POPLITEAL ARTERY ANEURYSM: A BIOENGINEERING STUDY ON PATHOGENESIS.

Francesca Condemi[(a)], Raffaele Serra[(b)], Stefano de Franciscis[(c)], Gionata Fragomeni[(d)]

[(a),(d)] Bioengineering Unit *"Magna Graecia"* University, Catanzaro, 88100, Italy
[(b),(c)] Vascular Surgery Unit *"Magna Graecia"* University, Catanzaro, 88100, Italy

[(a)]fccondemi@gmail.com, [(b)]rserra@unicz.it,[(c)]defranci@unicz.it[(d)]fragomeni@unicz.it

ABSTRACT
This study regards a computational fluid dynamics (CFD) model and a fluid structure interaction (FSI) model to describe the "Functional Entrapment Syndrome of Popliteal Artery" (PAES).
A stack of 127 slices, were acquired from RM of the right knee. The segmentation of the region of interest was performed on 3D Slicer, using the Single Region Growing. The final geometry was created in Comsol Multiphysics through the measure obtained by segmentation. To optimize the model's elaboration, we performed only the region of interest: the flow, the artery walls and the muscles soleus, medial gastrocnemius, plantaris and popliteus. CFD and FSI were performed using the commercial software Comsol Multiphysics 5.0 (COMSOL, Inc., Stockholm, Sweden).
In CFD section, in agreement with the experimental data, the popliteal blood velocity varied from 30[cm/s] to 70 [cm/s]. In FSI phase, the entrapment due to the gastrocnemius muscle caused a maximum displacement of the popliteal artery walls of 0.16 [mm]. When the entrapment is due to soleus muscle, the maximum displacement of the artery is about 0.3947 [mm]. The most important observation is the variation of contact pressure in two cases of entrapment. In fact, when the occlusion is due to soleus muscle, the pressure is higher than the precedent case.
The CFD model and the FSI model resulted in a detailed description of fluid dynamic and fluid-structure interactions useful to evaluate the pathology's features, independently, from the obstacles of in vivo analysis. These models can define the sites more solicited where there is the most probability to have an aneurysm.

Keywords: PAES, CFD model, FSI model, popliteal artery aneurysm

1. INTRODUCTION

Popliteal artery represents most common region of aneurysms after aorta.[1-3]In the period 1999-2007, 21patients (19 males and 2 females), (Age range 50-88), (mean age 69), with popliteal aneurysm were treated at our department.

We noted that 4 Patients (all males) with the right leg affected were bus driver. A bus driver uses repeatedly, for at least 6 hours per day, his right foot on the accelerator and break pedal of the bus and popliteal artery has an important anatomical relation with the muscles that control the movement of the foot. The evaluation of the leg muscles with MR imaging after the execution of particular movement of the foot and the leg, elaborated with mathematical and bioengineering tools, may correlate with the mechanical stress on the artery that may lead to the aneurysm formation.
This findings may identify those persons at risk of developing popliteal aneurysm especially in those subject (workers, athletes, etc) that acts repeatedly movement with the lower limbs.

2. METHODS

2.1. Bioengineering Study

The study, which was developed, regards the analysis of the popliteal artery aneurysm in people who aren't familiar history to atherosclerotic disease, abnormal anatomy of the muscles of the popliteal cavity or deviations of the popliteal artery course.
According to recent studies, in these situations, the formation of aneurismal sacs is attributable to the PAES[4].In this case, there is a regular anatomy of the popliteal pit, but during walking, competitive activities or any other effort to induce an involvement of the lower limb, it's possible that the axis of arterial leg from the groin to the foot, can be compressed, invarious levels, from bone structures - muscle - tendon. In the case of this study, the movement analyzed is flexion-extension of the foot. In this regard, we proposed a description of the type of movement exercised when driving a truck, the articulation of the foot and the affected muscles. Such movement repeated over time can induce muscle hypertrophy, in particular, at the level of the soleus muscle and medial gastrocnemius. For this reason, the drivers would be among the

categories that are more susceptible to the popliteal artery functional entrapment syndrome, which may lead to aneurysm formation.

