

**UNIVERSITÀ DEGLI STUDI DI PADOVA**

***Facoltà di Ingegneria***

***Dipartimento di Ingegneria dell'Informazione***

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Tesi di Laurea

**Computational framework based on computer aided design and  
finite element modeling for the development of a new medical stent  
with variable applications.**

**Relatore: Prof. Pavan Piero**

**Correlatore: Prof. Malvè Mauro**

**Laureando: Omizzolo Mattia**

**Matricola: 1182566**

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## **Abstract**

The main goal of this work is the development of a computational framework capable of designing and numerically simulating a new biodegradable medical device for cardiovascular and respiratory applications. This framework needs to be parametric since the geometry of the new device should be susceptible to be changed depending on the selected application. The new stent should be printable with the 3D printing technique with a biodegradable material to be chosen. This work is a part of the regional project PC086-087-088 CONDE financed by the Department of Economic Development of the Navarra Government. For designing the new device, two typical stent typologies have been used: Mesh-W and Mesh-T. Additionally, squared and circular sections have been tested for the stent strut. As parameters for the device, the strut thickness, the stent diameter and length, the length and the number of repetitive elements within a single stent unit-cell have been chosen. The main idea of the work is that, once a parameter is changed, all the design, computational mesh and boundary conditions will simultaneously actualize for allowing a new numerical simulation. The latter is necessary for estimating the radial compression of the device that is the most important feature of the device. Two biodegradable material have been selected: the PCL that has been characterized with a linear elastic material behavior and a Magnesium alloy (AZ31) that has been characterized using an elastic-plastic material. The main parameters that have been changed are the stent diameter (5 to 18 mm), the single unit-cell length (2 to 3 mm) the strut thickness (0.3 to 0.5mm) and the number of unit cell repetitions. As a conclusion, the computational framework is capable of designing, analyzing and characterizing the device with the constraints and the requirements of the project as for example the 3D printing and the biodegradable material to be chosen.



# ***Chapter 1***

## ***INTRODUCTION***

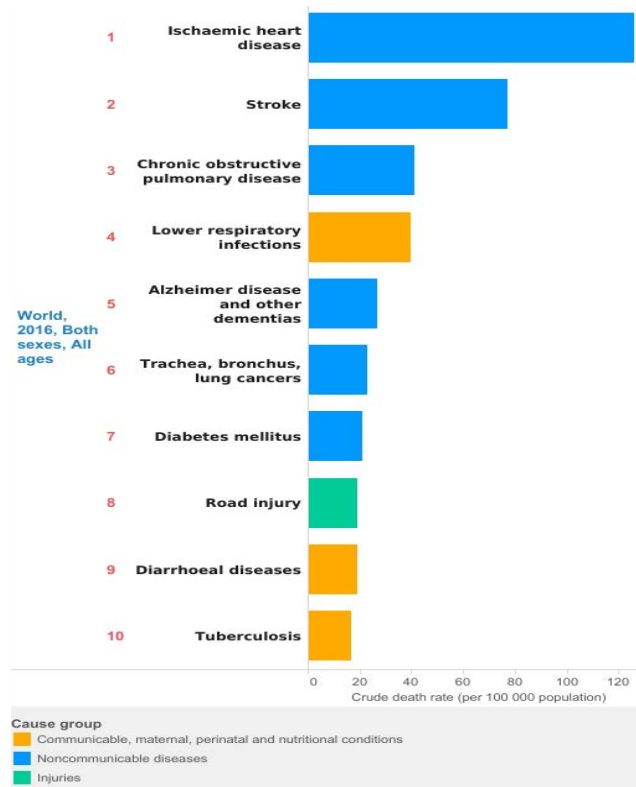
### **1.1 Stent definition**

A stent is a cylindrical structure in wire mesh, which is introduced into blood vessels and it is made to expand until its diameter is equal to that of the lumen.

### **1.2 Clinical background**

From the most recent data of Global Health Observatory (2016), can be seen how the incidence of the cardiovascular disease is the most important death cause in the world. From the below figure, where are presents the incidence rate of the first ten causes of death in the world, is clear that ischemic heart disease gets the most important role.

In particular, in the year 2016 the first ten death causes killed 56.9 millions of people, which correspond at the 54% of the entire world deaths, and of these 15.2 millions of deceases, are caused for the first death cause, the ischemic heart one. The trend is the same from the last 15 years. Is difficult collect this type of data, mostly in the poor countries and in this case are estimated. They are very important for the countries, because in this manner they can fix new politics to improve the health of the people.



**Figure 1** – Global Health Observatory (GHO) data (2016)

Only in the United States of America every year are implanted over than 1.8 million stents and, of these, approximately 965000 are used in the coronary applications. The remaining are for peripheral vascular implantation.

This data gives the importance of the development of the devices, which can help the medicine procedures to improve the technique to resolve this kind of problem in the society. In the last 30 years, from when was invented and applied the first stent (1986), there was a high impulse on the research groups to improve the characteristics of these devices. In a stent, there are many fields in which its possible to work to obtain a better device, but some of these are limited by the needs imposed, for example, by the material chosen, by the realization technique, by the design selected and by the application site.

The realization process of the stent is not so easy and for each case is necessary to design a new device. This is one of the most important problems in the stent productions. In this manner, it is difficult adapt one device to a different site from the cardiovascular one. The application range is important, because the stents could be used for all the organs which have a lumen. This generalization is the objective of this work. The innovation of the work will improve the stent realization process and the simulation testing part of these devices.

The guidelines at which all the companies watch to realize a useful device, contain the following features:

- Excellent flexibility and manageability
- High radial stiffness
- Shape such as the vessel
- Safe anchorage
- Radiopaque
- Patient specific
- Biocompatibility

### 1.2.1 Blood vessel

Is important to understand how is composed a typical blood vessel where the new device could be implanted. The artery wall is composed by three concentric layers:

1. The inner layer is the *intima*. It is positioned on a very thin thickness of connective tissue which is constituted by elastic fibers forming an inner elastic lamina;
2. The *media layer* which can be made mainly by elastic tissue in the artery with a large diameter, or by smooth muscular tissue in the artery with a medium or small diameter. The first are named elastic type arteries and the latter the muscular ones;
3. The external layer, named *Tunica externa or adventitia* is made by connective tissue and between this layer and the intermediate one is present an elastic external lamina.

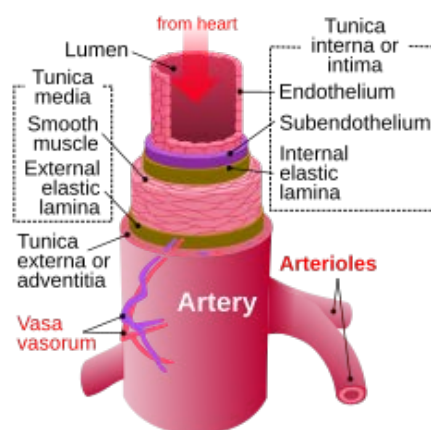


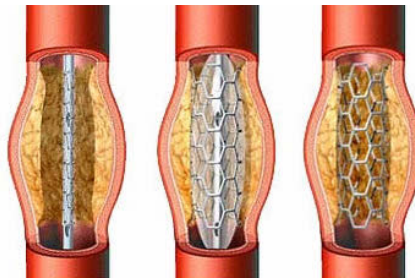
Figure 44 – Artery composition

### 1.2.2 Endothelial tissue

The endothelial tissue is a particular type of connective tissue, deriving from the mesenchymal one, which cover the internal wall of the blood vessel. The endothelial cells which compose the tissue are plane, polygonal and stretched to the blood flow. The apical face is oriented towards the vessel lumen and the nuclei are in the same direction. The cells contain a small number of elements such as Golgi apparatus, mitochondria, endoplasmic reticulum and ribosomes. An elevated number of pinocytosis vesicles for the transport through the endothelium wall and the electro-dense granules of Weibel-Palade which are present also in the platelets, are contained in the cytoplasm of the cells. In the granules membranes is present the P selectin which is inside the Willebrand coefficient which is the factor eight of the coagulation. The endothelial tissue has a very important role in the coagulation process, in fact is able to interact with the proteins involved in the healing process and with the blood cells. The secretion done by the endothelial cells can inhibit the thrombosis and the hyperplasia of the intima, which is the excessive growth of the smooth muscular cells causing the obstruction of the vessel lumen and are essential to guarantee the homeostasis and the maintenance of the vessel integrity. The application site of the secreted elements is different. In fact, the paracrine secretion happens near the cell for influence the vasal wall, but the endocrine secretion is in the flow and develop its function far from the cells, having functions such as the regulation of the blood pression. The endothelial tissue has a fundamental role in the remodeling, which is observed in the hypertension, in the stenosis after the angioplasty and in the atherosclerosis. Also, is important in the coagulation modulation and in the interactions between the blood cells, the platelets and the leucocytes. Moreover, the tissue is influenced by the mechanical signals deriving from the blood flow and by the neuro-hormonal signals deriving from the vasoactive mediators and has a control function of the arteries and the micro-flow. Two mechanical forces can be provoked by the blood flow on the vessel wall: the shear stress and the tensive stress. The first is caused by the friction of the blood flow on the vessel wall and influences only the epithelial cells, instead the latter is caused by the hydrostatic pression in the vessel and interested the endothelium, the fibroblasts and the smooth muscular cells. The shear stress causes the liberation of the vasodilators factors and the tension stress influence the vessel contraction. The net effect is the combination between the two phenomena. The studies for this behavior of the endothelium tissue were done by Holtz in the 1983.

### 1.2.3 Angioplasty: Surgical procedure

The surgical procedure used for the implantation of the stents is the Angioplasty. This is a minimal invasive technique. The first time was realized in 1977, by the German surgeon Gruntzig. The surgical procedure has a duration of about 1 hour. The angioplasty is performed under local anesthesia: the patient is therefore awake and conscious. The catheter, which contain the stent and a balloon, is insert from the percutaneous puncture of an artery, usually femoral artery or radial artery, and is carried up to the stenotic vessel. When it arrives in the correct position, the balloon that is present inside the stent, is inflated and the device restores the normal diameter of the vessel and the improvement of the blood flow. The medical device, thanks to its features will remain in situ and, at the end, the catheter will be removed and the surgical procedure end.



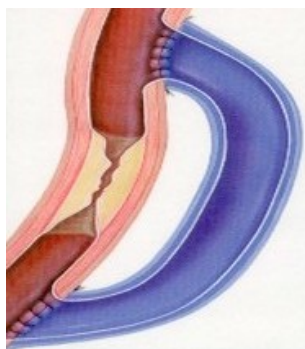
**Figure 2** – Angioplasty procedure

The plaque, which blocked the vessel, is pushed to the wall sides, but is not eliminated. After four months from the intervention, there is the complete endothelization that means that the device is full covered by the cells of the inner part of the vessel. There are several consequences after a stent deployment. One of these problems is the phenomenon called Restenosis and it is the partial obstruction of the vessel: in fact, the tissue grows up also between the mesh of the stent and can decrease the diameter of the lumen until the thirty percent.



**Figure 3** – Restenosis after stent application

The life of a metallic stent is typically of 20 years during which, unfortunately, the artery tends to re-occlude and cause slowly the usefulness of the device. The Bypass technique permits to avoid the obstruction connecting the healthy part of the blood vessel using a part of an artery or a vein (for the first one is used a tract of internal thoracic artery, and for the second one a tract of Safena vein taken from the leg of the patient). The procedure is done with the heart stopped, using the heart-lung machine, or with the beating heart.



**Figure 4** – Bypass example

It is important to remember that the application field of these devices is not the cardiovascular one but is also possible to use for Trachea applications, as for examples. In this work we focus on the Cardiovascular field, but in the future will be investigated also the tracheal one.

#### **1.2.4 Biodegradation**

For the aforementioned reasons, it would be of a great advantage that the stent disappears after complying its mission. In the last decades, new devices with a variety of materials have been developed with this aim. In particular, the biodegradable materials have been introduced as alternative of traditional metallic stents. The temporal presence of the stent avoids the long-term problems of the non-degradable devices such as fatigue structure fracture, in-stent restenosis and late stent thrombosis. Unfortunately, if this process is not controlled, could bring problems for the patient health. In fact, the healing process approximately persist for 6-12 month. Hence, it's necessary, that the device maintain its mechanical properties at least for this period. Theoretically, if the degradation process works properly, at the end could be the increase of local alkalization or hydrogen generation, etc. After the healing period, the stent would disappear degrading itself into non-toxic and non-inflammatory



products that are readily soluble inside the human body, without influencing the closed tissues.

### **1.3 Biomaterial and Biocompatibility**

A biomaterial is a substance used for the construction of devices able to substitute a living part situated in the human body. This is a generic description of the word, but in the last years was perfected by the researchers. The first definition of biomaterial was proposed in the 1974, at the 6<sup>th</sup> Annual International Biomaterials Symposium and presented the “Biomaterial as an inert substance for the organism and also for the pharmacologic point of view, designed for the implant or the incorporation in a living system” [1]. Now, the last recent version of the definition is correlated with the operative and functional approach. Actually, “a biomaterial is synthetic substance projected to be used for a long time in contact with biological elements, minimizing the damage reactions caused by the organism”. An important condition which the materials must have is the biocompatibility that is “the ability to determine, from the living system, a positive reaction when it is placed inside the human body, for a specific application” [2].

Since the ancient time, were present a lot of examples of biomaterial applications. The first was in the Egyptian era where the artificial prothesis were made of wood. The metallic materials were used for the first time during the American civil war. A famous episode was the utilization of a nail to fix a femoral fracture of a soldier. From that moment there was a development in the material research which permitted the utilization of stainless steels, metallic alloys, ceramics and polymers for the realization of the devices.

The biomaterials history can be summarized into three fundamental parts:

- First biomaterials generation is that which has the feature of minimizing the physics and chemical interaction between the material and the organism.
- Second biomaterials generation: the substance is bioactive which means that there is a rapid integration of the material with the organism that implies the formation of bonds and interactions with the physiological fluid, or resorbable, if the material is degraded by the living system, without damage or toxic effects for the organism.
- Third biomaterials generation: the material has to be bioactive and resorbable. The research, now, is following this direction.

The last category of biomaterials presented are also named biomimetics, because are able to interact with the tissues through process of biomolecular recognition mechanisms.

Is important to know that the biomaterials are also classified by their chemical nature into:

- Polymerics
- Metallics
- Composites
- Ceramics

## **1.4 Stent**

In the world market there are a lot of typologies of stent, characterizing for the presence and the absence of:

- a particular structure of the section
- a certain design
- made with a particular category of materials.

In the following, the two main types of stent will be presented, including their materials and characteristics. Also, the two designs selected for this work will be introduced and discussed in detail.

### **1.4.1 Non-biodegradable stents**

The first category presented in this work is occupied by non-biodegradable stents. Typically, these devices are made with metallic materials (BMS). They were used for the first time in 1987 [3] and their utilization is considered the second revolution in interventional cardiology [4]. The stents are made of stainless steel (316L), nickel-titanium and cobalt-chrome alloys, which are widely used in the arterial diseases. After the healing time usually occurring between 6-12 months, the metal stents remain permanently located in the arterial vessel of interest, though it becomes unnecessary. Its presence usually causes complications, as in-stent restenosis, subacute thrombosis, tissue inflammation and risk of loosening and fracturing, caused by long periods of cyclic loading of the stent [5][7]. Nevertheless, these devices have a good biocompatibility and mechanical properties and give sufficient scaffolding to the target arteries [5]. In the table below are summarized the features of this first stent category:

CHARACTERISTICS	<ul style="list-style-type: none"> <li>• High radial stiffness with a very thin thickness</li> </ul>
	<ul style="list-style-type: none"> <li>• Average life of 15-20 years</li> </ul>
	<ul style="list-style-type: none"> <li>• Neo-intima hyperplasia formation</li> </ul>
	<ul style="list-style-type: none"> <li>• Stent thrombosis</li> </ul>
	<ul style="list-style-type: none"> <li>• In-stent restenosis</li> </ul>
	<ul style="list-style-type: none"> <li>• Metallic material formation</li> </ul>

**Table 1** – Non biodegradable stent characteristics

In the following section, will be presented the principal stents of BMS category, present in the global market.

