Instituto Tecnológico y de Estudios Superiores de Monterrey

Campus Monterrey

School of Engineering and Sciences

Design of a Bioabsorbable stent as preventive treatment of complication in bariatric surgery RYGBP

A thesis presented by

Juan Manuel Jara Mendiola

Submitted to the
School of Engineering and Sciences
in partial fulfillment of the requirements for the degree of

Master of Science

In

Manufacturing Systems

Monterrey Nuevo León, December 5th, 2017

Instituto Tecnológico y de Estudios Superiores de Monterrey

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Declaration of Authorship

I, Juan Manuel Jara Mendiola, declare that this thesis titled, "Design of a Bioabsorbable stent as preventive treatment of complication in bariatric surgery RYGBP" and the work presented in it are my own. I confirm that:

- This work was done wholly or mainly while in candidature for a research degree at this University.
- Where any part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution, this has been clearly stated.
- Where I have consulted the published work of others, this is always clearly attributed.
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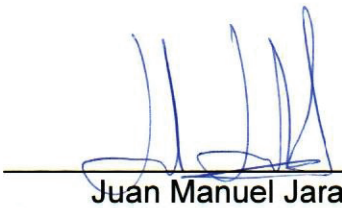

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Dedication

This is dedicated to my family for their support and encouragement in all the decisions that I made in my life and during this journey to get the degree of Master.

Acknowledgements

I would like to express my deepest gratitude to all my professors of the Tecnologico de Monterrey for their support and also to all the staff of the Anexo de Manufacura.

I'm very thankful for the opportunity of being part of the CONACyT program for post-degree students and for the support of living.

A special gratitude to my colleges who were with me during this journey, through those overnights, projects and exams for their support and advice, to those who became a second family for me.

I will always be grateful to my assessor Dr. Elisa Vazquez for the support and the guidance during my stay in the ITESM. Also, the counseling and advices from Dr. Ciro Rodriguez, Erika Garcia, Jan Lammel that were of great help in my formative growth.

A special thanks to Dr. Aida Rodriguez and the team form the Instituto de Biotecnología of Universidad Autónoma de Nuevo Léon, who were very supportive for the development of this project.

Design of a Bioabsorbable stent as preventive treatment of complication in bariatric surgery RYGBP

by

Juan Manuel Jara Mendiola

Abstract

A new approach to the treatment of complications of RYGBP is covered by the implementation of design methodologies as quality function deployment and theory of inventive problem solving, (QFD and TRIZ) to propose a Design of a bioabsrobable stent as a preventive treatment. In despite on the variability of documented results of degradation rates of bio polymers and bio metals, a new lab protocol is proposed to homogenize both families of materials degradation rates into comparable results. The usage of PLA and AZ31 into a new protocol proposal of degradation tests were carried on. The design resultant by the design methodologies were tested by finite element analysis to compare compression resistance, flexibility and compressibility. Three design proposals are shown with acceptable performance and an expected functional life time.

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1. Introduction

In this chapter, it will be discussed the main propose of the project by covering the history of the problems of obesity and other consequences, how this problem can be solved by bariatric procedures and quick limitations of this type of surgeries.

After the implementation of design methodologies to understand the full picture of the actual state of the usage of commercial stents designed for esophageal complications, an integral solution can be proposed.

The information documented about degradation rate of bio materials is very extensive but with poor comparability with each other, by using different mediums, the relation of volume of solution with surface exposed and even the ways to estimate the degradation rate. A new protocol proposal is designed to produce comparable data of degradation rates of biometals and biopolymers exposed to the same conditions, to estimate the functional life time of the design of the stent resultant in this document.

The design, product of the implementations of the design methodologies, will be tested on FEA simulations in SolidWorks Simulation to compare the performance of each proposal and be analyzed.

Once have discussed the state of the problem and the thesis objective, in the next chapters, will focus on the medical issues that are occurring during bariatric surgeries and how new medical devices or prosthesis can help to improve the healing process for the patients and a proposal design of a prothesis of biodegradable materials for post treatment of Roux-en Y gastric bypass.

1.1. Statement of Problem

To be diagnosticated with obesity, the body mass index (BMI) must be more than 40. Studies have shown that from 2000 to 2005, the rate of obesity in the US increased 24 percent. Evidence have shown also that the overweight present on infants and teenagers (until 18 years old) have premature mortality and physical morbidity when they reach the adulthood[1]. Now a days, the obesity is one of the main causes of death worldwide, because of all the context involved on the obesity topic, diabetes, heart diseases, cardiovascular complications, breathing complications as asthma [2]. To reach that level of BMI is not a thing of one day, it involves repetitive actions and behave of the person, also a specific routine of no exercise and long periods of being stationary, and a bad diet.

For young patients, strict diet, alimentary supplements and exercise is the best option, because they can change they life style, get new routines and behavior. But for older patients need to recur to something else, bariatric surgeries it's the most common[1]. The bariatric surgeries are a treatment of obesity through surgical intervention, where a portion of the stomach or small intestines are removed, this with the objective to reduce the volume of food required to satisfy the patient.