2.2. Image Acquisition

Data, 127 slices, were acquired from RM of the right knee. The subject was a healthy woman of 47 years old. 2D images have a resolution of 512 x 512 pixel, slice thickness of 4 mm, slice distance of 4mm and pixel dimension of 0.65 mm, Figure 1.

2.3. Geometry Reconstruction

The segmentation of the region of interest was performed on 3D Slicer, open-source software package for visualization and image analysis. In the first phase, the images were initialized using the definition of the Window/Level to discriminate little differences of density (of 0.5%), that are represented by different levels of gray, so we could increase the contrast of images. After the initialization, the segmentation was done using the Single Region Growing. The geometry was restituted in STL format (Standard Tessellation Language, native to the stereolithography CAD software created by 3D Systems of Valencia, CA, USA), Figure 1.
The final geometry was created in Comsol Multiphysics through the measure obtained by segmentation, Table 4. To optimize the model's elaboration, we performed only the region of interest: the flow, the artery and the muscles soleus, medial gastrocnemius, plantaris and popliteus, Figure 2.
Whereas, adipose tissue and the skin were simplified through a cylinder. The geometry was finished through form union, so it was only solid but the software could discriminate her different parts.
Finally, the meshing was realized using a free mesher that automatically created an unstructured mesh formed by tetrahedral and triangular elements. The mesh was chosen Fine and it restituted 56880 elements, Figure 2.

2.4. CFD Solver

CFD was performed using the commercial software ComsolMutiphysics. Therefore was used the module Fluid Dynamics – Incompressible Navier-Stokes.
Blood was assumed to be incompressible with a density of 1.050 kg/m^3 and dynamic viscosity of 0.0045 Pa*s.
The Navier-Stokes equation for a Newtonian and incompressible fluid formed a partial differential equation system[5-6]:

$$\rho\frac{\delta u}{\delta t} + \rho(u * \nabla) = \nabla * [-pI + \mu(\nabla u + (\nabla u^T)] + F$$

$$\rho\nabla * u = 0(3)$$

where v is the velocity field [m/s], F are the volume forces such as gravity [N/m^3], p is the pressure [Pa], ρ is the density of fluid[kg/m^3], μ is dynamic viscosity [Pa s].

To model the behavior of the arterial flow were specified the boundary conditions Inlet/Outlet pressure, no viscous stress, that are ideal because the variations of pressure, respect aorta, are known.
Therefore, we have been defined two functions that describe the variations from systole to diastole values, that characterized peripheral pulses, Figure 3. Finally, we have been imposed the condition of adhesions, i.e. a fluidin direct contact with a solid walladheresdue toviscous effectswithout giving rise to a relative flow. The condition Wall/No slipis precisely the adherence to a solid wall fixed in space.The Study of Time Dependent has been defined with t=(0:0.05:1), by which we derived the values of pressure and velocity along the artery.

2.5. FSI Solver

The module Structural Mechanics – Solid, Stress-Strain allowed to carry out structural analysis static or dynamic of all
types of geometry (3D, 2D and axial symmetry) and with various stresses (plane stress or plane strain, …). This module was exploited in order to consider the stresses suffered by artery that can induce the formation of an aneurysm. So, in this study, the problem has been addressed considering that:

- The surfaces of artery are in contact with the fluid, therefore, are subject to the forces due to pressure of the same.
- In functional popliteal artery entrapment syndrome, the walls are subjected to stress due to pressure exerted by the muscle.

In the first case, is set the rest condition of the knee, then the constraints relate to the
muscles around it. For the plantar muscle and popliteal has been imposed the condition of zero displacement, in this way the muscles can deform around the artery, but without inducing a load on it. For the muscles soleus and medial gastrocnemius, instead, in agreement to data reported on the literature, has been set a force of 758,313 [N], which varies parametrically, in such a way as to define the motion of the muscle. In the rest condition, the parameter that causes a change of this force is set equal to zero.
The value of the forces exerted by the fluid in contact with the wall is defined as:

$$F_A = \sigma * n \quad (4)$$

where F_A is the force per unit area [N/m^2], σ is the normal stress [N/m^2], n is the unit vector normal to the surface.
The PDE problems were solved using the solver PARDISO, by the solver Steady State Parametric, the parameter considered is the time.
It has been defined the time interval between zero and one, i.e. the time necessary for there to be the evolution

from the phase of systole to that of diastole, according to the course of pressure default.