### **1.4.1.1 Examples of non-biodegradable stents**

#### **Zilver Flex stent**

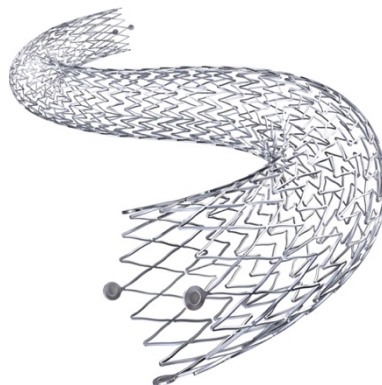
The Zilver® vascular stent is a self-expanding device made of Nitinol. Its intrinsic mechanical properties allow an excellent flexibility. Its shape is as a slotted tube, which is projected to provide support, while maintaining flexibility in the vessel upon deployment. After the application, the stent is designed to impart an outward radial force upon the inner lumen of the vessel, establishing patency in the stented region. The shape of the mesh is “W named” and it has a square section. The device is available in different sizes for the diameter and the length.



**Figure 5** – Zilver Flex® vascular stent

### **Innova stent**

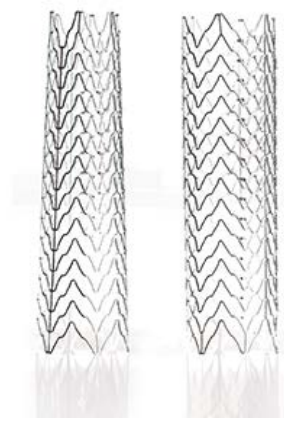
The Innova™ Vascular Self-Expanding Stent is produced by the Boston Scientific company. The device is a laser cut self-expanding stent made of a nickel titanium alloy (Nitinol). On both the proximal and distal ends of the device, radiopaque markers made of tantalum are present to increase visibility of the stent to aid in placement. The Innova™ stent has a very similar design to that of the Wallstent™ and it appears as its evolution. In fact, the main difference is that the initial and the final ends of the Innova™ are closed, instead those of the Wallstent™ are open. The Innova™ stent has a circular section and the shape of the mesh is “W named”.



**Figure 6** – Innova™ vascular stent

## **Acculink stent**

The RX Acculink Carotid Stent System is produced by Abbott. The device permits a high coverage to reduce embolic risk. There are both the straight and tapered stent options. It is made by Nitinol material which gives strength, crush resistance, conformability and flexibility. The stent is indicated for the treatment of patients at high and standard risk for adverse events from carotid endarterectomy who require carotid revascularization and meet the criteria outlined below. The device is not indicated for the patient which suffers hypersensitivity to nickel-titanium.



**Figure 7 – Acculink Carotid Stent**

### **1.4.2 Biodegradable stents**

The second category is that of the Biodegradable Stent (BDS). The scientists noticed that the permanence in the human body of the BMs device was not safety for the patient and for this reason the research went towards a way. BDS is considered to be the fourth revolution in interventional cardiology. [4] The biodegradable devices support the vessel inner wall for a limited period of about 4-6 months. After the healing period, the vessel will be healed and reorganized, while the biodegradable stent will be degraded and absorbed [4]. The vessel, after the disappearance of the BDS, is left free from foreign devices in the site where the disease was, thus there will be the retrieval of the vaso-reactivity with the potential of vessel remodeling [8]. Using BDS leads the vascular restoration, which is a great benefit because preserve the physiological integrity of the vessels, the long-term positive remodeling and the reactive vasomotion [9]. The

principal materials used to make the BDS are classified in two groups: the polymeric or the metallic ones. In the table below are summarized the features of the second category of stent presented:

CHARACTERISTICS	Low presence of in-stent restenosis
	Low stent thrombosis
	Fast degradation
	High radial stiffness, but with a greater thickness than the metallic one
	Made of metallic alloys or of polymeric materials
	degradation into non- toxic product

**Table 2** – Biodegradable stent characteristics

#### **1.4.2.1 Biodegradable polymeric stents**

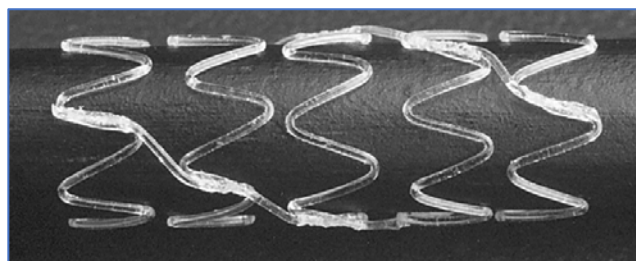
The polymeric materials are widely used in the medical treatment. A common example is the Collagen, which is employed from a lot of time. The research into biomedical applications of synthetic degradable polymers started only in the 1960s [10]. These materials present a very useful intrinsic properties, as the ability to be broken down and resorbed without removal or surgical intervention. The biodegradable polymers present a number of advantages over other materials for realizing devices. The main advantages are connected with the degradation time which is possible to adapt it to the different applications, modifying some parameters. In addition, the principal advantages in their utilization are good biocompatibility, low coefficients of

friction, easy processing and workability, ability to change chemically and physically the surface, and ability to immobilize cells or biomolecules within them or on the surface [11]. The synthetic biodegradable polymers most uses in the clinical application and the stent production are poly (glycolic acid), poly (lactic acid) and their copolymers, poly (p-dioxanone), and copolymers of trimethylene carbonate and glycolide.

#### **1.4.2.1.1 Examples of biodegradable polymeric stents**

##### **Igaki-Tamai stent**

The Igaki-Tamai stent is a biodegradable coronary stent. The two doctors, who invented this device, worked, for the realization, at Kyoto Medical Planning. It was the first biodegradable device applied in human body and the clinical studies started more than twenty years ago, or rather in 1998. But only from 2007 it is commercially available. Its design is “W named” and is made of a high molecular weight (321KDa) PLLA. The complete degradation occurs more of three years after the surgical procedure. The struct thickness of the device is 0.17 mm. it expands a certain temperature and there is no coating. The Studies showed the effectiveness, the feasibility and the safeness of the stent. The evolution of the Igaki-Tamai stent was implemented from the 2007 and it is used for the treatment of blood vessels in the lower extremities and it is known with the Remedy™ name.



**Figure 8** – Igaki-Tamai vascular stent

##### **Absorb bioresorbable vascular scaffold**

The Absorb Bioresorbable Vascular Scaffold (BVS) (Abbott, California) is a biodegradable stent that will fully resorb and is used to improve the vessel luminal diameter in patients with ischemic heart disease. The device

is made by poly (L-lactide) (PLLA) and it has a coating layer made by poly (D, L-lactide) (PDLLA) which is used to facilitate the release of drugs. The stent has a “W named” mesh, it has two platinum radiopaque markers and it is expanded with the balloon technique.

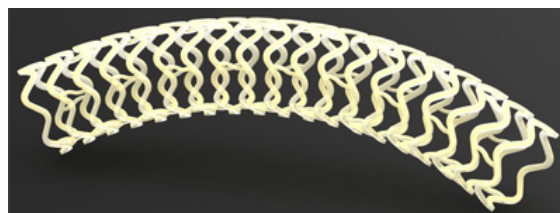
The device can be used only for the vessels, which have the diameter of 2.5 mm and 3.75 mm.



**Figure 9** – Absorb Bioresorbable vascular scaffold

### **Reva stent**

The REVA stent (REVA Medical, California, USA) is a medical device, made of biodegradable polycarbonate polymers derived from naturally occurring tyrosine amino acid. The bonds of iodine are covalent for radiopacity. The device, also, has the function to restore the natural vessel motion in one year and the complete resorption is with benign degradants. As all the other device, it provides strength during vessel healing period. The Reva stent has a struct thickness of 0.2 mm, which permits a safe expansion for the device and the function to gives the adequate radial force.



**Figure 10** – Reva stent



### **1.4.2.2 Biodegradable metallic stent**

The biodegradable metallic stent is the last way that the researchers are investigating with the objective to obtain the best device for the surgical applications. Biodegradable metals are defined as metals, which corrode gradually *in vivo*, with a proper host response induced by the products deriving by the corrosion, then, after the healing period, are absorbed with no implant residues [12]. Now, the materials most investigated are magnesium (Mg) and Iron (Fe) based alloys, but the studies are oriented on the magnesium. The biodegradable Mg alloys appear as the suitable biomedical degradable materials. Firstly, this type of materials is dissoluble in aqueous solutions, mostly in those where are contained chloride ion electrolytes, since of their very low corrosion potential [13]. Secondly, the Young's modulus of the bone tissue (15-20 GPa) is close to that one of the magnesium alloy (45GPa). Those of the stainless steel and of the Nitinol are very different. For this reason, the stress shielding effect is avoided. Thirdly, the Mg cation is one of the essential elements in the human body and the fourth most abundant. The daily quantity of Mg intake in a health adult person is 300-400 mg and greater amounts of this element are harmlessly and efficiently excreted in the urine [14]. But this element has a limitation in the degradation. In fact, Mg has a very high corrosion rate and commonly this involve the degradation before the healing period end. To improve the resistance to the corrosion can be used:

- alloys;
- particular structure design;
- surface modification.

These are the technique which gave the manner to solve this limitation.

#### **1.4.2.2.1 Examples of biodegradable metallic stents**

##### **Dreams stent**

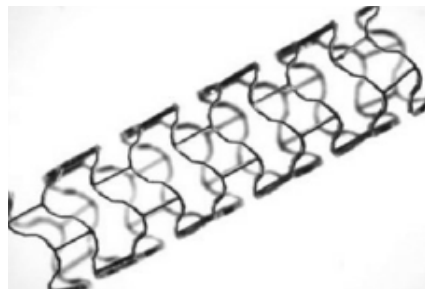
The DREAMS stent is an evolution of the AMS device, produced by the Biotronik company. The AMS stent was the first biodegradable stent produced by the company. It was made for the 97% by Mg and for the 7% by rare earth metals. The improvements that are present in Dreams biodegradable device are essentially four:

- now is used a Mg alloy with a slower resorption and a higher collapse pressure;
- the struct thickness is reduced;
- there is the changing between rectangular to square structs;
- is added an antiproliferative drug-eluting polymeric coating.

Actually, the resorption time is augmented from 2 months of the AMS device until 9-12 months of this one. There are two generation of the stent. In the first, the coating layer has a thickness of 1  $\mu\text{m}$ . In the second generation, are improved the design, which gives to the device a great radial stiffness comparable to the metallic stent and received the CE mark in the 2016 [15].



**Figure 11** – Ams vascular stent, 1<sup>st</sup> generation



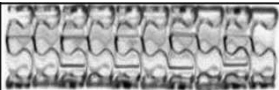







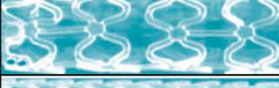

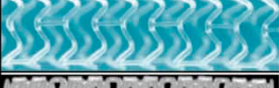


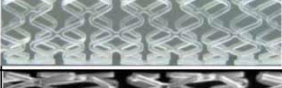

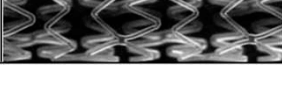
**Figure 12** – Dreams vascular stent, 1<sup>st</sup> generation



**Figure 13** – Dreams vascular stent, 2<sup>nd</sup> generation

### 1.4.3 Stents available on the market

In the table 3, it is possible to see all the stent available on the world market. The table allows a general view of the devices for a better visual comparison of the design and of the material (identifiable only from the color). The principal stents and the most interesting for the features are been described before. There is a lot of work to do in the research field to obtain a better device which could help the medicine to improve the ischemic disease treatment. Possible and necessary improvements are also responsible of the stent companies, as did the Biotronik company for the Dreams devices.

AMS 1		DESolve	
DREAMS 1		ART	
DREAMS 2		ART18Z (ART 2 <sup>nd</sup> Gen)	
Igaki-Tamai		IDEAL BTI	
BVS 1.0		IDEAL BioStent	
BVS 1.1		Amaranth	
REVA		Xinsorb	
ReZolve		ON-AVS	

**Table 3** – Stents available

## 1.5 Mesh design

In the world market, the devices, which have more success, because have better mechanical properties, have two typologies of mesh structure: The type-T and the type-W.

The starting point in the development of the new device was to take the most improved design presents in the literature. The idea was to use these designs as base for the new improvements which give better mechanical properties to the stents and permit the fabrication of the devices. The software used was SolidWorks and all the design possible were limited from the constraints deriving from the method used for their production.

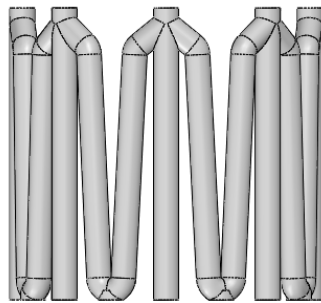


Figure 14 – W mesh

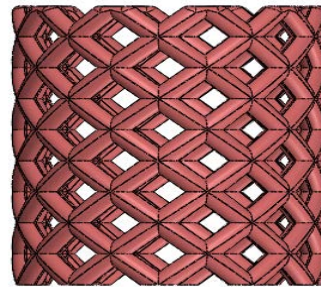
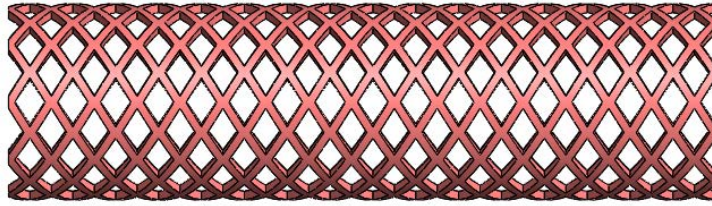


Figure 15 – T mesh

## 1.6 Struct

Studying the literature and searching in the world market is clearly possible to notice how the favorite shapes for the realization of a stent are the type-W and the type-T configurations. The W mesh design presents a W trend between a certain number of wires that run through all the device. In the market, there are a lot of variations for the positions of the support poles in the stent but is always possible to recognize the two fundamental parts, which compose the device: The W trend and the support poles. Where the geometry is more complex, there will be more tension in the compression studies. The T mesh design is similar to a wire wrapped mesh. The dimensions of the holes and the thickness of the wires can be changed. Another interesting think is that the ends of the device can be open or close. In fact, the choice between the two different configurations could influence the healing period, in that these determinates the contact between the device and the tissue and the blood flow through the vessel. In the new devices the direction is to use a closed shape of the border meshes, and almost all the devices presented follow this trend.



**Figure 16** – Square section



**Figure 17** – Circular section

## **1.7 Fabrication methods for biodegradable stents**

Typically, for the fabrication process of the stents two main approaches are possible: The first one is the bottom-up, where the technique provides an additive process of the material deposition, starting from a solid support. This technique is used from 3D (dimensional) printing and from solvent casting techniques. The second one is the Top-down process, instead, is a subtractive technique usually starting from material blocks and removing all the unnecessary pieces to obtain the desired shape. Laser machining, molding and electroforming use these typologies of process.

*3D printing technique* in the last years has become one of the most used production processes. In fact, it presents a lot of advantages and, in the engineering field, is also used to fabricate tissue scaffolds, because exploits the dispensing based rapid prototyping technique. The advantages include the ability to adapting to a widely scale of materials, from liquid to solid paste, the great repeatability, the good precision and control over microstructure and the simple production condition, such as no high temperature, no toxic solvent needed and efficient and rapid fabrication process. The 3D printing technique is widely used for the realization of biodegradable stent, not only for polymeric ones, such as made by PCL, PLLA and PLA, but also for which made by metallic biodegradable materials, like based on

magnesium alloy. There are also some disadvantages but are all connected with the minimum thickness limit that is possible to imprint.

