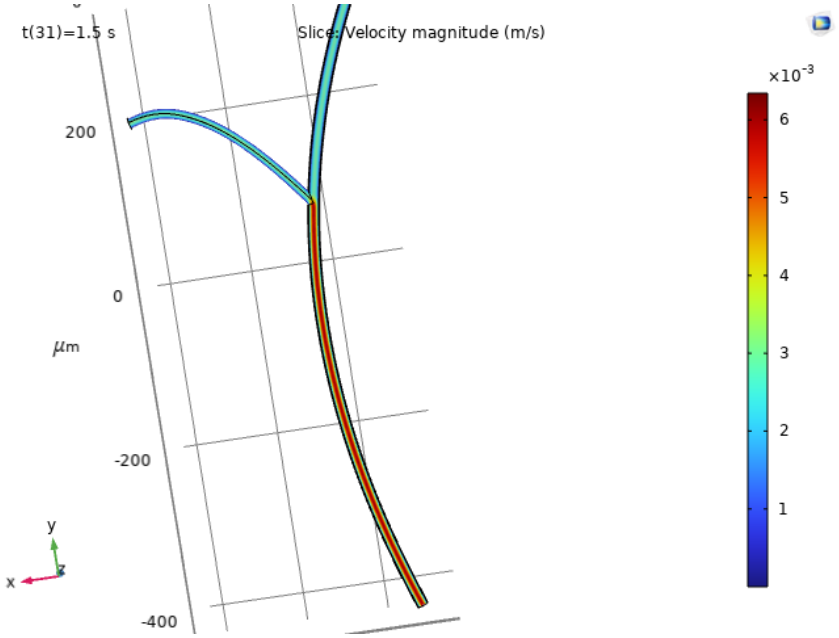

Figure 18. Similar representation in the figure 12, of velocity, containing diabetic values, it is important to pay attention to the caption, that even though the figure looks the same, the scale of the results are altered.

In the pressure variation we have two interferences, the function of the heartbeat that increases in a period and the evolution of the condition, which tends to increase the values as well, so in the results we can see this elevation both in the minimum and maximum data, figure 19.

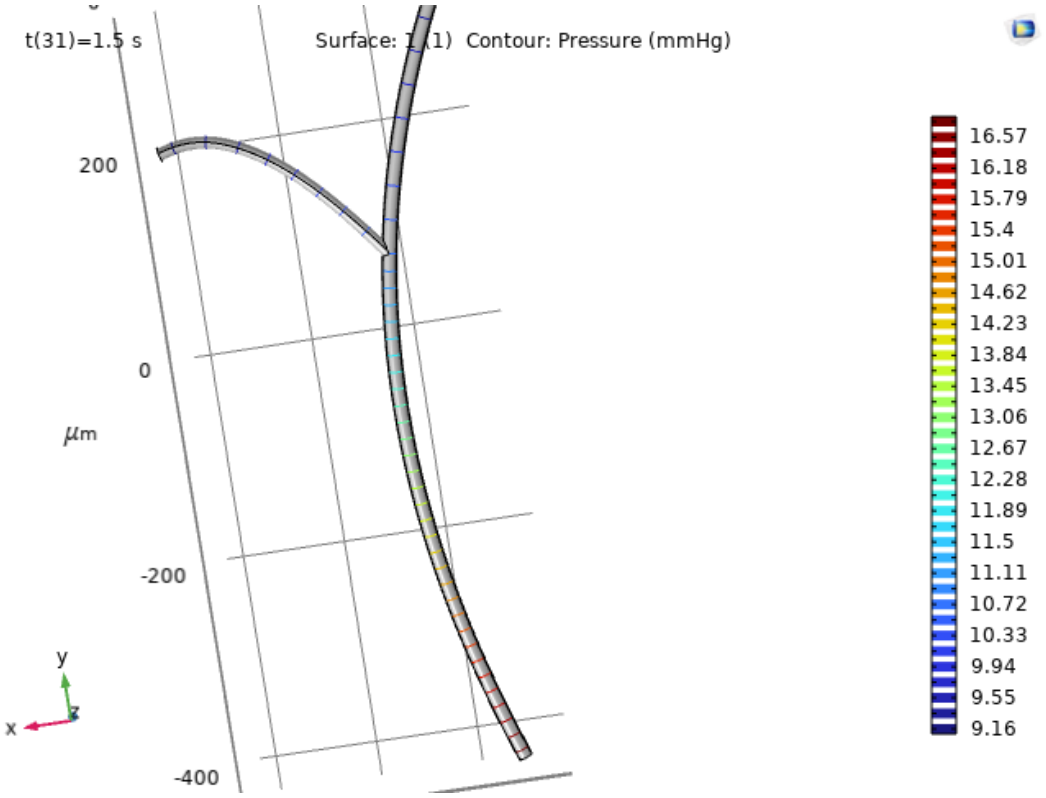

Figure 19. Similar representation in the figure 13, of pressure, containing diabetic values, it is important to pay attention to the caption, that even though the figure looks the same, the scale of the results are altered.