In the second case, was analyzed the stress due to the load exerted from the soleus muscle, in the distal section, and from the medial gastrocnemius, in that medial.

This condition, in particular, is found in the lorry drivers, for whose posture, in the movement of flexion-extension of the foot is induced a constant stress of these muscles, which undergo hypertrophy and, consequently, in the exercise, they intermittently compress the artery. Therefore, has been defined a maximum force, as a function of which the muscles undergo a shift, such as to cause the trapping of the artery, it has been defined to be zero along x and z, while along y the force varies according to a parametric function:

$$P\_max\cdot((para<=1)\cdot para+(para>1)\cdot(2-para)) \quad (5)$$

where the parameter, para, varies between zero and one, so the initial condition is the rest state, then the trapping and again the release of the artery.

In the case where the entrapment is exercised by the soleus muscle such a force acts on it.

It follows the movement of the muscle in the flexion-extension of the foot and the subsequent entrapment of the artery in the distal region.

For the plantar muscle, popliteal and gastrocnemius is imposed the condition of zero displacement, in this way the muscles can deform around the artery, but without inducing a load on it.

Conversely, in case where the entrapment is charged to the medial. In this case, the displacement of the plantar muscles, soleus and popliteal is set to zero along the three cartesian axes. While there is provided, according to the same principle of the soleus muscle, the displacement of the gastrocnemius along the y-axis, (Eq 5).

The solution of this study is for medal ways in the stationary case, with respect to time, and dependent upon the parameter that indicates the shift of the muscles involved.

In both cases, the mechanical properties of the soleus, medial gastrocnemius, plantar, popliteus and external tissue are: Lamé constant (μ) 7.20e6 [Pa], Lamé constant (λ) 20· μ-2· μ/3 [Pa], Density 1200 [kg/m^3].For walls Lamé constant (μ) 6.20e6 [Pa], Lamé constant (λ) 20·μ-2· μ/3 [Pa], Density 960 kg/m^3.

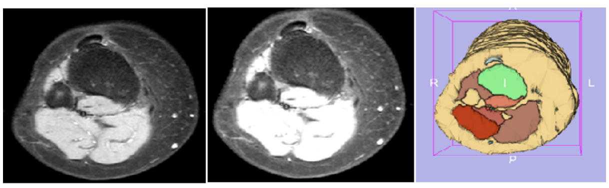

Figure 1: The first figure on the left represents one of 127 slices were scanned, the second the same slice pre-processed, the last on the right shows the segmentation result in 3D Slicer.

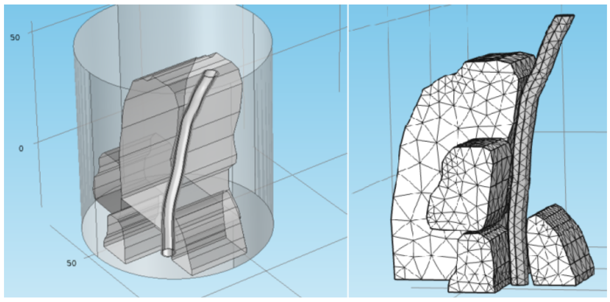

Figure 2: On the left is represented the full geometry, on the right the mesh.

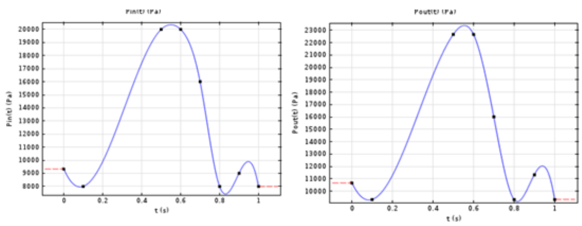

Figure 3: On the left inlet pressure, on the right outlet pressure that characterized peripheral pulses due to the peripheral resistance.