*Fused deposition molding (FDM)* is a particular production technique, where the object is made by the repetitive deposition of thin material layers, such as polymeric one, which create the 3D object. Moreover, the *melt spinning technique* is used for polymeric fibers with the thickness included between 150 to 200  $\mu\text{m}$ , which then can be woven or knitted into stent devices. The fabrication process described is new and further studies are necessary for a better knowledge of this technique and to improve the process. A limitation is due to the obstacles caused by the melting points of the materials.

*Injection and compression molding processes* are very indicated for the polymeric materials for their intrinsic thermoplastic behavior. The recent development is oriented in the optimization of micro and Nano molding processes. The ICM technique combines the injection and compression molding processes. The advantages of this technique are in the increasing of the micro-surface precision and the reduction of the flow distance/wall thickness ratio. Is difficult to obtain a perfect process because problems, such as the melt penetration to the parting line caused by late compression or incomplete filled caused by early compression, could happen.

*Laser machining* is the widely used method generally for metallic stents. The technique is formed by two parts, or rather the formation of the tube and the cutting phase, done by the laser which gives the desired meshes to the device. This process has a high resolution. Also, an advantage is the ability that the laser machining has, is possibility to gives complicated structure and design at the stent with a so high accuracy. In the other side, the process requires a lot of time and for the biodegradable polymeric materials is not recommended, because the heat, produced in the process, could damage the physical and chemical properties of the material and the covalent bonds between the atoms and molecules. This technique was used to the production of the biodegradable polymeric Reva stent.

In the table 4 the advantages and the disadvantages of the fabrication techniques for the production of biodegradable stents described above are reported.

<b>Fabrication Technique</b>	<b>Advantages</b>	<b>Disadvantages</b>
<i>3D printing technique</i>	<ul style="list-style-type: none"> <li>• High efficiency</li> <li>• Low cost</li> </ul>	<ul style="list-style-type: none"> <li>• Nodde diameter limitation</li> </ul>
<i>Fused deposition molding (FDM)</i>	<ul style="list-style-type: none"> <li>• Fast fabrication</li> <li>• High precision</li> <li>• Control production</li> </ul>	<ul style="list-style-type: none"> <li>• Heat effects</li> <li>• Nodde diameter limitation</li> </ul>
<i>Injection and compression molding processes</i>	<ul style="list-style-type: none"> <li>• Fast production</li> <li>• Low cost</li> </ul>	<ul style="list-style-type: none"> <li>• Design restriction</li> <li>• Difficulty</li> </ul>
<i>Laser machining</i>	<ul style="list-style-type: none"> <li>• High resolution</li> <li>• High accuracy</li> </ul>	<ul style="list-style-type: none"> <li>• Heat effects</li> <li>• Incompatible for all the materials</li> </ul>

**Table 4** – Fabrication technique and properties

## 1.8 Motivation aim and scope

The main goals of the master thesis work are the development of a computational framework capable of designing and numerically simulating a new medical device. This tool needs to be parametric to be used for several applications and to be patient specific.

Moreover, the present work is an improvement in the stent realization process for the following aspects:

- Specificity of the device for the patient
- Avoid of time consuming in the realization
- Wide application range

In addition, the stent should be fabricated with a biodegradable metallic alloy of Magnesium. Finally, it should be 3D printable. The collaboration between three companies for the realization of this project led at the division of the research fields. In fact, the UPNA (Universidad Publica de Navarra) is in charge of the design and of the computational testing such as, the simulation of the compression test studies for determining the radial strength. The AIN (Asociación de la Industria Navarra) is in charge of assembling the necessary materials of the device, and NAITEC (Centro Tecnológico de Automoción y Mecatrónica de Navarra) will perform the experimental tests and the biodegradation process. In the following chapter the workflow and the corresponding software used for each step done for creating the computational tool are described.



## *Chapter 2*

### **MATERIALS, INSTRUMENTS AND METHODS**

In this chapter the materials analyzed and used in this master thesis work, with their features and the motivation for the choice done will be presented. Moreover, the descriptions of the software used for the design and the simulation parts, with the presentation of the tests carried out and the motivation of the meaning of the simulations are exposed. How described in the first chapter, the new stents will be designed with the two most typical struts geometrical organization such as T-mesh and W-mesh.

#### **2.1 Materials**

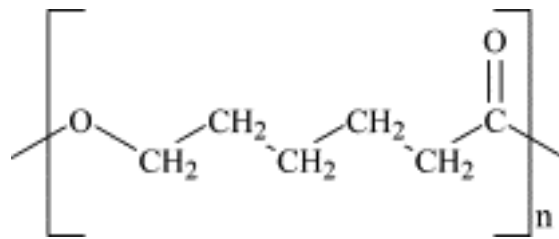
The material used for the realization of this project is based on Mg. The composition of the alloy is made by the AIN company. The materials used for the simulation tests and for the realization of the first samples has different physical properties.

In fact, one has a linear-elastic behavior and the second has an elasto-plastic conduct. The first used, the linear-elastic, belong to the polymeric materials and it was the Polycaprolactone (PCL). The latter, and closer to the definitive one, was the Magnesium alloy AZ31.

The idea for choosing the material is to select one with an elasto-plastic behavior. This because the plastic behavior is important for the position of the stent in a vessel and because using this kind of material is impossible that the device could move along the vessel. But, the analysis of the differences between two kind of behavior give a complete definition of the scene and permit to do very important considerations. In the last chapter, the analysis of the compression tests and the final consideration about the designs and the material compositions of the stents will be presented and discussed.

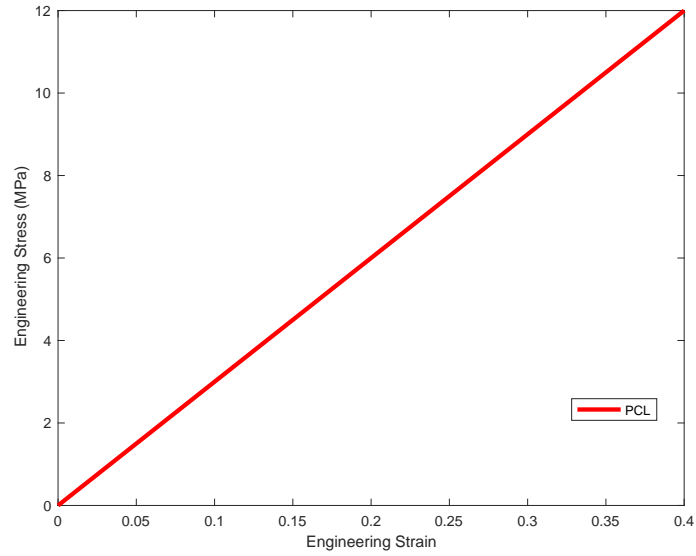
### 2.1.1 Polycaprolactone

The polycaprolactone (PCL) is a biodegradable synthetic semi-crystalline polymeric material. In the biomedical field it is widely used for its high thermal stability. Moreover, it presents a chlorine, oil, water and other solvents resistance. The PCL is made by polymerization with ring opening, using as catalyst agent the stannous octanoate. The polycaprolactone has a melting temperature including between 59-64 °C and a glass transition temperature close to -60°C. This is very low compared to other bioabsorbable polymers, used for biomedical applications. The decomposition temperature is 360°C. The degradation process of the PCL is the hydrolysis, because the polycaprolactone has ester bonds within the molecule structure. Was observed that the polyester, after two years from the implantation, present a significant decrease of the molecular weight, highlighted by the decreasing of the relative viscosity of the order of 80-90%.



**Figure 18** – PCL molecular structure

The behavior in the stress-strain test is linear-elastic. In particular, for this reason, there is no residual deformations or plasticity problems. But this not eliminates the breaking point that will be present with a particular value of stress. The stress values are in the Megapascal (MPa) range and the strain have not the measure unit, because is described as the ratio between the deformation minus the initial length of the sample, divided for the initial length.



**Figure 19** – elastic-linear behavior of the PCL

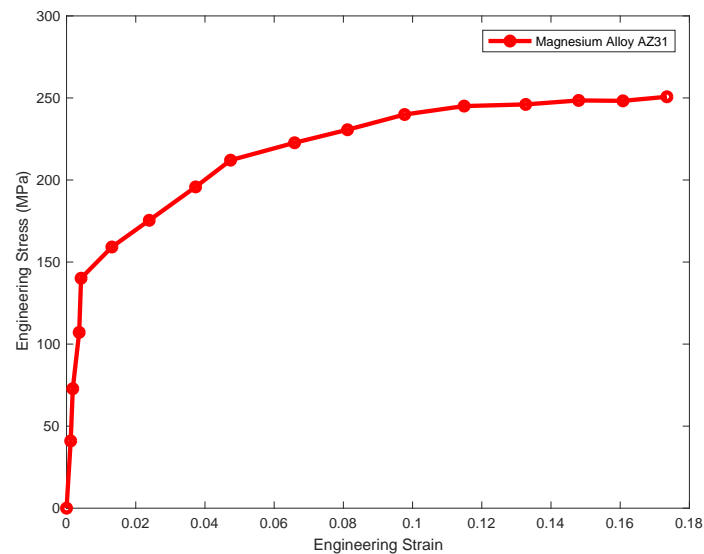
In the following table, are summarized the principal properties of the material used for the devices with the relative values.

Material Characteristics:	
Density:	1440.8 Kg <sup>m</sup> <sup>-3</sup>
Young's Modulus:	400 Mpa
Poisson's Ratio:	0.33
Bulk Modulus:	3.9216 E+08 Pa
Shear Modulus:	1.5038 E+08 Pa

**Table 5** – PCL physic characteristics

## 2.1.2 Magnesium Alloy AZ31

The Magnesium Alloy AZ31 is a biodegradable alloy made of 3% Aluminum, 1% Zinc, 0.05% Copper, 0.04% Calcium, 0.02% Manganese, 0.01% Silicon, 0.005% iron and 0.005% nickel. Alloy is a monophasic or polyphasic mixture, constituted of two or more elements of which at least one, the principal, is metallic and its name is base metal. The AZ31 alloy is produced by the Norsk Hydro ASA (Oslo, Norway), with a particular technique called Twin Roll Casting. This involves direct continuous casting inside two counter-rotating and water-cooled cylinders. Today, the magnesium alloys are studied in the biomedical device research field. In fact, the high presence of the Mg inside the human body allows the realization of instruments made by this material. The mechanical behavior of the Magnesium AZ31 alloy is elasto-plastic. In fact, if we consider only the stress values under 120 MPa, it is possible to see an elastic-linear behavior. The loading and un-loading processes follow the same straight line. But when we increase the stress value the behavior of the material become plastic. In fact, the two phases of loading and un-loading in the tests follow different paths. In the end, remain a residual deformation which transform the sample from the initial one. It is not possible return to the initial configuration of the specimen, if the force applied is reduced in the way it was increased. These mechanical behaviors changes with the temperature values. But from the medicine studies the body internal temperature and the material properties are known. It is also possible to notice this trend observing the figure below:



**Figure 20** – elasto-plastic behavior of the Magnesium AZ31

It is important to know that higher is the stress force, higher will be the residual deformation. Augmenting the force at a specific level the rupture will be reached. In the following table, the principal properties with the relative values are summarized.

Material characteristics:	
Density:	1770 Kgm <sup>-3</sup>
Young's Modulus:	44.8 Gpa
Poisson's Ratio:	0.35
Yield Strength:	138 MPa
Ultimate Tensile Strength:	245 MPa

**Table 6** – AZ31 physic features

## **2.2 Work flow**

For the realization of the projects two software are used: SolidWorks and Ansys. The first was utilized to create the design of the stents and to parametrized it. In fact, with this technique, the device is able to change some important parameters, allowing changes in its geometry and dimensions. The parametric designs of the two mentioned stent types were imported in the Workbench of Ansys in which the computational radial tests were performed.

### **2.2.1 SolidWorks**

SolidWorks is a solid modeling computer-aided design (CAD) and a computer-aided engineering (CAE) computer program. The software permits the realization of 2D and 3D geometries. The company was founded in 1993 by the Massachusetts Institute of Technology. The first version of the program was released in the 1995 and now the last one is the “SolidWorks 2019” that are present in the market from the October 2018. The approach to the project can be top-down or bottom up. The SolidWorks program is a solid modeler which utilizes a parametric feature-based approach. In fact, it is important to know that the parameters refer to constraints whose values define the geometry of the project or the assembly. The parameters can be numerical and/or geometrical: the first are line lengths or circle diameters and the second, are the bonds of parallel, horizontal, vertical, concentric, tangent or coincidence. It is possible to associate one numeric parameter with another simply using relations, that allow them to capture the design idea. The design idea is to permit the optimization of the device according to the needs. It is possible with SolidWorks to specify what are the parts which can be modified changing also one parameter. The features are connected with the building blocks of the part. They are the operations and the shapes of which the part is composed. Shaped-based features start with a 2D or 3D sketch of the desired shapes and then these are extruded or filled with the addition or the diminution of material.

In the present work, the parametric part connected with the software was very important. In fact, all the measures of the devices implemented are connected to seven fundamental parameters. Changing the value of one of them, there is the actualization of the stent design and consequently the characteristics of the device respond to the requisites deriving from its application. As an example, it could be possible to generate patient specific devices. In the program, is possible to change the parameters opening a particular window and varying the desired parameter.

Once the designs are ready, these can be imported into the commercial package Ansys. In the Workbench tool of Ansys, the computational process corresponding to the conventional finite element modelling can be performed. The different tools of Ansys allow the generation of the computational meshes and the definitions of the material modellings and boundary conditions.

The great advantage of the parametric tool is that when a geometrical parameter changes in SolidWorks will have a consequent effect on the finite element model: once the design changes, the computational model will be consequently updated. Since the designs realized can be subjected to considerable changes due to the industry requirements, the created framework represents a useful tool for managing the development of a new device that is the main goal of the work.

### **2.2.2 Ansys**

Ansys (Ansys Inc., Canonsburg, PA, USA) is an engineering simulation software based on the finite element method which was invented by John Swanson in 1970. In the 1993, the founder sold the company and from the 1996 is listed on the Nasdaq. From the 2000, the industry bought another society expanding the engineering knowledge in fluid dynamic, electronic design and physic analysis fields. The Ansys software was invented and product as a finite element analysis program employed for the simulation of engineering problems. The program permits the additional creation of structures or machine/electronics components to tests the strength, toughness, elasticity, temperature distribution, electromagnetism, fluid flow, and other characteristics in a simulation level. The objective of the program is to identify and quantify how a device will work with different conditions, without the real construction of tests products or conducting crash tests. A clear example could be the realization of a new instrument with a new design and less material without sacrificing the safety. The majority of the simulation applications are done with the Ansys Workbench, which is one of the most famous software of the company. Also, the present work is realized using this software. Moreover, Ansys users divides larger structures into small components that are modeled and tested individually. Finally, is possible to start by defining the dimensions of a device and then adding force, temperature, pressure, weight, etc.

### 2.2.3 Ansys Workbench

The ANSYS Workbench environment is an intuitive up-front finite element analysis tool that is used in connection with CAD systems and/or Design-Modeler. ANSYS Workbench is a program for simulating structural, thermal, and electromagnetic analyses. In the present Master thesis Work, the utilization of the Workbench involves the static structural part. In the block of the tests, are present the following parts, which have to be completed in order to perform the analysis:

- Engineering Data
- Geometry
- Model
- Setup
- Solution
- Results
- Parameters

*Engineering Data* is important in the definition of the material components. In fact, opening this field, the material parameters can be defined. Is also possible, to upload the mechanical behavior curve of the element (stress/strain curve) and the material features of the device will adapt to the one loaded. In the engineering data section are present a wide material list where is possible to select the one desired. In figure 21, the main window presents in the left all the mechanical behaviors which is possible to select. Choosing, example “isotropic elasticity”, a second window will open, and it will be possible to complete the fields in it with the more adequate values. In the upper part, the main material categories are presents and, in the right one, the mechanical curve with the set parameters is showed.