In all the surgical procedures, it will be always a probability of failure, like in all the events or processes in the industry, the purpose of the medics and the researchers is to keep this value of failure at the lowest possible and keep at minimally the invasive of the bariatric interventions.

The gastric bypass operation is one of the most common procedures for surgical treatment of obesity, even is called "*The Golden Standard for surgical treatment of obesity*" [3], Even when bariatric surgeries can be classified in malabsorptive, restrictive or combined malabsorptive-restrictive procedures, in most of the procedures has to be a cut of the stomach or intestine or both, and this can produce a risk on the process of healing, the most common, foregut leaks[4].

To prevent foregut leaks, it has been used medical devices or prosthesis to help with this issue, but the procedure it's not completed yet, lots of topics can be evaluated to improve the procedure and offer a good proposal to the patients.

It's well known on the literature the usage of prosthesis, stents, to prevent foregut leaks. The stents used for this scenario were designed for other usage, those stents need to be placed when the complications are presented in the patient and require to be removed after the healing processes is done. Some other complications can be presented after the placement of the stent, this happens because of the usage of a product designed for another application, and can be prevented by the design of a new product specialized for this usage.

1.2. Thesis Objectives

The focus of this thesis is to design a medical device as a preventive treatment for RYGBP complications, that design will be product of the analyze the most popular bio absorbable materials in the literature and the stents available in the market used in this scenario. After select the materials more viable to perform this task, it will be putting on a degradation test, the results will provide data to develop a product specifically designed for this area of opportunity, and offer a product that will maintain its mechanical properties during the time expected. The main goal is to provide a medical device that will be absorbed by the body completely to save a second medical intervention to remove the prothesis, improving the healing process and providing a better quality of service by reduce the number of medical interventions.

2. Literature review

In the next chapter, it will contain the findings in relevant topics of our project, introduction to the medical issue that it is the obesity, how big is this issue in the world for the health of the population. Later, it will be discoursed the term of bariatric surgery, how it works, the benefits and areas of opportunity. New materials to produce medical devices and prosthesis with bio-absorbable properties, and how these materials will change the medical procedures and increase the life quality of life of everyone.

The result of our research is to understand the importance of our project, see the causes and consequences of the obesity and how to improve the actual procedures by the develop of integral solutions.

2.1. The Obesity, causes and consequences

The obesity is a condition that most of the population of the USA and México have, this two been the countries with the biggest rate of obese population on the last 5 years [5].

According to the World Health Organization (WHO), obesity is defined as abnormal or excessive fat accumulation that may impair health [6]. The way to know who and who is not consider as obese, the Body Mass Index (BMI), for adults, must be greater than or equal to 30, if the BMI is between 25 and 30 is considered as overweight. BMI is defined as a person´s weight in kilograms divided by square of his height in meters (kg/m^2).

In these last years, overweight and obesity are linked to more deaths worldwide than underweight. There are more people around the world who are obese than people who are underweight, with the exception of some parts of Asia and Africa [6].

The cause of the obesity and overweight is the number of calories consumed over pass the calories expended, this imbalance is caused for different factors:

- The easy access of food in high fat.
- The inactivity of the people who lives in very industrialized regions of the world.
- The sedentary way of life that is more and more common on the big cities. This involves the modes of transportation and the urbanization of more cities.

This changes on the way of living of the residents of urbanized cities, are associated with the social and economic changes like, sedentary work stations, food processing, distribution marketing, lack of urban planning, and poor develop of supportive policies in sectors like, health, agriculture, economics and transportation [6].

According to the OECD, the obesity rates of countries like USA and Mexico show that one of three adults is overweight or obese. In the Figure 2.1, its shown how countries like Korea, Italy, and Switzerland have increase very low their rater, but also, we can see that countries like Australia, England, Canada, Spain, have increase their rate very fast in the past 10 years.

In these countries are most of the people with overweight live, and most of them are adults, this means that at least, over the past 30 years, these people have been living an unhealthy lifestyle.