As changes were considered only in blood parameters, there were no changes in Von Mises and deformation graphs. However, when we relate velocity to Von Mises tension, we see that it may be related to vessel rupture, using the von Mises failure criterion, see image 20.

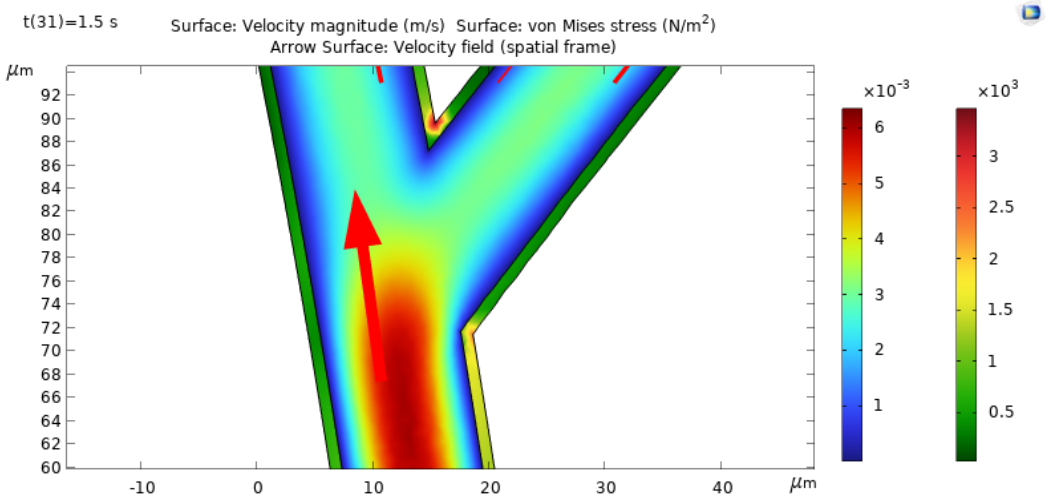

Figure 20. Representation of the diabetic vessel relating the Von Mises tension to the fluid velocity, containing direction vectors, which shows how the incidence of the fluid on the wall weakens it and that, in this case, the values intensify with the pathology, comparing with the figure 16.

3.3. Shear rate

As previously presented, the shear stress cannot be measured solely in the blood fluid because it is a non-Newtonian fluid, so in the image 21 it is possible to see how the shear stress behaves over time.