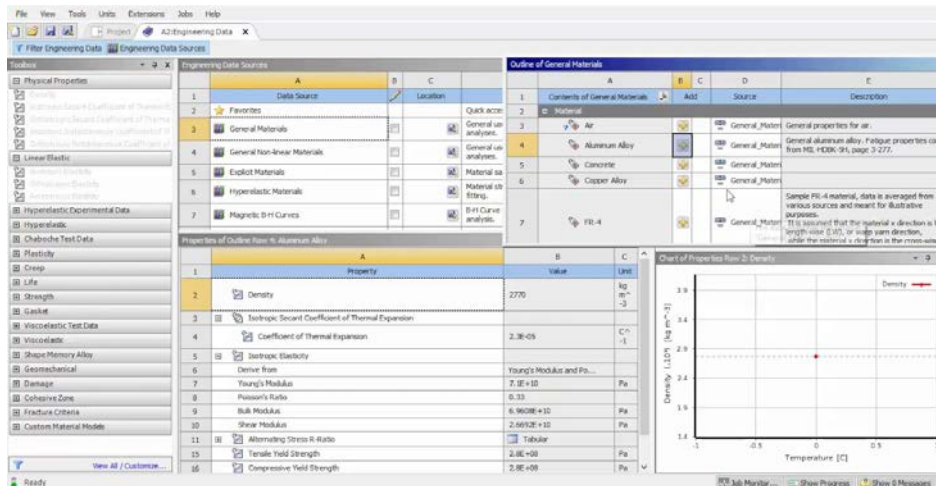


Figure 21 – Engineering data

*Geometry* is one of the most important fields of static structural analysis. In fact, the geometry of the device has to be uploaded and the software has to show correctly all its parts. The measures have to be adequate and do not always happen. The geometry of the device can be directly implemented in the workbench or can be imported from other design software, such as SolidWorks. For the latter, two different uploaded ways are possible. Firstly, the SolidWorks project with the “. IGES” is saved and the Workbench will read the file in the geometry section. This choice does not permit changes in the device structure and to modify the project it is necessary to update the instrument measures in the design software, re-save the project with the extension and then re-upload in the workbench. All the border conditions have to be reset. The second is to connect the design program, in this case SolidWorks, directly with the Ansys Workbench software, as did in the present work. In this manner, all the modifications done in the device structure are automatically imported and actualized in the workbench geometry part. The border conditions, in the model part, are actualized without doing anything. At the beginning, to implement the second manner is more difficult than to use the first, but then there are advantages.

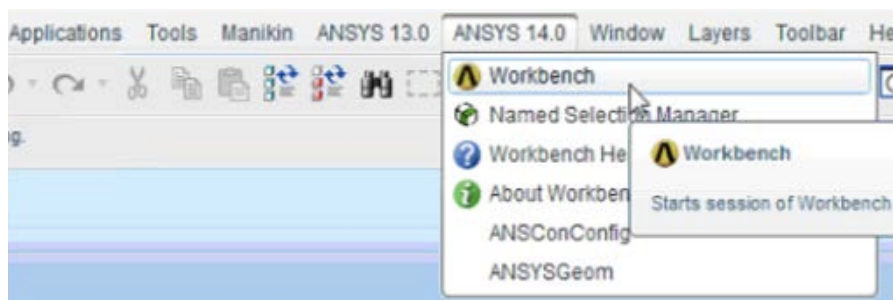
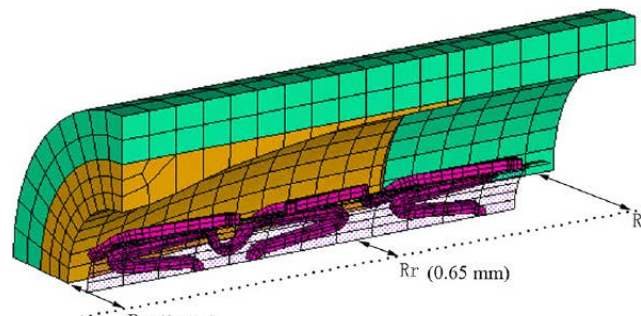


Figure 22 – design import process

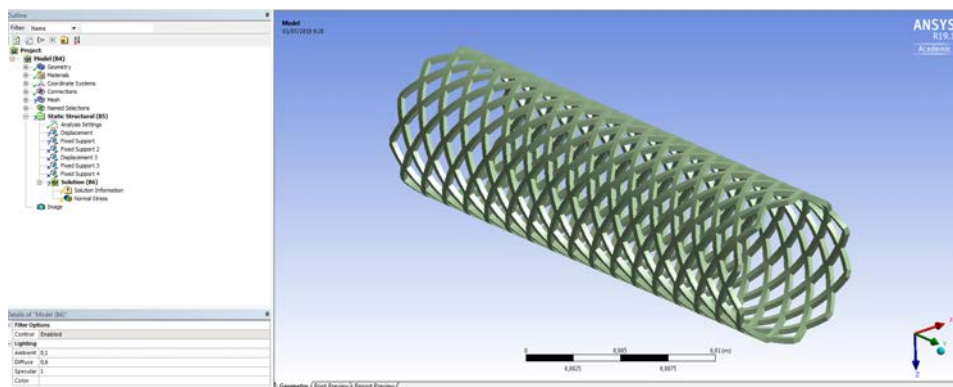
*Model* is the part of the test definition which is more complex and long to obtain. After the geometry importation, the first step is to define the coordination system. In fact, the software gives a default system, but is possible to change it and to move the application place of the system. Moreover, it can have more than one coordinate system, such as the absolute and the relative ones, and it can be chosen between the cartesian, polar and cylindrical systems. The second step, if there are contact regions is the selection of contact typology and the solution method used in that region, such as MPC, Augmented Lagrange. The following step is the mesh definition. This is a very important step which can influence the final results. In fact, ad adequate number of elements has to be selected for a specific model. However, a very high number of elements, i.e. a very high number of elements promotes high computational costs while a low number of elements has limited costs. Hence, it has to be found a compromise between the precision necessity and the computational cost. After the implementation of the mesh size, the program will report the number of elements created with the dimension used and the number of nodes. The Workbench offers the possibility to choose between three shape types of mesh: triangle, tetrahedron and pyramid. The software permits the creation of named selections which are useful in the force application in the testing part and are important in the definition of the nodes orientation when are present curve structures.



**Figure 23** – different mesh dimension examples

*Setup* part there are all the border condition such as the force and/or movements which the testing object can undergo. In fact, to analyzing a particular device behavior under the force application or under a controlled deformation it is necessary to set all the parameters. Moreover, it has to be selected if the object can have a linear or nonlinear behavior, the solution method which is used to arrive at a solution, if the convergence or the deformation have to be controlled

or forced, and all this parameter are mentioned only for the static structural analysis typology. In fact, in this part there are the Analysis Settings panel, where are to be imposed the Step Controls and the Solver Controls and then the fixed supports, the displacement and/or the forces applied, their intensity values, the coordinate reference system, the place where are applied and the orientation. In the Workbench software an applications menu, where can be selected the desired feature and when one of these is chosen, a new window is open with all the parameters which have to be inserted is present.

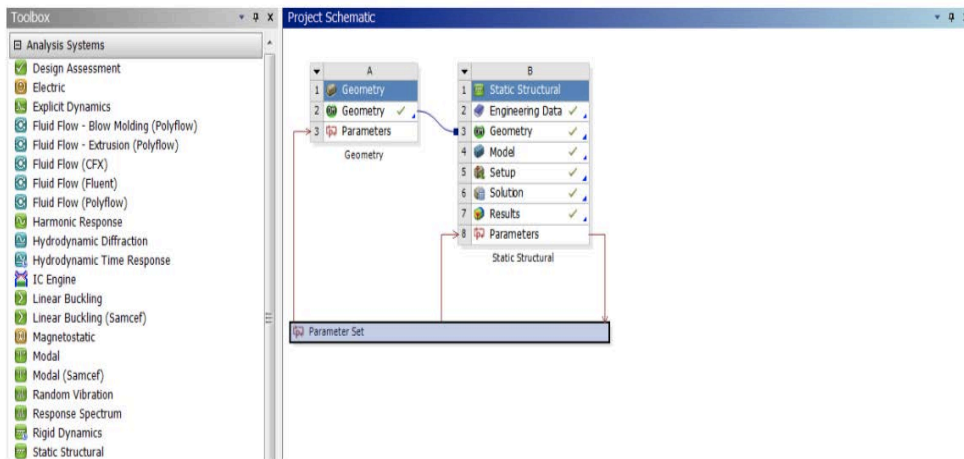


**Figure 24** – Ansys Workbench configuration

*Solution and Results* in the simulation test processes it is necessary to understand how the device react to the imposed conditions. In fact, the software permits to analyze the data coming from the test and visualizing the results obtained. In the solution part, the user has to select what it is important to check, the coordinate system in which wants to see the solution, in what part of the instrument to observe the results, the observation time and which variable need to be exported. Is also possible to apply an augmenting or decrementing force/displacement. In the same time, the program offers the possibility to see some different features and for each one gives the numerical data, a visual overview under a movie shape and the maximum, the minimum and the average value measured. Also, all the data can be downloaded and automatically the software prepares a written relation, where are present all the parameters and the solution methods used to obtain the results. Moreover, is possible to save on the program the data and the configuration prepared. The visual part, because is immediately understand what the problems in the configuration are, where the device presents higher tensions and how to change the simulation setup is very important.

*Parameters* could be change when start the tests and all the features are correctly present. The workbench offers the possibility, in the model configuration, to select a number of parameters which can be modify from the blocks window without changing the border conditions of the entire simulation test. This increases the velocity in the process and contributes to automatize all the analysis part. In this manner, it is always possible to control the process and avoid trivial errors.

In the block diagram is present a section called “parameters” where these are located in a scheme the selected ones with their own values. Is also possible to insert a certain number of parameters deriving from the solution data and so that they can be elaborated and analyzed.



**Figure 25** – Ansys Workbench blocks diagram

## 2.2.4 Matlab

The software used for the calculation of the force and for the graphic representation was MATLAB (Matrix Laboratory). In fact, this software was used for the analysis part and for the comparisons of the obtained results. MATLAB is a multi-paradigm numerical computing environment and proprietary programming language. It permits the matrix elaboration, plotting data, realization of algorithms, implementation of user interfaces, and communication with programs developed in other languages, such as C, C++, Java, Python. Essentially, the utilization of MATLAB was concentrated in the realization of the arrays structures to represent the data and the calculation of the Normal Force, which is the value analyzed in the compression and dilatation studies. The version used in the work is the R2017b, which is adequate for the analysis. Now is possible to download the license for the last one, which is the R2019a.

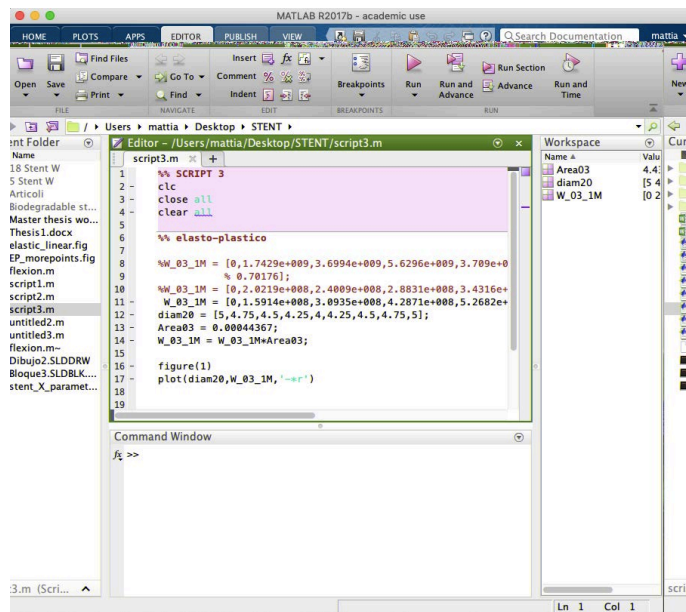


Figure 26 – Matlab interface

The upper figure shows the typical Matlab interface. Is possible to see the main blocks which compose it:

- Script is the part where is usually written the code. In fact, the only way to save the coding part is to write on it.

- Command window is also used to write the code but cannot be saved. Is also the place where are indicated the eventually errors when the code is controlled, before to execute the program.
- Workspace is the place where all the variables are indicated with their respective values.
- Current folder indicates the working ambient were the user is coding and in what folder the progress will be saved.

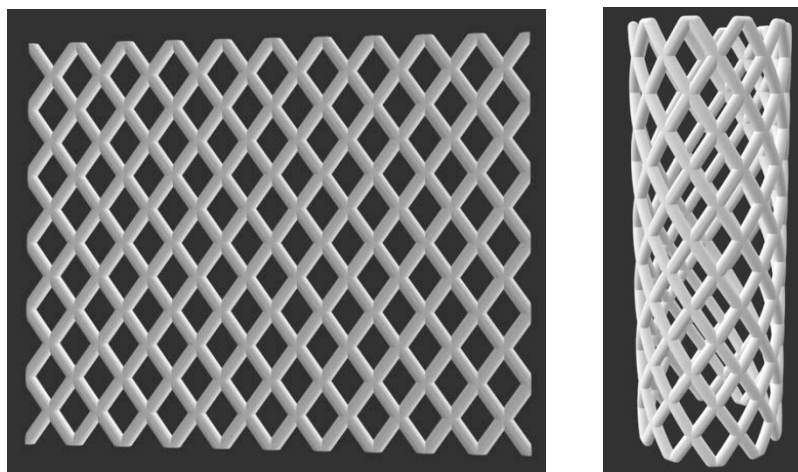
To verify the program the user has to press the bottom “Run” and if the function provides a figure, it will appear in a new window which can be modify with a lot of function.

### 2.2.5 3D printing technique

The two devices design and described are produced by the Naitec company with the 3D imprinting technique. The realization process consists in:

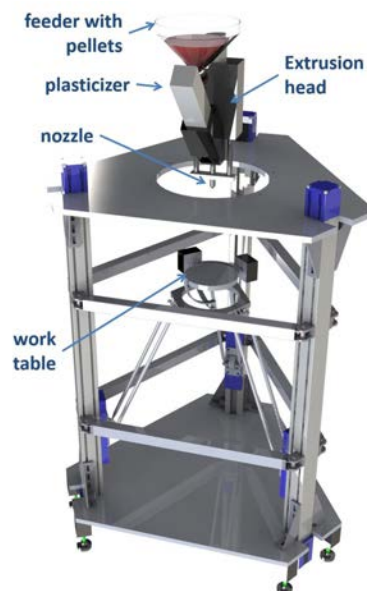
- Saving the design file with the “. STL” extension
- Sending the data to the NAITEC company
- The company controls the stent design and their printing method
- NAITEC gives limitation and possible issues deriving from the fabrication process

To research the best way to fabricate the stents, the files contain two version of the devices. In fact, the stents were designed in a 3D and in a plane version.



**Figure 27** – Files “. STL” of the two version of the same stent typology

The realization process tried to use all the two ways to obtain the devices with the best resolution and precision. The fabrication of the device, for the first draw, was with a bottom-up strategy. This one provides the material deposition from a support, which at the end will be removed. The advantage of the approach is the realization of the device, without weak points, that are present if it is necessary to merge the stents in some parts of it. Unfortunately, some issue arises due to the resistance, because as layers build up, the inferior part has to be solid and to stand the increasing weight. For this the deposition velocity has to be controlled and the design has to be optimized. NAITEC studied and determined the adequate parameters for the realization of the stents. The second strategy, provides the 3D printing of the stent in a plane way and then to close it, obtaining the circular shape. Certainly, the latter technique is faster than the first one, permits the realization of particular design, but the presence of the merging section can influence the physical and chemical properties of the device. At the end, for the realization process of the devices, was used the first technique, that influenced the devices design, but permitted to have the best precision and resolution as described before. In the figure below, there is a representation of the 3D imprinting machine, but in this case the layers deposition occurs in the horizontal direction, and with the utilization of a support cylinder [16].