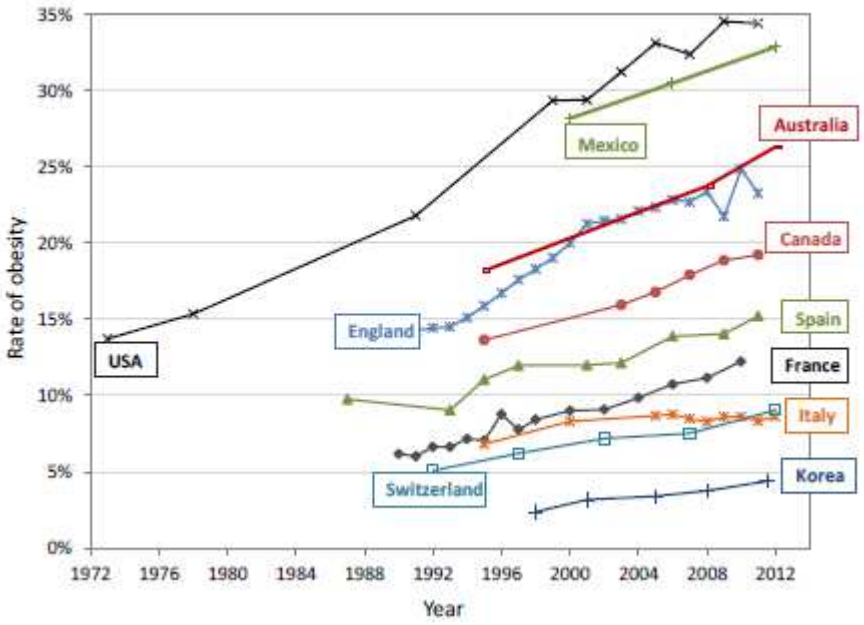


Figure 2.1.- Rate of obesity 2012 of the OECD
Image subtracted from the Article "Obesity Update 2014" of the OECD [5].

The consequences of being an overweight or obese person have major health risks. The way that organism is used to work change when we over pass the caloric levels over the calories expend, the assimilation of nutrients goes low, and the absorption of fat grows, some of the organs start to be capped and some veins and arteries closeup, because of the saturation of fat on the blood [7].

The most common health consequences of the overweight are:

- Cardiovascular diseases (heart disease and stroke) [2][7]
- Musculoskeletal disorders [6]
- Osteoarthritis [6]
- Cancer (breast, ovarian, prostate, liver, kidney, colon) [8][6]

The numbers of people with overweight have in comparison between sexes, the females a bigger percentage than man, this is related with the pregnancy. Women gain weight during the pregnancy, and most of them never reach their original weight, they even gain more, that's why the number on women are slightly bigger than men, and is more common in some countries that more physical job being preform by men, like construction, logistics, etc.

In the Figure 2.2 by the OECD Health Statistics of 2014, its shown how is distributed the percentage of women versus men on percentage of the populations in overweight. This is very important to know the size of the market, and which countries need an integral solution to this issue. In this

Figure 2.2 we see that USA and Mexico had the highest percentage of overweight of population of 15 years old and older, having the 35.5 and 32.4 percentage respectively. The three countries with more population with overweight are, United states, Mexico and New Zealand, respectively, in all these three countries, the woman present more percentage of overweight in comparison with the males.