3. RESULTS

3.1. CFD results

The results for the values of pressure and velocity of the fluid have been developed in the first part of the analysis. We were imposed as boundary conditions the pressure, which evolve over a period of one second, from thediastolic value in the systolic, then defining the pulsation that characterized the peripheral pulses. Therefore, the values of the average speed, for each instant of time, vary between about 70 [cm/s] and 30[cm/s], Table 1. Assuming thatthe artery has constant cross section, these results show that the speed varies with the cardiac cycle. Furthermore, having assumed that the flow islaminar, the speed at the centerof the vessel is greater than that which is locatedat the edges andthisphenomenon is called *Parabolic Profile Velocity*.

3.2. FSI results for the rest condition

In the analysishas been supposed that the flow is continuous due to the elasticity of the arterial walls: they, after having dilated during the cardiac systole to accommodate the blood, in diastole retract thereby ensuring a forward thrust to the mass of blood. The arteryis affected by the compression force of blood flow, as a function of which will have in the systole phase an increase in diameter of the wall, which is equal

to $4.1 \cdot 10^{-3} \cdot 10$ [mm], while t = 1 [s], during diastole, is equal to $1.85 \cdot 10^{-3} 10$[mm].
The average pressure suffered by the wall varies between about 2900[Pa], in diastole, and 6000[Pa], in systole.
However, the hypotheses of the study are: young and healthy patients who did nothave risk factors or family history of atherosclerotic disease. Under these assumptions, the analysis does not focuson the definition of Shear Stress suffered by thevessel wall, which can be, also, a risk factorfor the onset of aneurismal disease.
However, even thisstage of the analysis has a certain importance in order to consider, first of all, the physiological condition of the artery and the stresses it undergoes in this case, and secondly, a full analysis can't be separated fromall the phenomenathat may occur.

3.3. FSI results duringthe flexion-extension of foot

The purpose of this experimental study is to define the prevalence of the popliteal artery occlusion during the active plantar flexion-extension, in young volunteers who lead physical activity. The analysis was carried out in such a way that could be induced the same condition suffered by the wall in case of exercise repeated.[7]
In the pathological case, we have distinguished two conditions: the first caused by entrapment soleus and the second by medial gastrocnemius muscle. Whereas the force exerted by the gastrocnemius muscle, the maximum displacementof the wall is about 0.16 [mm].
Comsol Multiphisycs provides a series of tools by means of which it is possible to derive the pressure over the entire wall. The value of the pressure undergone by the vessel is obtained by integrating the value of the pressure with respect to the surface of the wall itself:

$$P = \int_A p dA \qquad (1)$$

The average pressure is calculated by simply dividing the load applied to the area of the wall:

$$p_m = \frac{P}{A} (2)$$

The values, obtained, were plotted with respect to the variation of the force and the time, Figure 4 (a-b). The latter part of the analysis made possible to compare the physiological and pathological data, Table 2.
As was expected, there is a marked increase in the average pressure over the entire artery. In addition, Figure 4 (a) shows how varying the pressure on the vessel as a function of the movement of the muscle: it is verified that the occlusion of the artery occurs intermittently, therefore, the rising phase of the function indicates the trapping during exercise, in the second part indicates the release of the artery, returning to the resting.

Finally, it was considered the pressure experienced by the side section of the artery, in contact with the muscle Figure 4 (c), according to equations 1 and 2, and subsequently, has been considered the stress undergone by that section, Figure 4 (d). It is evident, Figure 4 (c), that at the medial, that is, considering the length of the artery of 80 mm to about 40 mm, there is a peak pressure. This peak corresponds with the region where the trapping occurs due to the gastrocnemius muscle[8] compression on the artery.
Moreover, comparing the two curves of Figure 4 (c) and the two curves of Figure 4 (d), these show that in the region urged there is a pressure increase of an order of magnitudean increase in stress on artery and, therefore, according to the experimental data that are now known[9], these repeated stresses may be such as to induce a reduction in the elasticity of the artery, resulting in the expansion and formation of an aneurysm sac.
The same type of analysis has allowed to solve the problem in the case where the occlusion is due to the force exerted by the soleus muscle. In this case,the maximum displacementof the wall is about 0.3947[mm].
We have been defined the variation of pressure respect force and time, Figure 5 (a-b), the contact pressure and the stress suffered by vessel, Figure 5 (c-d). What it should be emphasized is, in this case, the pressure increase in the pathological condition, compared to the case previously considered, Table 3. About this, today, there are not sure explanations. The only assumption that can be advanced is that: the soleus muscle is characterized by a high pinnation and by I type fibers, while the gastrocnemius has a pinnation lower and prevalence of II type fibers, so the first serves to generate for a long time static force, the second generates lessforce, for less time, but faster. Consequently, for a given applied force, since the application time increased, the pressure and the induced stress will be higher.