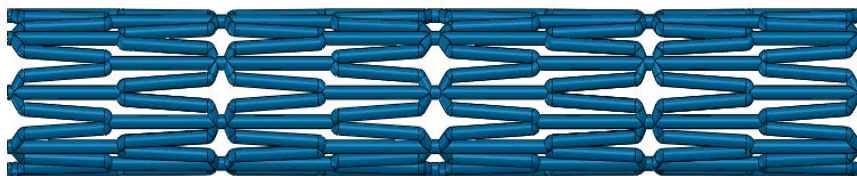
**Figure 28** – 3D imprinting technique

## 2.3 Methods

In the present section the finite element analysis used for the testing part with the Ansys Workbench software will be described. Moreover, the devices will be presented, along with its main parameters. Also, will be described the set-up of the experiments.

### 2.3.1 Stent design

As described before, the final devices design implemented for the realization of the two biodegradable stents present different characteristics. First, the design will be inspired from the two most used configurations: T-mesh and W-mesh. These configurations, as will be described in the next chapter, guarantee to have the necessary characteristics to be implanted in the vessel of the human body. Second, the devices section is circular, and this was due to fabrication requirements, the selected section is circular and not squared. In the following figure is possible to have a visual presentation of the devices and to notice the design differences described before.



**Figure 29** – Circular W stent



**Figure 30** – Circular T stent

The W stent present alternating supports which connect the meshes. In this manner, the configuration gives stiffness to the device and can be printed with the 3D technique. In fact, in the first version designed, the supports were in the same longitudinal line, causing problems in the realization process. The T one has a grid mesh and the shape permits an easy fabrication process.



### 2.3.2 Model's parameters

From the analysis of the literature and to have a device that can be used for being adaptable to the patient exigences and for the characteristics that the device should possess, seven main parameters were fixed. All the measures of the stents structure depend from these values, which can be changed promoting an automatic updating of the model set up. In the following section the seven fundamentals parameters and the consequence caused by of their change are presented. The parameters are:

- Diameter
- Length
- Thickness
- Mesh Length
- Mesh Width
- Number of Length Mesh Repetition
- Number of Radial Mesh Repetition

#### 2.3.2.1 Diameter

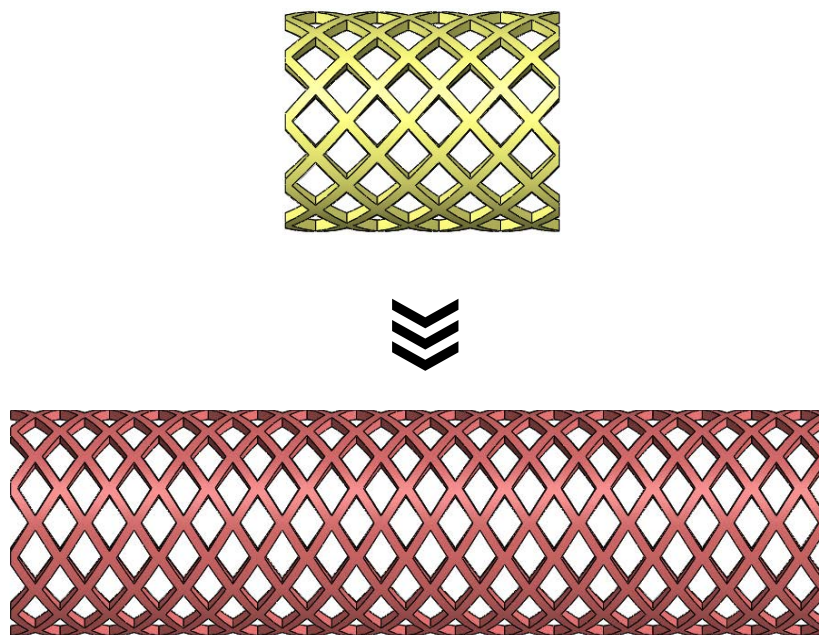
The first parameter investigated is the diameter. This is fundamental for the application vessel in which the device has to be implanted. In fact, an artery vessel such as Aorta has a diameter that is bigger than a coronary one. The example reported previously is connected to the blood vessels, but the field of application is wide, because the device can be used also for the tracheal conduct.



**Figure 31** – Diameter variation

### 2.3.2.2 Length

The second parameter which is possible to change is the stent length. The number of the mesh remain the same but the mesh dimension changes. The parameter depends from the patient disease and adapting the correct length to the device the healing period will be faster, because the degradation time of the stent will be the correct one and the damages caused by the insertion of the device involves a less part of the vessel. Having this possibility, the advantage for the production process is to save material.

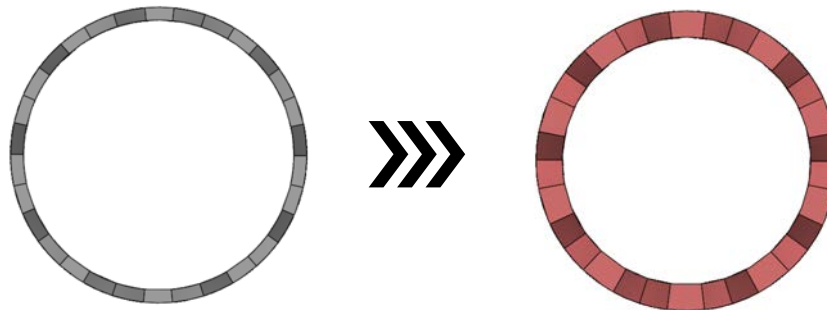


**Figure 32** – Length variation

### 2.3.2.3 Thickness

In the literature it is stated that for metallic stent, the strut thickness commonly used is 0.1 mm. For biodegradable stents, the thickness is usually larger due to the material and the consequent resistive capacity (0.3 - 0.5 mm). This parameter can be changed to satisfy this limitation and to adapt the stent to several materials. In fact, is possible to tests the device with the different thicknesses to use the best one which guarantee the mechanical features and the necessary degradation time in order to preserve the healing period. Is not possible for the biodegradable stents to have thickness less of 0.3 mm. On the contrary, a thickness larger than the 0.5 mm is not useful for the medical

application. The stent design implemented in the devices can be used with a widely range of materials.

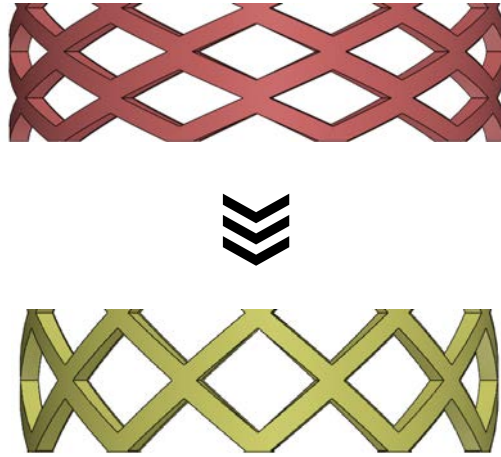


**Figure 33** – Thickness variation

#### **2.3.2.4 Mesh Length**

In the development of a new stent another important parameter is the mesh length. Modifying this value, there is the variation of the size of meshes in a longitudinal direction. Consequently, the number of meshes changes and the mechanical properties of the device are different and new. The most important one is the radial stiffness. The stent implanted has to resist to the compression rate imposed by the hearth activity which reflects in the movements of the vessels wall. For this reason, it is important the study of the variation of this parameter. One of the goals of the present work is the analysis of the devices involved in the variation of the parameter, mostly in the field of the compression test.

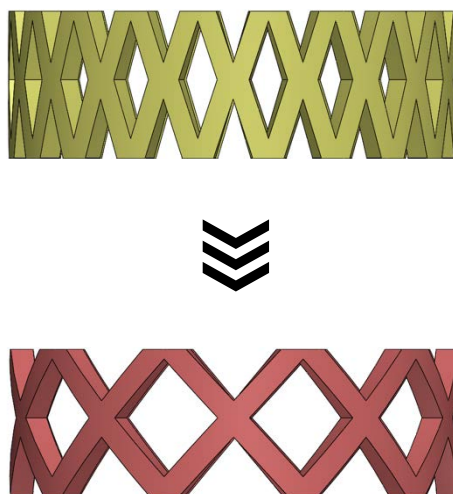
Modifying the length of the single element of the mesh, all the parts forming the cell are automatically adapted to the new measure. This is useful if the vessel disease tract has a particular trend or if has a very small diameter and is necessary to change the properties of the stent. From the following figure is possible to understand how in the same vertical length the cell dimension is changed. In fact, in the upper part there are two meshes in the longitudinal direction instead below there is only one cell. But the longitudinal dimension the length value is the same.



**Figure 34** – Length mesh variation

### 2.3.2.5 Mesh Width

Another parameter is the mesh width. In fact, it is possible to change the parameter maintaining the same diameter of the device. This influences the mechanical properties of the stent such as the flexibility and the radial force. Also, in this case, changing the width of the single cell is an improvement for the medical application, because the device is able to follow better the trend of the vessel. Moreover, due to the wide field of application, the stent should be capable of adapting to different situations. It is important to analyze the effects deriving from the variation of this value. Further studies could be done to investigate this topic. In this work the focus was on the radial stiffness tests.



**Figure 35** – Length width mesh variation

### 2.3.2.6 Number of Length Mesh Repetitions

Another useful parameter in the definition of the stent structure, is the number of the mesh repetition in the longitudinal direction. In fact, is possible to change this parameter maintaining fix the device length. In fact, to guarantee acceptable mechanical properties, and considering the small thickness of the device and the functions that have to do, is fundamental the possibility to augment the number of the mesh repetitions. Augmenting the value of the parameter, will be present more meshes in the same place. This cause an increase of the stent material in the vessel and consequently the degradation time will be longer. A determinate value has to be found. In fact, the desired mechanical properties have to be maintained and the correct degradation time has to be researched. The figure, is possible to have a visual presentation on how the parameter influences the struct of the stent, having the same longitudinal length. Unavoidably, the dimensions of the single mesh are optimized for the parameter choice.

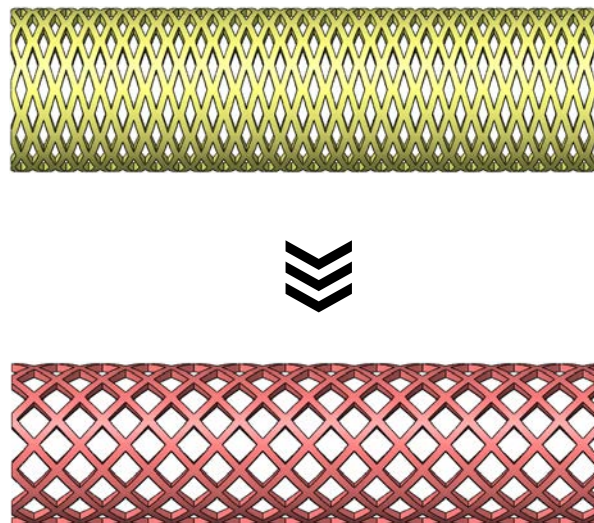
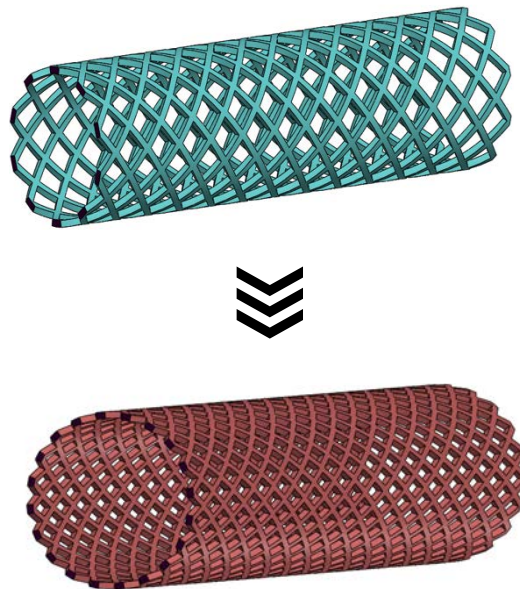


Figure 36 – Number of Length Mesh Repetition

### 2.3.2.7 Number of Radial Mesh Repetitions

The last parameter chosen and described is the Number of Radial Mesh Repetition. As for the number of Length Mesh Repetition, it can influence the mechanical properties of the stents, in particular the radial stiffness of the device. In fact, augmenting the mesh cells in the circumference direction of

the stent, there is a higher maximum radial stiffness value. This can be proved touching a physical realization of the device. The number of elements is chosen considering shape of the vessel involved in the disease. In fact, vessels with twisted shapes need a very flexible device which follow the development of the tube. On the contrary, for “linear” shapes can be chosen more rigid devices. More element will be present, more the vacuum spaces will be inferior, causing a less presence of in stent restenosis. All the measures, when the parameter changes, are immediately adapted ad optimized, using the relationship functions implemented for the parametrization of the stents created. In the figure, is possible to understand better how, changing the parameter, the structure modifies its design. The blue device has a smaller number of elements in the radial dimension than the red one, but they have the same diameter, thickness and length.



**Figure 37** – Number of Radial Mesh Repetition

### 2.3.3 Finite Element Analysis

The Finite Element Method (FEM) is applied to susceptible physics bodies at the division into a certain number of elements with a definite shape and a limited dimension. In the continuum, each component is considered a numeric integration field with homogenous features. The main characteristic is the discretization process through the mesh creation, composed by primitive shapes. For each element the problem solution is done from the linear combination of functions, named “shape functions” [17]. To arrive to the FEM, is necessary to follow a specific process:

- *Modeling* is the first step. There is the passage from the physics system to the mathematic one. In this way, there is the abstraction of some important features, focusing into a smaller number of variables. The model choice influences the presence or absence of an error and to quantify it, experimental test has to be done.
- *Discretization*: in a simulation process is necessary to limit the number of the degree of freedom (DOF). In fact, in the continuum the DOF in the space or in the time are infinite, but in the simulation process, has to be few. In this manner, an error is introduced and can be valued with an adequate mathematic model of the structure.

Each element can be 1D, 2D or 3D. The nodes are particular points which indicate the geometry [18]. At the nodes are connected joint reactions or displacement values. The number of this values for each node are the degree of freedom and for each node are present external forces or the joint reactions. Moreover, exist a linear relationship between the forces and the joint reactions: the “u” indicates the DOF vector and the “f” the external forces vector on one node.

The equation is:

$$\mathbf{K} \cdot \mathbf{u} = \mathbf{f}$$

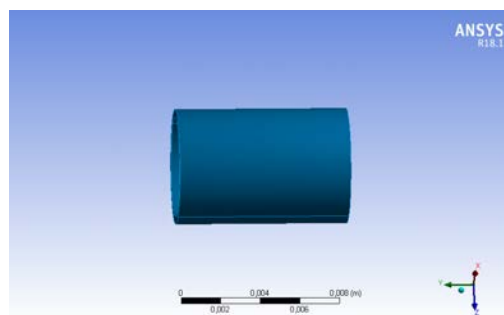
Where the  $K$  is named stiffness matrix. The  $K*u$  value is the work done by the external forces. The last concept that has to be explained is that of constitutive features which is the description of the element property and its behavior [18].

### 2.3.4 Radial stiffness evaluation

The simulation part involves the studies of the radial stiffness. In fact, from the literature there is a lot of research in the field of the force for the stent insertion in the catheter, and studies of the expansion phenomenon when the device is placed in the blood vessel. But on the radial force exerted by the vessel on the stent and vice versa little is known. There are not upper or lower bounds in which the stent has to stay. The experiments that we did, are concentrated in the analysis of the two types of stents made by the two different materials described before and a comparison of them. In the next chapter, will be presented the initial configurations with the choices done, the obtained results and the final considerations.