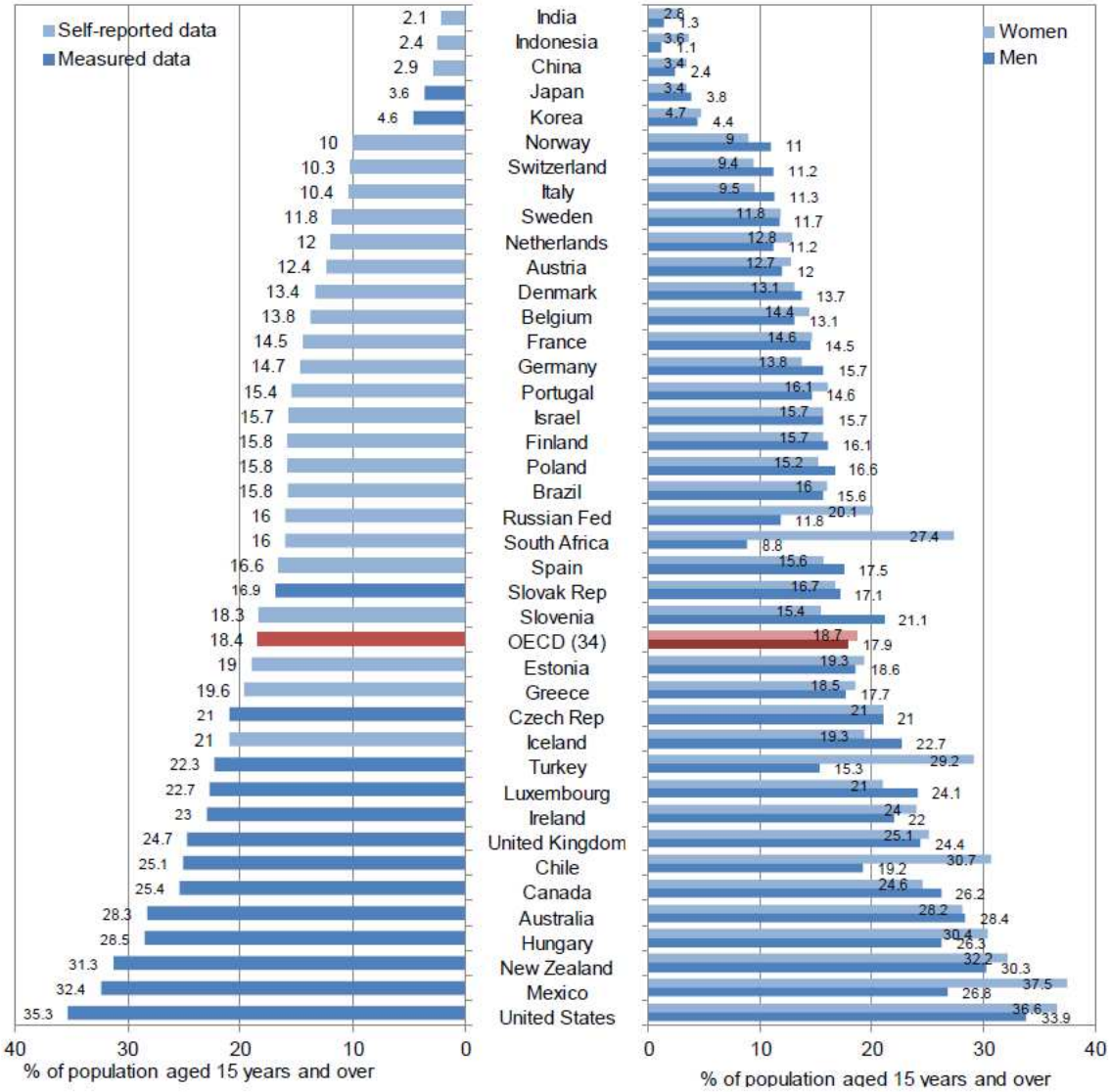


Figure 2.2 OECD Health Statistics 2014 percentage of population with overweight worldwide
The image was subtracted from the article "Obesity Update 2014" of the OECD [5].

The overweight and the obesity is curable. When is present in childhood, with an strict diet and exercise the children can eliminate the overweight and prevent all this diseases, but when the adult is the one with overweight, it's more difficult to lose weight [6]. Sometimes the bones are too damage to resist heavy exercise, or the lungs cannot assimilate oxygen during the exercise, also the

heart struggle to pump blood trough the body. Because all this, the bariatric interventions are very attractive to improve the quality of life of all those patients with overweight [1].

2.2. Bariatric Surgeries

The treatment of obesity by surgeries with the finality of having a significant post operating weight loss. The bariatric surgeries can be categorized by their approaches, the malabsorptive, restrictive and the malabsorptive-restrictive procedures.

Our design of product is centered on the complications of a very specific bariatric surgery, The Roux Y bypass. But it's very relevant to understand why we focus in this precise bariatric procedure.

2.2.1. Types of gastric bypass

The restrictive procedures focus in reduce the volume of the stomach, which leads to getting full of smaller meals, that means less consumption of caloric volumes equal to loss weigh. The popular procedure are the gastroplasty, gastric pacing, gastric banding, sleeve gastrectomy and Intragastrical balloon, just to mention some of them, Fobi et al. in 2008 explain who brought this procedures in medicine and some pros and cons [9].

In the Figure 2.3 its shown some of the most popular procedures, who design them, year and a little illustration of the principle to restrict the amount of caloric income to the stomach as a weight loss procedure. The Horizontal gastroplasty and the midway gastroplasty, presented by Mason 1971 and Pace 1979 respectively, consist on restrict part of the stomach to reduce the income of food, these procedures where not so effective and the patients presented re-gain of weight after the procedures, also the oblique gastroplasty by Long 1978, present un ineffectiveness.

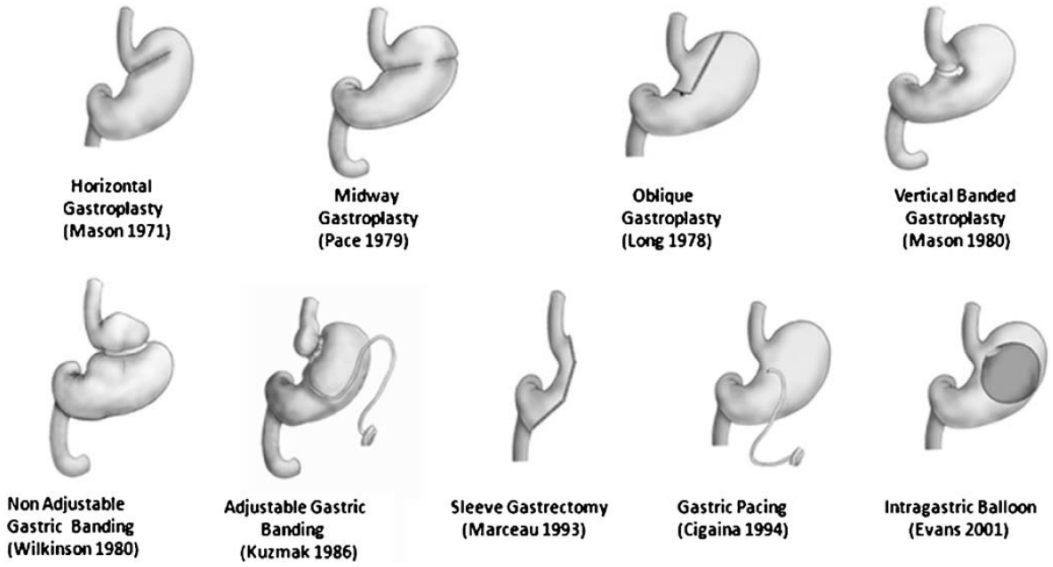


Figure 2.3 Restrictive procedures, extracted form Fobi et al. in 2008 "The bariatric surgeries: The past, present and the future"[9]