4. DISCUSSION

Popliteal aneurysms constitute 70% of peripheral aneurysms with an incidence of 4.5-7.5 new cases out of 100.000 inhabitants per year in the world[1-3].
Natural story of poplitea artery aneurysms is characterized by high rate of thrombotic and thromboembolic complications which may determine an increased risk towards aserious damage of peripheral artery vessels.
Their clinical interest is due to frequent serious complications which may cause limb amputation. Various trials report a frequency rate of 18 -57 % ofcomplications like embolism, thrombosis and rarely rupture [10-12]
Acute ischemia may occur for acute thrombosis of aneurysm, chronic ischemia
is usually due to progressive occlusion for multiple thrombotic apposition in aneurismal sac [13].

About one third of patients are asymptomatic at first diagnosis [10]. Acute or chronic peripheral ischemia for thrombosis or distal embolism are most common clinical presentation [1,14].
Less frequent symptoms, often underestimate or not known, are those related to aneurysm compression on adjacent venous and nervous structures. Symptomatology, in these cases, may vary from pain (nervous irritation, venous outflow obstruction),oedema (marked venous outflow obstruction) to popliteal vein thrombosis (related to aneurismal sac dimension) [15].
Anatomy. The popliteal artery is the continuation of the superficial femoral artery, and courses through the popliteal fossa. It extends from the opening in the Adductor magnus, at the junction of the middle and lower thirds of the thigh, downward and lateral ward to the intercondyloid fossa of the femur, and then vertically downward to the lower border of the Popliteus, where it divides into anterior and posterior tibial arteries. In front of the artery from above downward are the popliteal surface of the femur (which is separated from the vessel by some fat), the back of the knee-joint, and the fascia covering the Popliteus. Behind, it is overlapped by the Semimembranosus above, and is covered by the Gastrocnemius and Plantaris below. In the middle part of its course the artery is separated from the integument and fasciæ by a quantity of fat, and is crossed from the lateral to the medial side by the tibial nerve and the popliteal vein, the vein being between the nerve and the artery and closely adherent to the latter. On its lateral side, above, are the Biceps femoris, thetibial nerve, the popliteal vein, and the lateral condyle of the femur; below, thePlantaris muscle, the lateral head of the Gastrocnemius and the Soleus muscle. On its medial side, above, are the Semimembranosus and the medial condyle of the femur; below, the tibial nerve, the popliteal vein, and the medial head of the Gastrocnemius [16]. Popliteal artery is located in a compartment in which different muscles work. These muscles, expecially Gastrocnemius and Soleus, after specific movements apply pressure force on the vessel itself.
Erdoes LS et al. showed that, in normal population, sonographic examination can show arterial compression elicited by maneuvers such as plantar flexion and dorsiflexion of the feet. Although this finding is consistent with the diagnosis of popliteal artery entrapment syndrome, previous studies have shown occlusion in up to 59% of asymptomatic subjects. In those patients, normal anatomy was confirmed on MRI, and the popliteal artery occlusion was at the soleal sling site as a result of compression by the soleus muscle, lateral head of the gastrocnemius muscle, plantaris muscle, and popliteus muscle.
In the period 1999-2007, 21 patients (19 males and 2 females), (Age range 50-88), (mean age 69), with popliteal aneurysm were treated at our department.
We noted that 4 Patients (all males) with the right leg affected were bus driver.
This kind of working activity may represent a risk factor for popliteal aneurysm formation as bus drivers generally use repeatedly, for at least 6 hours per day, his right foot on the accelerator and break pedal of the bus. The break pedal offer, in fact, a certain resistance to the flexion of the foot. In this condition the generation of anomalous local forces in the popliteal fossa may attempt the arterial wall integrity that may lead to aneurysm formation.