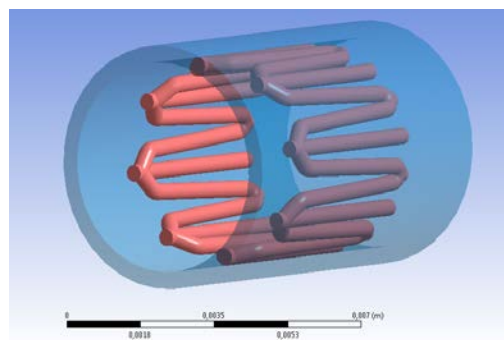
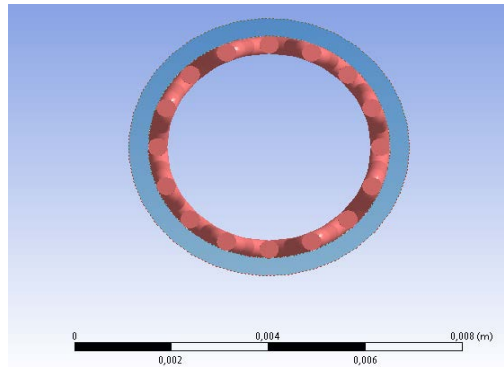
### 2.3.5 Set up of the computations

All the tests for the numerical simulations for the study were done using the Workbench of Ansys. As described before the program was connected with SolidWorks and in this manner, it was possible to optimize the device projects. On the workbench it was selected the Static Structural panel and to simulate the radial stiffness, we created a cylinder, with a length dimension 2 times bigger than the device one, with a thickness of 0.5 mm, made by Structural steel, to avoid deformation, which represents a typical artery vessel with a diameter of 5 mm. Below, two different perspectives of the “vessel”- stent configuration are presents.



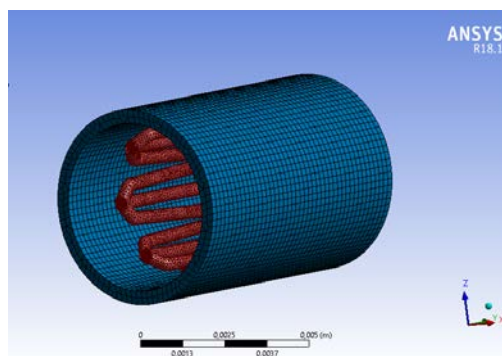
**Figure 38** – Model of blood vessel





**Figure 39** – Frontal and ¾ visions

A sliding contact is imposed between the device and the cylinder surfaces. The values used for the meshes were: 0.0001 [m] for the stent and one of 0,0002 [m] for the cylinder. With these values the obtained results had an acceptable precision and the computational cost was reduced.



**Figure 40** – mesh modeling

Statistics	
<input type="checkbox"/> Nodes	119185
<input type="checkbox"/> Elements	46299

**Table 7** – number of mesh elements

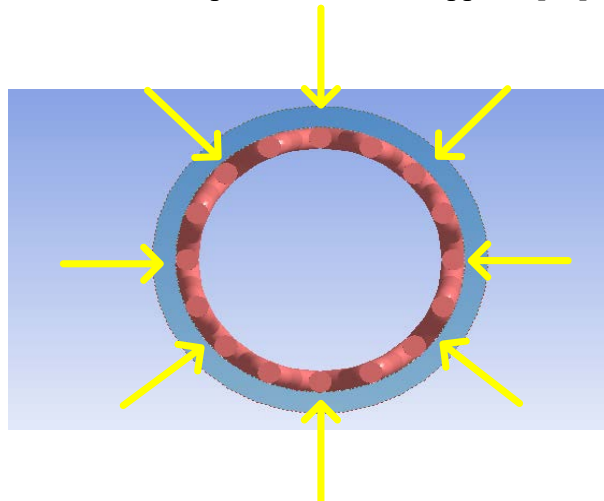
### 2.3.5.1 Radial Compression displacement imposed

the stent was compressed and expanded by means of the cylinder [19]. In fact, were imposed to the internal surface of the vessel, the following range of displacement values:

0	5	10	15	20
15	10	5	0	

**Table 7** – % values of the initial diameter of the stent

The applied values are the percentual values related to the initial diameter of the structure, or rather 5 mm. The displacement is applied along all the inner surfaces of the cylinder at the same time [20]. In the following figure is possible to see how the displacements were applied [21].



**Figure 41** – direction of the displacement application

The procedure was applied for the two types of stents, each one made by PCL or magnesium alloy AZ31. The evaluated radial force of both materials was finally compared.

### 2.3.5.2 Material properties used

As described before, in the engineering data of the workbench were inserted all the parameters necessary to define the material characteristics. For the PCL the required structural properties were Young's modulus and Poisson's ratio, having respectively the values of 400 MPa and 0.33. For the Magnesium alloy AZ31, a stress-strain curve was provided. The latter was extracted by literature data [Grogan et al, journal of the mechanical behavior of biomedical materials 12 (2012)]. the required features were the Young's modulus of 44 GPa, the Yield strength of 138 MPa and the stress-strain values, which are reported in the following table, where in the left part are present the strain values in mm and in the right the stress values in MPa.

Properties of Outline Row 3: Blood vessel				
	A	B	C	D E
1	Property	Value	Unit	
2	Material Field Variables	Table		
3	Density	7850	kg m <sup>-3</sup>	
4	Isotropic Secant Coefficient of Thermal Expansion			
6	Isotropic Elasticity			
7	Derive from	Young's M...		
8	Young's Modulus	2E+11	Pa	
9	Poisson's Ratio	0,3		
10	Bulk Modulus	1,6667E+11	Pa	
11	Shear Modulus	7,6923E+10	Pa	

Figure 42 – Material properties for blood vessel

Properties of Outline Row 4: PCL Stent				
	A	B	C	D E
1	Property	Value	Unit	
2	Material Field Variables	Table		
3	Density	1140,8	kg m <sup>-3</sup>	
4	Isotropic Elasticity			
5	Derive from	Young's Mo...		
6	Young's Modulus	400	MPa	
7	Poisson's Ratio	0,33		
8	Bulk Modulus	3,9216E+08	Pa	
9	Shear Modulus	1,5038E+08	Pa	

Figure 43 – Material properties for PCL Stent

Properties of Outline Row 3: AZ31 Alloy Stent				
	A	B	C	D E
1	Property	Value	Unit	<input type="checkbox"/> <input type="checkbox"/>
2	Material Field Variables	Table		
3	Density	1,77	g cm <sup>-3</sup>	<input type="checkbox"/> <input type="checkbox"/>
4	Isotropic Elasticity			<input type="checkbox"/>
5	Derive from	Young's Mo...		
6	Young's Modulus	44000	MPa	<input type="checkbox"/>
7	Poisson's Ratio	0,35		<input type="checkbox"/>
8	Bulk Modulus	4,8889E+10	Pa	<input type="checkbox"/>
9	Shear Modulus	1,6296E+10	Pa	<input type="checkbox"/>
10	Multilinear Isotropic Hardening	Tabular		<input type="checkbox"/>

**Figure 44** – Material properties for AZ31 Alloy Stent

Strain (mm)	Stress (Mpa)
0	0
0.0012	41
0.0018	72.8152
0.00365	107.1412
0.0042	140.1415
0.0131	159.1796
0.0239	175.4517
0.0373	195.7952
0.0474	212.0804
0.0659	222.6965
0.0812	230.629
0.0977	239.9098
0.1149	245.0537
0.1327	246.0606
0.148	248.4946
0.1608	248.2319
0.1735	250.7185

**Table 8** – stress-strain tabular values

### 2.3.5.3 Boundary condition

The initial and final ring of the cylinder were blocked to avoid a movement of the entire structure during the tests. The forces were applied on the internal surface of the cylinder. The decrease of the diameter was progressive and the solution method for the contact area was, for the stents made by elastic-linear material, MPC, instead, for the devices made by the elastic-plastic alloy, was the Augmented Lagrange, which permits a nonlinear behavior.

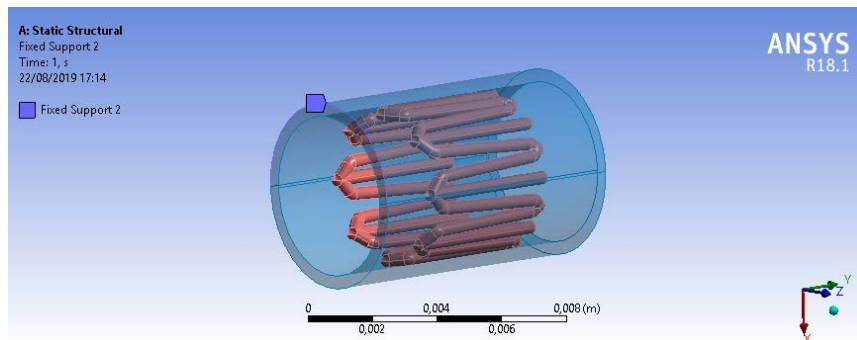


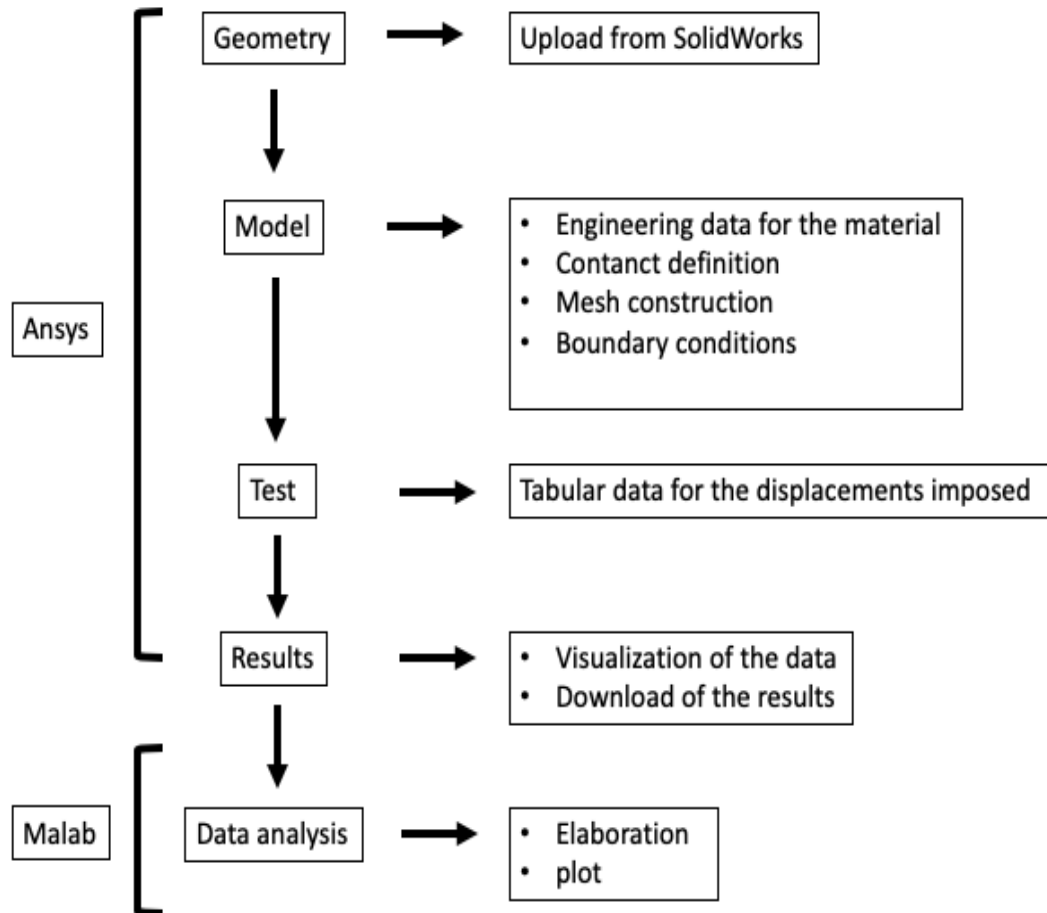
Figure 45 – Fixed support in the external rings

### 2.3.5.4 Force evaluation

To obtain a force measures we had to take as the output of the computations the average Normal Stress in the longitudinal direction along, in this case, the Y axis of the coordinate system, which was positioned along the stent axis. The measures were expressed in megapascal. The normal force was estimated using the stress field computed during the compression/expansion and the area of the stent [22].

### 2.3.6 Test procedure

In this section, the entire process is summarized by means of a block-structured workflow. The software used for these objectives are Ansys 2019 and Matlab R2017b. With the diagram is easier to have a complete scheme about all the operations which have to be done.



**Diagram 1** – Radial compression test procedure

## ***Chapter 3***

### **RESULTS AND DISCUSSION**

In the next paragraphs are presented the results obtained from the radial compression tests and a discuss about the analysis of the data calculated. The thickness used are 0.3 and 0.5 [mm]. Only one ring of meshes was used and a circular section was employed.

#### **3.1 Thickness limits**

The chosen thickness for the stent is derived from a limitation imposed by the 3D printing technique. In fact, the NAITEC industry guarantees to be able to produce the devices with at least a thickness equal to 0.4 millimeters. The lower limit deriving from the literature for biodegradable stents was of 0.3 mm and the upper one was of 0.5 mm. For this, we realized the 0.4 [mm] device, but it was decided to analyze and to test the devices with the limited thickness found in the literature to have a complete knowledge about the behavior of these stents. In fact, the fabrication technique can be improved in the next future, because the 3D printing is a recent process which have to still be completely studied and analyzed. The behavior of the devices with the thickness imposed by 3D printing process has to be considered as the average trend of that of the upper and lower bounds.

#### **3.2 Number of length mesh repetition**

All the devices studied for the analysis and the comparison have only one ring of meshes in the length. The reasons are:

- The first, and the most important, is that there are no significative differences in the behavior between the devices with one or more ring of meshes for the radial compression test were found. This derives for the relatively small dimension of the meshes and the influences of the number changes little in the final value measured. For other kind of trials such for example the flexibility tests, it become very important.

- The second, derives for reducing the computational costs and perform more cases. In fact, to preserve the simulation time there was the need to limit the number of elements in the finite element analysis.
- The third, to have a sort of equilibrium and parallelism between the devices struct and configuration for comparison purpose between the two configurations.

### **3.3 Struct limit**

As discussed, the strut section used in this work is circular. In fact, this was another limit imposed by the fabrication process. The project has the objective to arrive at the final stent with all the properties fixed and for this motivation the decision to do simulation trials only on the devices having the correct structure which was effectively useful for the development of the final stent. However, the square section was also tested. The presence of sharp angles causes an increasement of the local tensions measured in the stent during the compression dilatation process.

Is also important to do not forget that the objective of the regional project PC086-087-088 CONDE, financed by the Department of Economic Development of the Navarra Government, is to arrive to have a specific design to be produced and fabricated. For this reason, specific analyses were performed for analyzing all possible characteristics.



### 3.4 W mesh stent test results

The W mesh stent test presents a very interesting results: in fact, from the simulation software it is possible to see some increase of tensions in specific region of the device, where the geometry is more complex. In the compression part of the trial in the places where are presents curves, discontinuities, configurations more difficulties, are measured the higher stress values. The differences between the initial configuration and that one with the biggest displacement imposed are clearly discernable. In the figures below, are presented the distribution of the normal stresses along the devices in the initial and in the most compressed configurations.