The malabsorptive procedures are considered as high invasive because of their nature. To make the digestive system to absorb less sugars and fat of the meals, its common to section the stomach.

Some of the procedures of malabsorptive are presented and explained by Saber et al. in 2008 [9],in Figure 2.4.

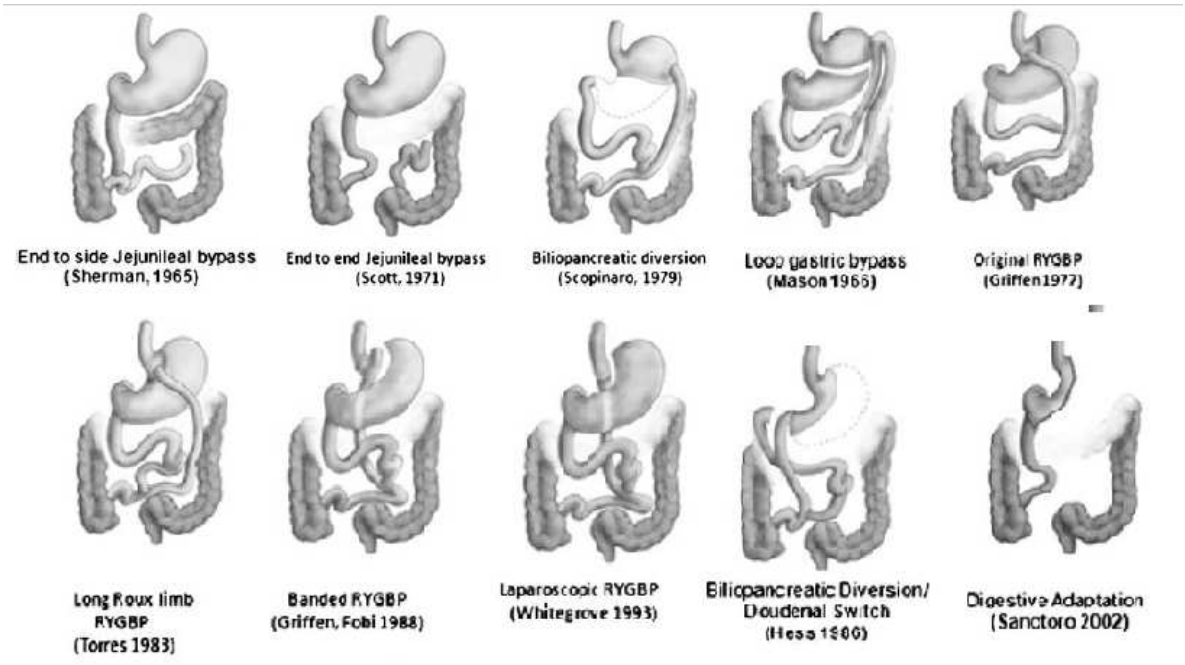


Figure 2.4 Malabsorptive Procedures, extracted from Saber, A. 2008 [9]

The Roux Y bypass it's the more common and popular procedure as a treatment for obesity, also known as *"The Golden Standard for surgical treatment of obesity".* The Roux Y it's the one in which were going to focus because of its popularity and for being the most used.

One of the main reasons of why the Gastric Bypass (GBP) effectiveness on the weight loss function, it's because of its fat malabsorption without affecting the absorption of protein and carbohydrates.

This procedure doesn't allow a normal sequential mixing of food with bile and pancreatic secretions, that result in missing steps on a normal sequence of the digestive process, and the fats and fats non-soluble nutrients absorptions is decreased, having as consequence a decreases caloric absorption[3].

The impact of bariatric surgeries is bigger than we think, economic and society sectors have been affected with this topic, because of the amount of people asking for this alternative as quick weight loss procedure. Even though, the effectiveness is really high on elderly people [10].

2.2.2. Diseases and Complications after GBP

The Roux-en-Y GBP is a combination of restrictive – malabsorptive procedure, that why this procedure has been used as the Golden Standard and has a good long-term result.