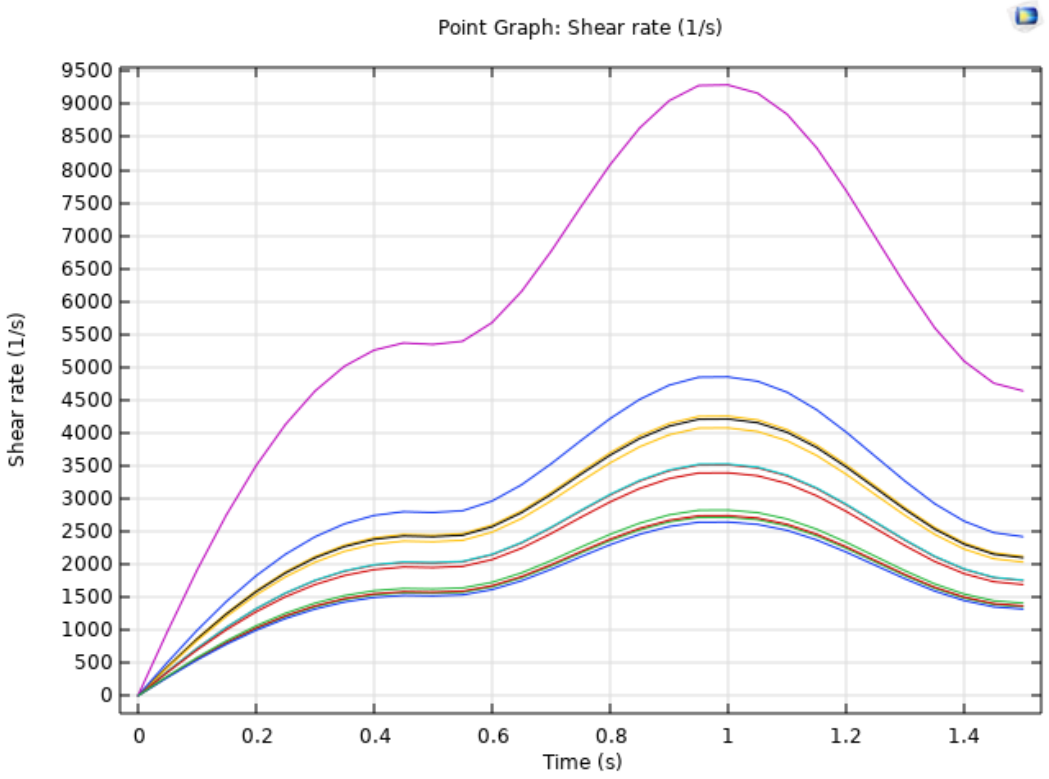

Figure 21. Behavior of the shear rate that resembles the heartbeat function and has values according to the amount of fluid, as it is a non-homogeneous fluid.

3.4. Endothelial cells

Endothelial cells are responsible for composing the vascular structure and the capillary vessel has a single layer in its composition, which makes it 100% endothelium. [11]

Thus, by assuming that the wall is isotropic to obtain the influence of the stress variables [11], the vessel deformation was measured and it was possible to analyze how the pathological blood inflicted on the model.

4. Discussion

The capillary vessel is the structure with the velocity smallest of the human body, this structure is 8 μm in diameter and 1 μm thick and consists of only one layer of endothelial tissue, in this vessel, when in a healthy state, flows a fluid at a pressure of 22.8/12.8 mmHg and density 1040 g/l, this vessel is already thinner and more fragile than the others, and is responsible for the exchange of nutrients with the other tissues.

When pressure and density increase, this exchange becomes more difficult and can lead to several consequences, in the case of the studied vessel, diabetes is induced in a short period of time (1.5 s) and changes are verified in this vessel, the pressure of the vessel, now pathological , becomes 25.3/13.6 mmHg and the density 1100 g/l.

In addition to these data, the plastic viscosity is changed from 0.00142 Pas to 0.00231 Pas and the temperature rises from 37ºC to 44ºC, the vessel starts to release more energy and, as mentioned, it is a more sensitive structure, a way to alleviate this high energy it is through vessel deformation, which occurs constantly, but this deformation has a limit and this limit is where this article hits.

The diabetic foot presents several anxieties before suffering complications and some can be observed in the blood of the patient who, when evolving to the condition, undergoes changes.[19] One of these changes is related to blood pressure, which in the capillary has a gain of 10 mmHg, at minimum and maximum values.

This pressure interferes with blood flow data, but even without changing the vessel, it is also possible to observe a change in its structure, seeing that it becomes more susceptible to rupture when in contact with diabetic blood.

It can be seen in the analysis of von Mises in which, although it did not present variation when accompanied, when placed side by side with the velocity of the blood, it shows this higher tension, which refers to the capture that occurs when one is exposed to the disease.

Another aspect that can be observed is the location of this tension, it occurs in the branching of the vessel, which even when perceiving a relief of speed and pressure has this Boundary Loads localized tension. This is also noticed in the Boundary Loads graph, where the vectors intensify at the beginning of the branch.

On the other hand, the deformation of the vessel is more associated with its length, which has an intensification in the middle and decays along the branching, this is a way to avoid shearing of the structure, relieving the attributes.

Finally, it is possible to see that the shear stress oscillates and has several propagations according to the variation in blood viscosity, which has a direct influence on the heartbeat function, for this reason the shape of the function is similar.

5. Conclusions

The hypothesis established for the development was confirmed with reservations, a clinical analysis of the data is necessary to obtain more parameters, in order to develop a model that addresses all alterations relevant to diabetes.

Despite these caveats, it is possible to conclude that the objective of the work of establishing a mathematical and computational model for a healthy vessel and a diabetic vessel, which by definition of the researchers, opting to vary parameters in the blood that referred to the condition of diabetes, was achieved.

It is possible to conclude from the images that from the pressure, density, viscosity variations, the 3D model is able to identify sensitive punctual parameters that can lead to a complication in the diabetic vessel, it should be taken into account that this work observes the evolution of a healthy vessel for diabetes and what other parameters may change.

As seen in the previous topics, we can see that changes resulting from diabetes can make a vessel with the same condition more susceptible to rupture or congestion, something that in future studies may be associated with diabetic foot wounds.

Due to the difficulty in finding physical parameters in the diabetic model for future research, it is also proposed to use physical parameters obtained through in vitro or in vivo tests of the evolution of the disease, as they are not usually evaluated in clinical trials, validating the model.

Another possibility of working from this model is a direct relationship with the organ-on-a-chip, using our work to create a vase that will be printed on a bioprinter and implement the chip.

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