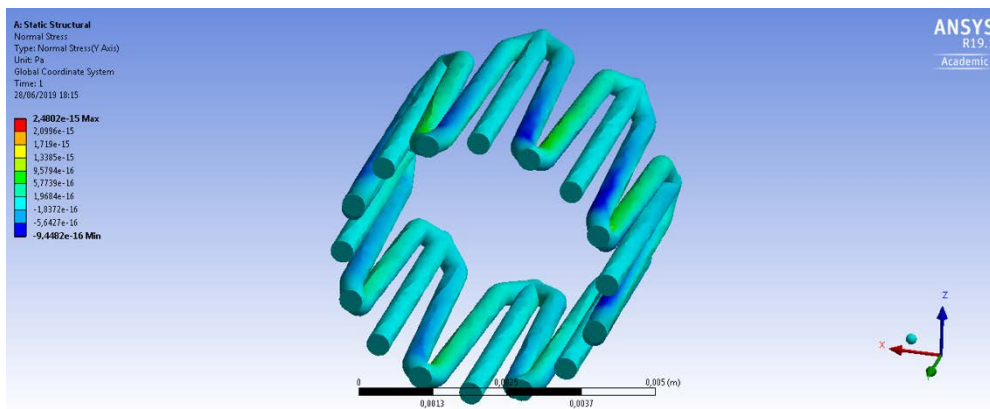
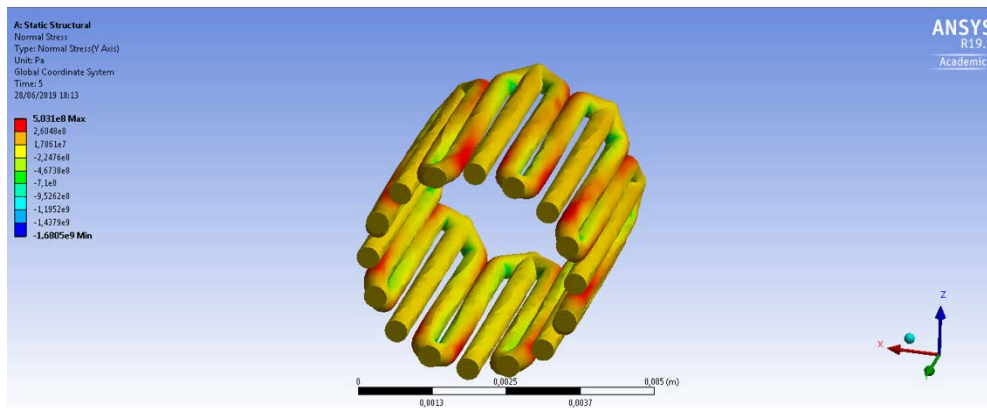


Figure 46 – 0% compression value

The figure describes the normal stress values measured along the Y axis in the configuration where the displacement imposed is the 0% of the initial diameter of the device. In fact, the measures are very low and is also possibly to see a minimal difference between the parts with a linear geometry and that one with a more complex trend.

From the initial configuration to the most compressed one is possible to notice the increase of the stress values along all the structure, but the higher values, which are represented with the red color, are visible only in specific only in some specific regions. The compression displacement imposed and shows in the next figure is the 20% of the initial diameter which was of 5 mm. In fact, the tests were done simulating a typical artery vessel, that is the main application of the developed stents.

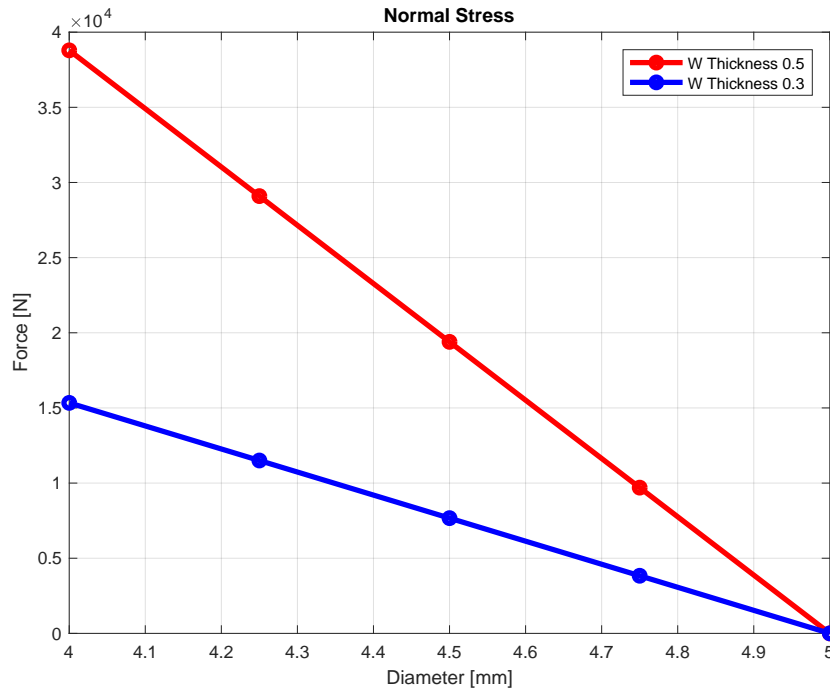


**Figure 47** – 20% compression value

The normal stress measured are so different from the previous image and the values are significant higher. In fact, more increase the compression displacement, more the different parts of the stent are closed, and as a result, it is produced an increase of the stress values in the regions where the geometry is more complex. The phenomenon is the same whatever is the material which compose the device. To understand the variations, it is necessary to plot the data measured with the same axes. The next step was to use Matlab to represents the values and to analyze the results obtained. Now, will be presented the differences in the behavior between the two devices with the same mesh design, but made by two difference materials.

### 3.4.1 Linear-Elastic W-mesh comparison

Firstly, using the strut diameter of 0.3 and 0.5 mm and the same design, the characteristics of the two materials were compared. In the Y axis are reported the normal stress measured and the X one, the diameter values are presented. In the figure, the points represent the values obtained and the line is their interpolation. The slope of the curves can give an idea of the different stent stiffness.



**Figure 48** – W-mesh PCL device data

From the figure is possible to do some important comments. Firstly, the load and unload process follow the same way. In fact, being an elastic-linear material, the present behavior was expected. The maximum compression value is not so high and for this reason will not arrive to the limit. This is important for the patient application and means that the device can be compressed until to have the diameter of 4 mm in safe conditions. Also, after the compression, the device will return back to the initial condition without having damages to the structure and ready for a next compression test. The thickness influences the normal stress values, and as it was expected, increasing its value in the device we obtain that the forces measured are higher for the normal stress compression, but the behavior for the devices does not change. To have a value for the analysis can be used the maximum normal stress result measured or the slope of the curves and measures the ratio.

### 3.4.2 Elastic-Plastic W-mesh comparison

The second analysis for the W-mesh device was done with the elastic-plastic material, or rather the Magnesium alloy AZ31, with the limit values of thickness, i.e. 0.3 mm and 0.5 mm. In the Y axis are reported the normal stress measured and the X one, the diameter values are presented.

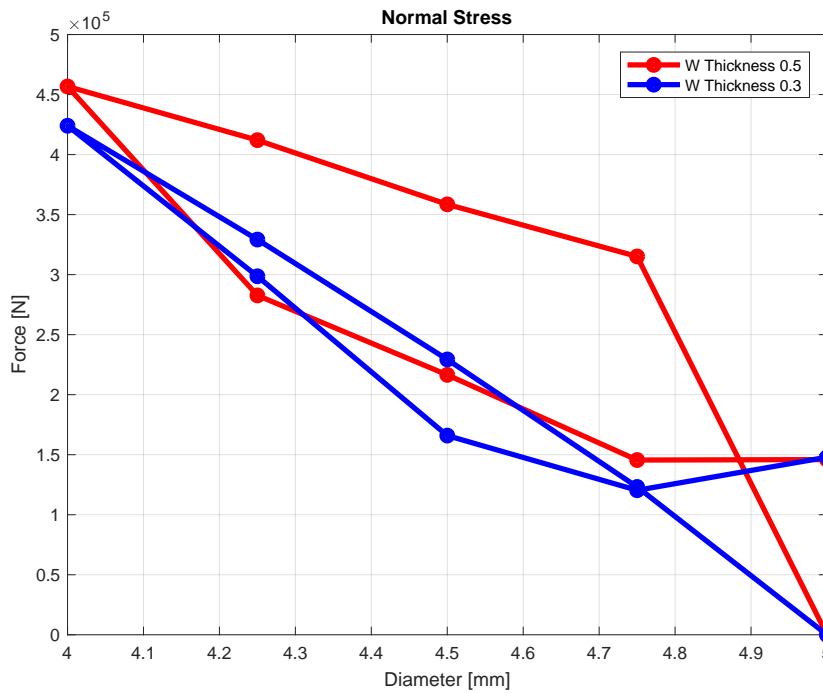


Figure 49 – W AZ31 device data

The loading and unloading processes follow different ways. In fact, as expected, the compression requires a higher force than the expansion. The radial compression and expansion do not follow in fact the same curve. Moreover, it is possible to see the residual deformation. In fact, at the diameter of 4.8 mm, there is a change of force trend with a new increase. In the normal condition, the experiment finish in that value, but considering that in the boundary conditions we imposed the slider contact between the vessel and the device, there is a constriction caused by the cylinder that causes the arrive at the final of the trial. It is necessary an additional force to bring the stent back to its initial configuration. Also, in this case, increasing the thickness of the stents it will have a higher force necessary for the compression. Finally it is possible to see that an increase in thickness promotes an increase of the area of hysteresis. Moreover, it is possible to notice that the area of the device with the smaller thickness is included almost totally inside that with the bigger thickness.

### 3.5 T mesh stent test results

Observing the figure below is possible to see the differences between the two types of devices. In fact, the new configuration of this stent permits to have a lower normal stress values both for the initial and final configuration. Also, in this configuration, the presence of discontinuities in the design and a rapid change of direction causes the increase of the normal stress values. Moreover, also in this trial we decided to use a interval of compression values between 0% and the 20% of the initial diameter of the device which is 5 mm, equal to that used before.

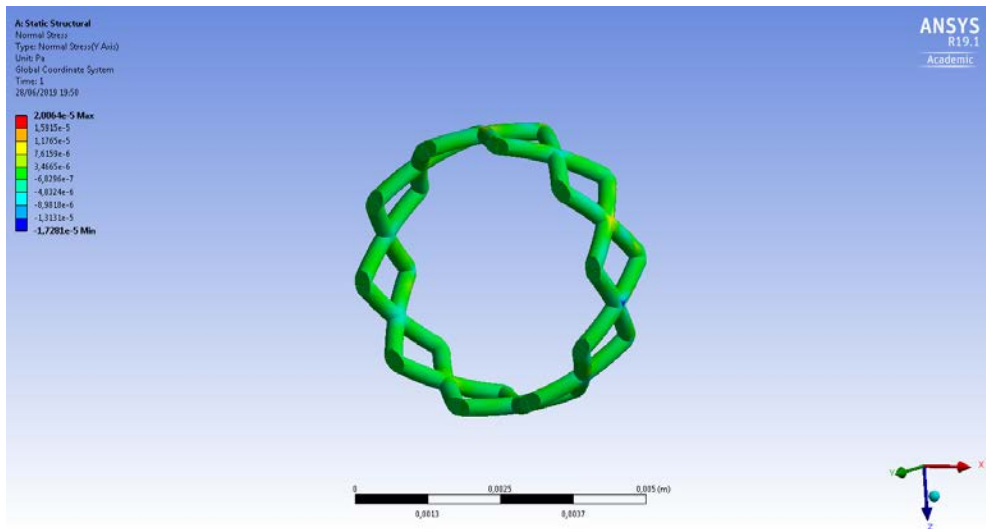
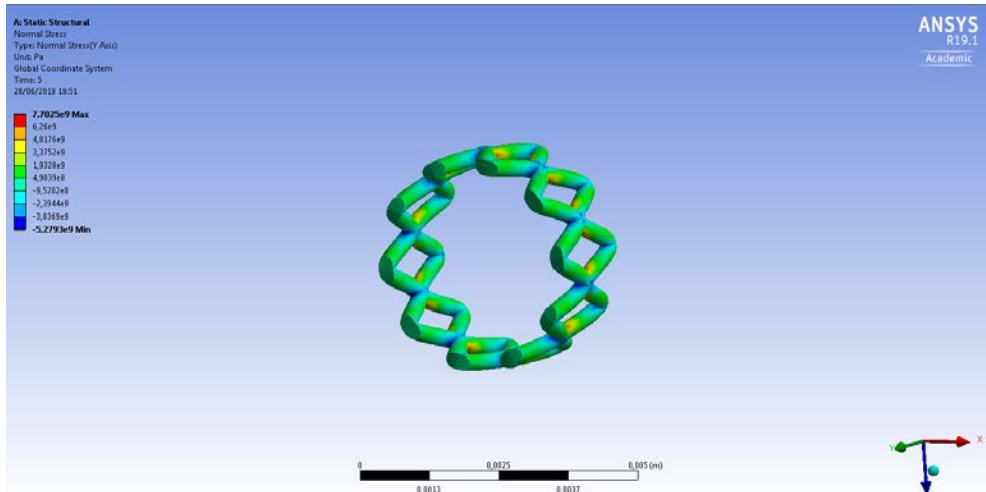


Figure 50 – 0% compression value

The tension values measured in the initial condition are a slightly higher than which detected before with the other configuration. Also here, there is a minimal difference of the elements with a complex geometry compared to the rest of the stent. The values measured are the normal stress along the Y axis. The following figure describes the forces detected at the moment of maximum compression, or rather when the diameter of the stent was of 4 mm. The red zones represent the ones in which the tensions are higher.

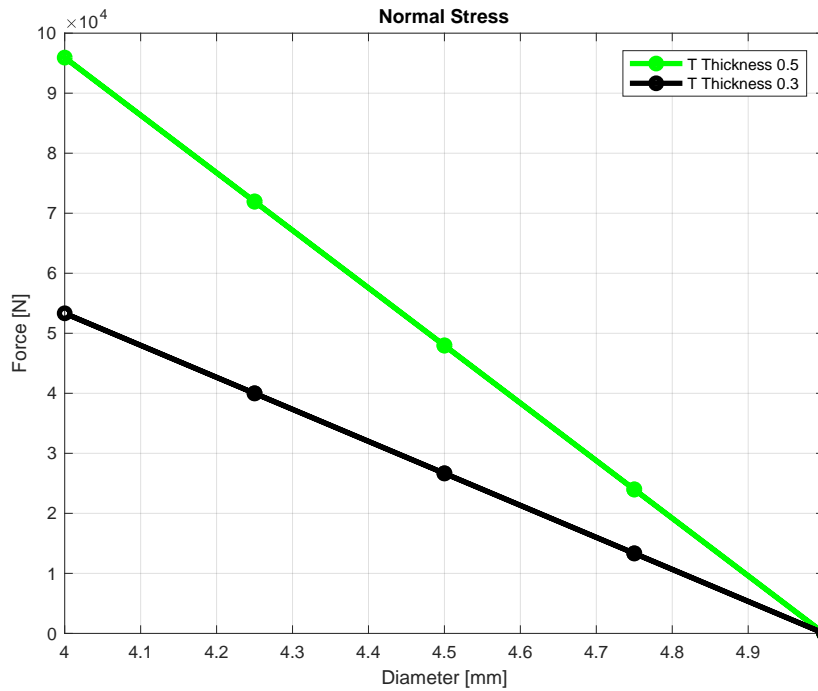


**Figure 51** – 20% compression value

Only considering the visual comparison is possible to understand that with the T mesh stent, the normal stress distributions detected are less than the one described above with the other mesh design typology of stent. In fact, the red zones are smaller and located only in the less points which present discontinuities. Moreover, the differences between the figure 51 and the figure 50 are very few. The necessity to have the same interval of the trial before is given by the necessity to have the same conditions to do the final analysis. Certainly, increasing the displacement value it can be arrived to have the color range close to that one of the before trial. The visual analysis is only a superficial method to have the first knowledge about the regions in which will be present the higher tension and which can be different from that ones expected. The qualitative information that can be extracted from the Figures can be quantified again using MatLab. In the figure is not present the cylinder which simulates the blood vessel. This was done to have a better view on the entire device. In the following section the numeric results obtained and an analysis between the behavior of the devices with the two limit thicknesses with two different materials will be presented.

### 3.5.1 Linear-Elastic T-mesh comparison

The third analysis presented is that one related to the behavior of the stents with T meshed fabricated with PCL material. The devices used have a bound value of thickness which are 0.3 mm and 0.5 mm. In the Y axis are reported the normal stress measures and the X axis, the diameter values are presented.



**Figure 52 – T PCL device data**

For this configuration and for this case, the behavior of the two devices is as expected. In fact, they present a linear-elastic trend and follow the same trajectory for the loading and unloading process. As expected, the device with a thickness of 0.5 mm needs higher normal forces to be compressed until the 20% percent than the stent with the thickness of 0.3 mm. The behavior of the device with the realizable thickness, or rather of 0.4 mm will have a stiffness which slope lays between the lines represented in the two Figures. An important thing is that also for this configuration we are not arrived at the limit point. To have a value for the comparison can be used the maximum normal stress result measured or the slope of the curves and measures the ratio.