As its well explained in Andrés et al. in 2007 [11], this bariatric procedure was first introduced by Mason and Ito in 1967. The procedure consist in a gastric pouch of 15–20 ml, having as result a division of the small bowel distal to the ligament of Treitz; and the distal segment is brought up to the pouch antecolic through the transverse mesocolon to create the gastrojejunostomy of 15 mm diameter approximately, the Roux limb can be short of 100 cm long and is connected as well as the defunctionalized stomach, duodenum and variable length of jejunum, also known as the biliopancreatic limb, and this can be either stapled or sutured jejunojejunostomy[11]. In the Figure 2.5 is shown how the digestive system is before and after the RYGBP.

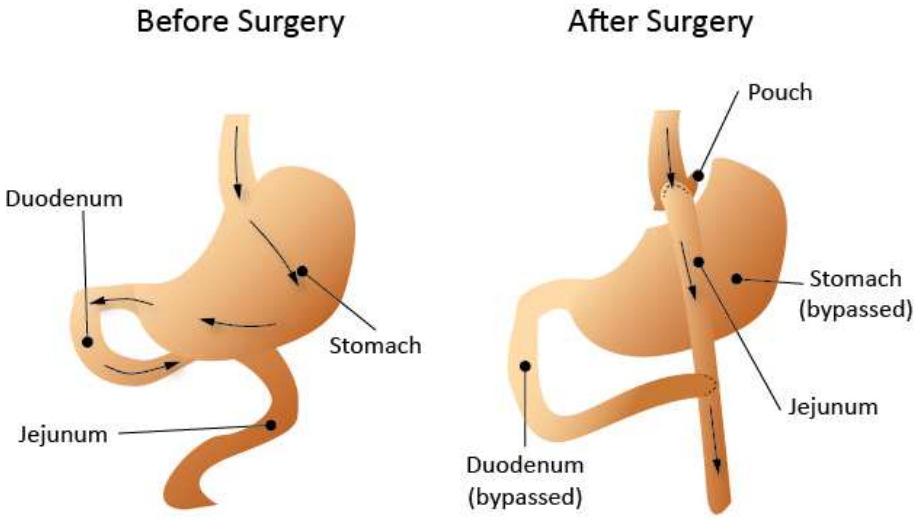


Figure 2.5 Roux-en Y Gastric Bypass (RYGBP)

Even when this procedure it's popular of the medic field, as all the medical procedures, has a rate of success. As late complications after a GBP Fobi et al. in 1998 [3] can be named:

- Stomal stenosis (c)
- Gastric staple line dehiscence(d)
- Leaks(d)
- Jejunal and gastric necrosis
- Loculated fluid collection
- Celiac trunk stenosis

Stenosis is an abnormal narrowing or contraction of a body passage or opening, called also arctation, coatraction and stricture. These complications are located at gastrojejunostomy or jejunojejunostomy. In the Figure 2.6 its graphically shown how the c) stenosis, d) the inflammation may cause the foregut leak and how the e) usage of prosthesis can help in these complications.

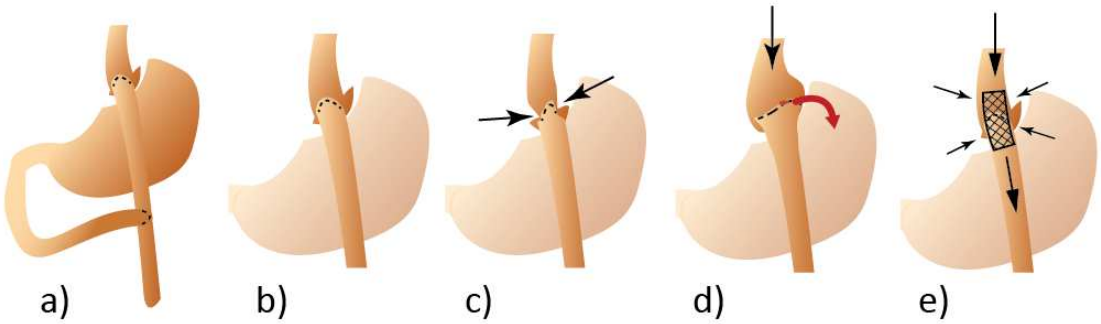


Figure 2.6 Most common complication after RYGBP
a) The new digestive system has two locations where the intervention has done, those locations are duodenum and jejunum, b) the jejunum is where is more common to present complications such as c) stenosis, where the gastric tube closes, either for inflammation or as a consequence of the healing process trying to close the section done by the physician, d) the inflammation also may result on the excessive stretching of the staple zone having as a consequence the rupture of the tissue producing the leak, and also by the excessive income of food, e) most of these complications can be prevented by the usage of a prothesis.

Even though of this complications this procedure has just 10 percent of morbidity post-surgery and the success of weight loss is about 80%, and the 50% of the loss weight is accomplished in the first two years after the surgery [3].