Table 1: Values assumed by the speed input and output in the different phases of the cardiac cycle.

t	Average velocity input[cm/s]	Average velocity output [cm/s]
0	0.00661	0.00472
0.55418	0.74669	0.41618

Table 2: The Table shows the data physiological and pathological fort he time instants which indicate the transition from diastole to systole and vice versa.

t	Pressure in the physiological case [Pa]	Pressure in the pathological case [Pa]
0	2988.76593	2780.45252
0.45	5991.35984	11989.54278
0.5	6352.6332	12645.33149
1	2797.42349	30899.26342

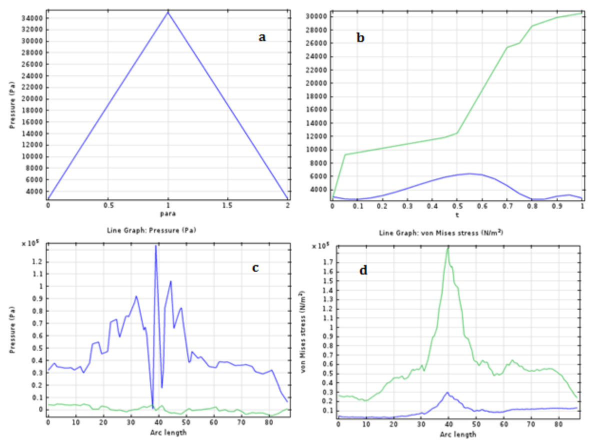

Figure 4: (a) Variation of the pressure exerted by the muscle; (b) in blue is shown the average pressure acting on the vessel in the physiological case, in green in the pathological case; (c) pressure suffered by the side section of the artery in contact with the muscle, the physiological condition in green, blue in the pathological; (d) the blue line represents the stress suffered by vessel under physiological conditions, the green stress in pathological conditions.

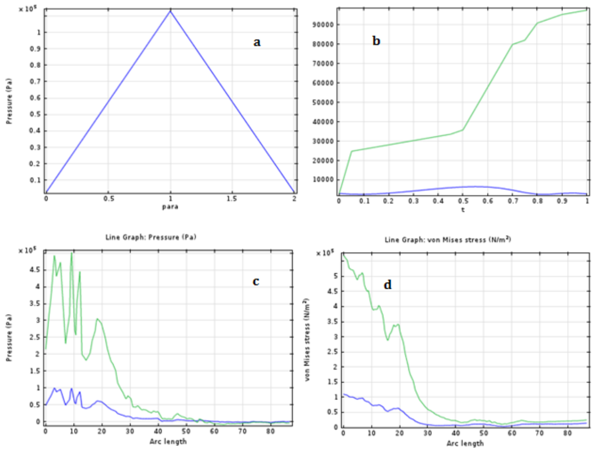

Figure 5: Variation of the pressure exerted by the soleus muscle; (b) the blue line represents the stress sufferedby vessel under physiological conditions, the green stress in pathological conditions; (c) pressure suffered by the side section of the artery in contact with the soleus muscle, the physiological conditionin green, blue in the pathological; (d) the blue line represents the stress suffered by wall sunder physiological conditions, the green stress in pathological conditions.

Table 3: The Table shows the data physiological and pathological for the time instants which indicate the transition from diastole to systole and vice versa.

t	physiological case (Pa)	pathological case gastrocnemio(Pa)	pathological case soleus (Pa)
0	2988.76593	2780.45252	2797.42345
0.45	5991.35984	11989.54278	33569.644
0.5	6352.6332	12645.33149	35769.99161
1	2797.42349	30899.26342	97510.95427

5. CONCLUSIONS

In functional popliteal artery entrapment syndrome, the walls are subjected to stress due to pressure exerted by the muscle. This is the final aspect studied in this analysis, from the consideration that: in young patients, who aren't familiar history to atherosclerotic disease, in fact, the increase in diameter of the artery due to stress caused by the fluid is negligible. In fact, what causes the pathological condition, i.e. the formation of the aneurysm sac, is the stress due to the load exerted from the soleus muscle, in the distal section, or from the medial gastrocnemius, in that medial.

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