### 3.5.2 Elastic-Plastic T-mesh comparison

For the last test presented, the analysis of the T device was done with the elastic-plastic material (the Magnesium alloy AZ31) with the limit values of thickness, i.e. 0.3 mm and 0.5 mm.

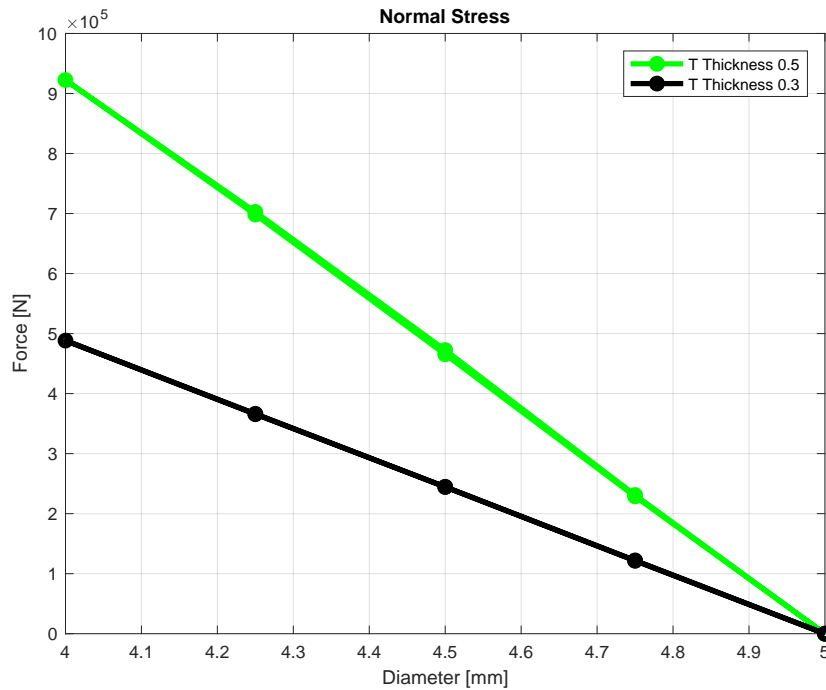
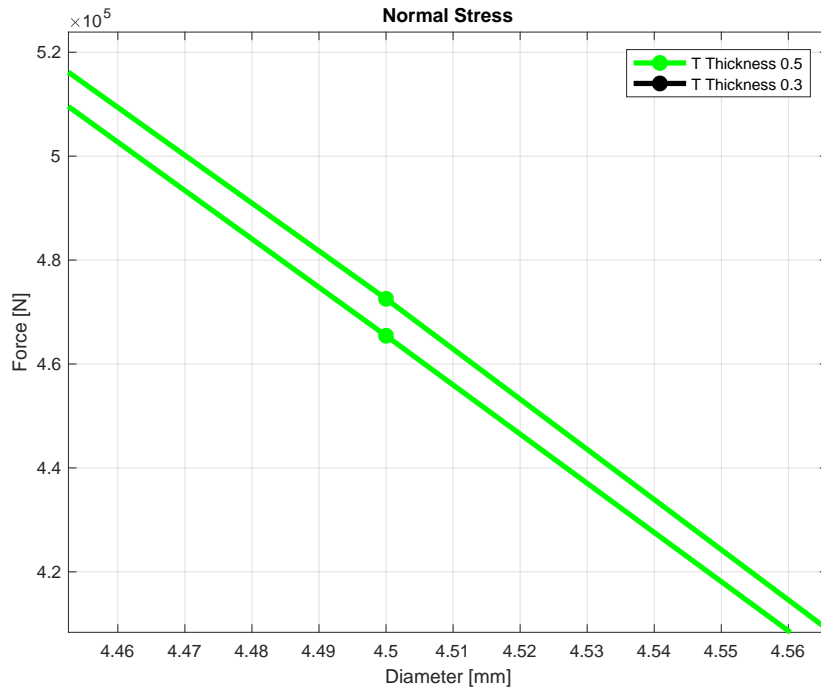


Figure 53 – T AZ31 device data

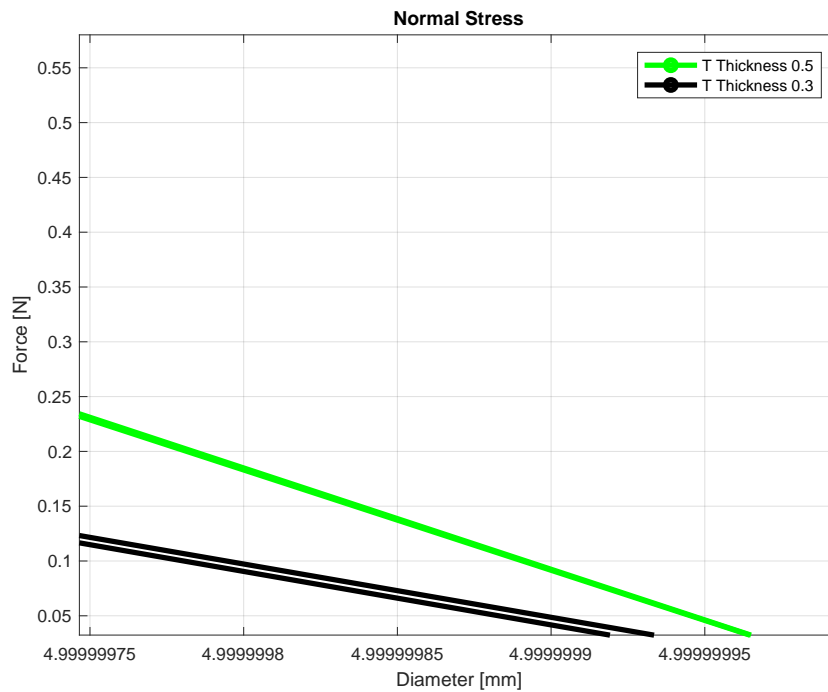
In the figure are present the stiffness of the stents tested. The trend looks like that one of a linear-elastic material, but observing the central part is clearly distinguishable, easier for the device with the thickness of 0.5 mm, the differences between the trend during the loading process and that during the unloading one. It is possible to notice a slight hysteresis in the Figure.





**Figure 54** – Zoom on hysteresis area

There is also the residual deformation, but the values now are very close to the initial diameter.



**Figure 55** – Zoom on residual deformation

With the zoom on the hysteresis shown in the figure is possible to have an idea of the residual deformation, which is very small. It is possible to increase the testing interval, but to have a same condition for all the trials, we decided to stop the simulation at the 20%. Consequently, there would be a major hysteresis area, and the residual deformation would be bigger.

### 3.6 Comparison between the T and W devices made by PCL

Finally, all the presented computational results will be compared for having a general overview.

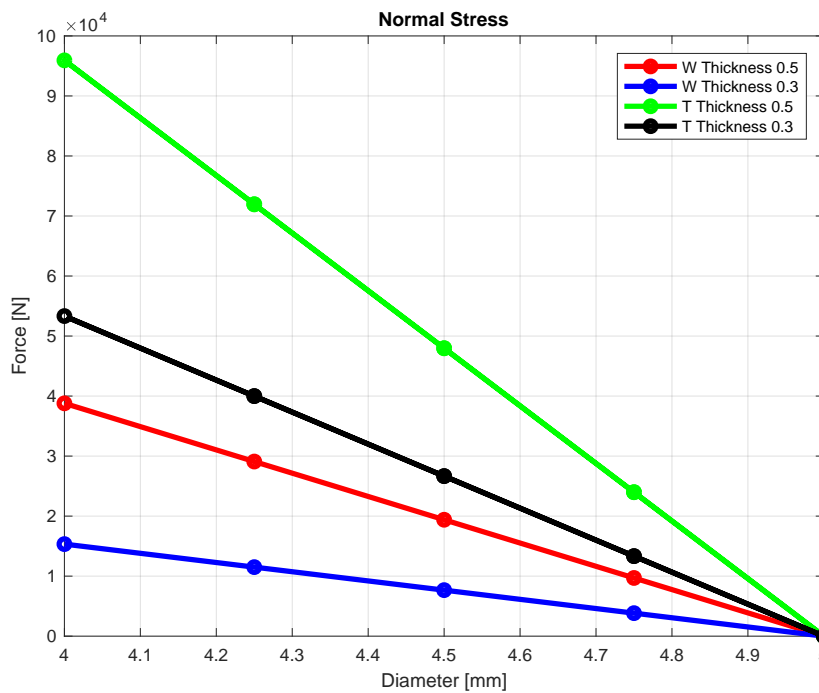


Figure 56 – T and W PCL device data

In the X axis of the plot are presented the different diameter correlated to the percentages presented in the methods part. In the Y axis are reported the Normal Force values measured. The force necessary to arrive at the limit compression value is bigger for the stents with the T mesh design. All the stents have the same trend in the loading and unloading process and the normal stress values are in the 1000-10000 N interval. The comparison allows to understand how the design of the device can influence the mechanical behavior of the stent. The limit of the compression values imposed, in this case, is sufficient to have differences between the behavior of the stents with the two types of meshes, but to obtain a complete knowledge about their mechanical features could be important to compress the devices until the breaking point.

### 3.7 Comparison between the T and W devices made by AZ31

The comparison between the behavior of the two typologies of devices made by the same elastic-plastic material, the Magnesium alloy AZ31, is very interesting.

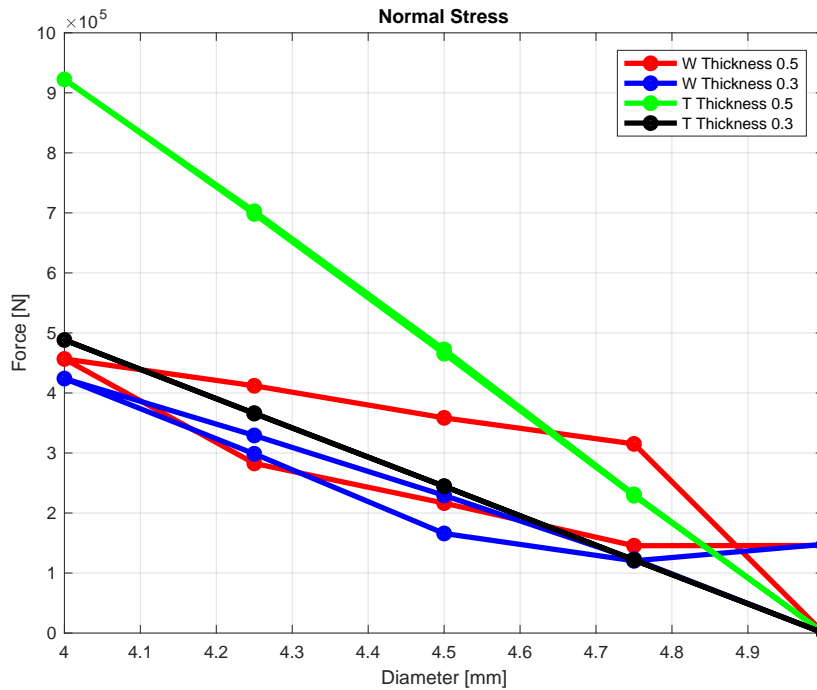


Figure 57 – T and W AZ31 device data

From the figure is possible to notice how the devices with the T mesh have a more rigid behavior in the radial compression trials. In fact, to arrive at the final diameter of 4 mm, is necessary a higher force than the stents having the W mesh. The differences between the two typologies of design are very evident although are made with the same elastic-plastic material. It is incredible how the design can influence the presence of the stress values. The choice can be done also considering the place where the stent has to be implanted, or rather thinking about the diameter of the vessel, its conformation and the entity of the disease. Also, in this case, we are not arrived at the limit point of the devices. The T mesh device with the 0.3 mm has a mechanic behavior which is similar to the W mesh devices, because the maxima forces measured are very close, but there is a significative difference with the stent having a thickness of 0.5 mm and a T mesh. Its radial resistance is so high and probably the best choice could be to use a device with the intermediate thickness value, or rather of 0.4 mm. To have a better mechanical property for the W mesh there are the possibilities to increase the thickness of the stent, but in this case is not useful, because could not be used or could have a very limited range of application or changing the length of a single ring of meshes. It was important the

comparison done, because was possible to understand the differences between the two typologies of devices implemented.

### **3.8 Final considerations**

The results obtained from the realization of the thesis permit to have a parametric tool which allows the design of a stent. In particular, in this framework is possible to modify the device only changing the value of the desired parameter. The parametric tool was created for analyzing different types of device so that every change on a specific parameter directly modifies the geometry. In this way, either is possible to study the effect of each single parameter on the stent performances such as the radial compression stiffness.

The final goal of this work is the design and optimization of a new prototype of stent which has to be made by a biodegradable material and has to be fabricated with a 3D printing technique [23]. The created parametric tool allows the analysis and computation of the stent structure and the numerical simulations that provide its main performances. The materials used were biodegradable and the realization process was obtained with a 3D printing technique.

The effects obtained augmenting the thickness are an increase of the force necessary for the radial compression of the devices.

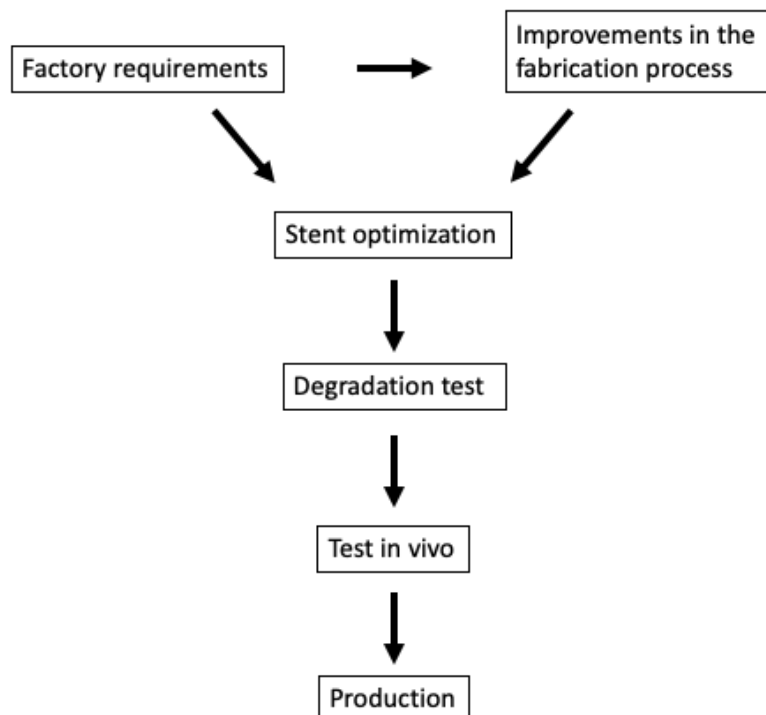
The T-type, in the same conditions resulted more rigid than the W-type. In the work, two different biodegradable materials are used: the PCL which has a linear-elastic behavior and the Magnesium alloy AZ31 which behavior is elastic-plastic. Finally, the field of application of this new type of stent is very wide, because the device should be used for all the organs which presents a lumen. For this reason, the lumen diameter and stent length are two of the parameters defined in the structure among others.

This allows lastly a patient specific personalization of the device.

### 3.9 Future improvements

In the future will be possible to have the definitive material properties and a new type of trial which permit to have a complete knowledge about the potentialities of the devices. Certainly, will be present an optimization of the design, improving the parameters exposed before to satisfy all the characteristics deriving from the fabrication process. Also, there will be the improvements of the factory realization method which consequently will involve another requirement. The next step will be the degradation test which will be conducted by the NAITEC company and the in vivo trials before to test the devices in the humans. In the end, the last passage will be the final production of the device.

Below there is a diagram containing all the future improvements which are yet established. In the future, having the properties of the material used, it is possible to evaluate, in the T-type with 0.4 mm thickness of the strut, which are specific imposed, the effect of the various parameters and according to the application, to generate the final prototype.



**Diagram 2** – Future improvements process







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