2.2.3. Areas of opportunity

It's well known in the literature that some of the complication listed on the last section, can be treated with medical devices[4], [12]–[21]. These medical devices are called Self-Expanding Metal Stent (SEMS) or Self-Expanding Polymer Stent (SEPS). These devices were design with the finality of treatment for esophageal complications as esophageal ulcers, benign strictures, rupture, perforations and fistula, malignancy, achalasia[22]. But because of their attributes can be also as relatable alternative. These devices are stents of in oxidable steel, titanium, nitinol or even of some polymers as silicone and polypropylene. The complications are form the obstruction of the gastrojejunostomy or jejunojejunostomy or the failure at the staples or suture causing leaks, these devise act as an oppositional force to these obstructions and as a patch for the leaks. The attributes, advantages and disadvantages will be discussed on the next section 2.4 of the document.

2.3. Medical devices for GBP complications

In the past 3 decades, esophageal stents have become a very attractive alternative as treatment for dysphagia resulting from esophageal and gastric cancers. With the pass of the years, these stents have taken another uses because of their good performance and their attractive characteristics for different benign treatments as post-surgical foregut leaks.

As a successful treatment of malignant and benign conditions, the self-expanding metal stents (SEMS) and or Self-Expanding Polymer Stent (SEPS) placement has presented a high rate of success for gastric anastomotic leakage, staple line dehiscence, perforation and general gastric trauma, conditions that can be life-threatening for the patient[12].

The most common complications after the insertion of the prothesis, this device for some reason may tear tissue in one of the anchors placed to keep the device in its place, also the device may migrate into another place of the digestive system of failure anchors, weak tissue or inflammation, once the device is no longer in its place and it's not protecting the area as it have to, the patient may have discomfort on the abdominal area, as a consequence of device on a wrong place, rapture of the tissue or even a foregut leak, as is shown in the Figure 2.7.

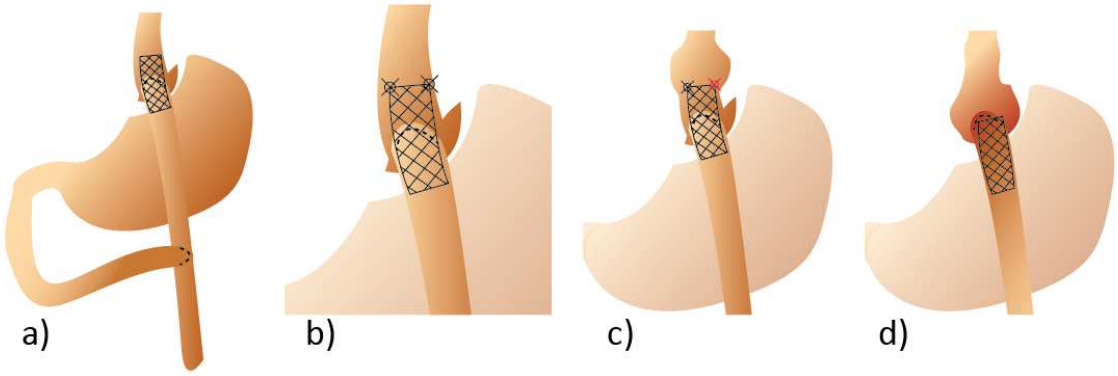


Figure 2.7 Complications after the placement of the prothesis
a) Once the device is placed, its fixed by b) anchors placed to keep the device in its place but these anchors for some reason may tear tissue having a small rapture of the gastric tube, also the device c) of failure anchors, weak tissue or inflammation, d) may migrate into another place of the digestive system once the device is no longer in its place and it's not protecting the area as it have to, the patient may have discomfort on the abdominal area, as a consequence of device on a wrong place, rapture of the tissue or even a foregut leak

The USA is one of the more advanced medical technology worldwide, also the biggest influent in the economic and social sectors for Mexico. The USA and Mexico have the highest overweight rate of their respective population, that's we are focusing on devices approved on USA by the Food Drug Administration (FDA). The FDA main propose is to protect the public health by regulating medication for human and animal consumption and other biologic products, medical devices, cosmetics, alimentary supplements and products that emit radiation as well. It also provides scientific based data of the medicaments and food to improve the health. The FDA has responsibilities in all USA and some Latin-American countries.

It's have been well documented the usage of esophageal and tracheal devices for the use of post-treatment of GBP complications as stenosis and foregut leaks.

In the next section will be discussed about the available products in the market used for this type of complications for GBP.

2.4. Benchmarking

By consulting the American Society for Gastrointestinal Endoscopy (ASGE) has been documented a review of the most important stents for gastrointestinal usage[17].

- Ultraflex

By Boston Scientific, Available in distal or proximal release, suture removal release mechanism, 48%-54% foreshortening with deployment; indicated for resectable and nonresectable malignancies.

Figure 2.8 Ultraflex by Boston Scientific

- Wallflex

By Boston Scientific, Low-profile 18.5F coaxial delivery system with reconstrainability up to 75%, proximal and distal flares, proximal removal suture, endoscopic transition zone for deployment under direct visualization; indicated for resectable and nonresectable malignancies and concurrent esophageal fistulae.

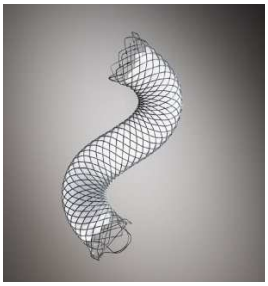


Figure 2.9 Wallfelx by Boston Scientific

- Evolution

By Cook Medical, Silicone coating on the exterior and interior stent surface, proximal and distal uncovered flanges, lasso loop for repositioning immediately after placement, controlled-release trigger deployment and re-capturability, 30 - 40% foreshortening.

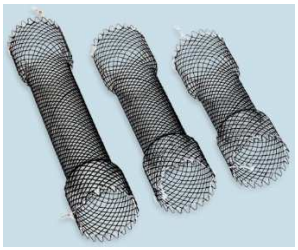


Figure 2.10 Evolution by Cook Medical

- Alimaxx-Es

Merit Medical Systems, Laser cut nitinol design results in virtually no stent foreshortening or elongation. Stent contains antimigration struts that reduce stent migration. Polyurethane cover helps to decrease tissue ingrowth. Silicone lining provides a smooth inner lumen. Soft distal and proximal flares allow patient comfort because of controlled circumferential stent expansion. Indicated for maintaining esophageal luminal patency in esophageal strictures caused by intrinsic or extrinsic malignant tumors and for occlusion of esophageal fistulae.

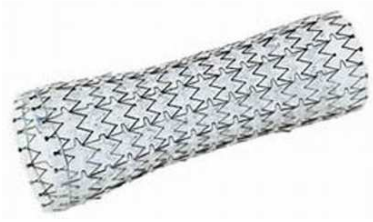


Figure 2.11 Alimaxx-ES by Cook Medical

- Polyflex

Boston Scientific, Indicated for refractory benign strictures, resectable and nonresectable malignancies. Studies have demonstrated safe removal weeks after placement, manual loading onto delivery system required, has radiopaque markers at ends and center, 36%-41% foreshortening with deployment.

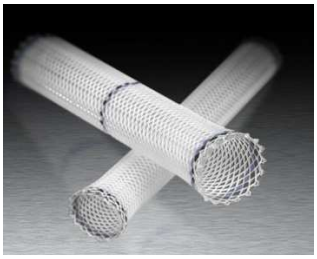


Figure 2.12 Polyflex by Boston Scientific

- Niti-S Stent

By TeaWoong Medical, the device combines two specific characteristics, which presumably could reduce, if not eliminate, stent migration. First, the Niti-S stent flares at both ends. Second, it has a double-layer configuration with an outer uncovered nitinol wire tube to allow the stent to fix itself in the esophageal wall.

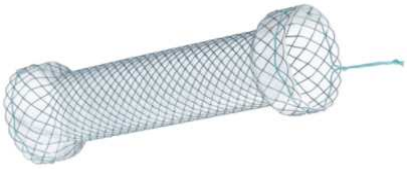


Figure 2.13 Niti-S stent by TeaWoong Medical

- Bonastent

By EndoChoise Inc., Hooked crosswire geography offers greater conformability.

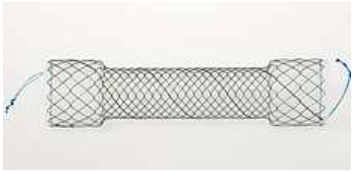


Figure 2.14 Bonastent by EndoChoise Inc.

- EndoMaxx

Merit Medical Systems, its design of hooked crosswire offers conformability and prevents migration of the anchors on the self-stent.

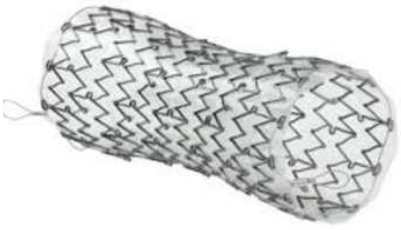


Figure 2.15 EndoMaxx by Merit Medical Systems

- BD Sx-ELLA

By CS ELLA, the placement procedure is by endoscopy as well as the SEMS, its design is for patients with esophageal cancer, dysphagia.

Figure 2.16 BD Sx-ELLA by CS ELLA

- Hanarostent

Mendo Medikal, Stent designed as post-treatment for gastric sleeve or as alternative as malabsorption procedure for weight loss, further research needed for the rate of success of this usage.

Figure 2.17 Hanarostent by Mendo Medikal

Need to be mention that the Harnarostent and the BD SX-ELLA are not approved for the FDA but because of their popularity and relevance as products of high level of innovation on their performance, needed to be taken on this document on the benchmarking for the proposal of a new design of product.

By consulting the data bases of the FDA, we collected documents of the medical devices approved by this organization and were compared on the scientific data bases for the most used on the field to list the products used as treatment for GBP post-surgical devices[23], [24].

In the Table 2.1 and Table 2.2. It's shown a matrix of the geometrical and technical attributes of each stent, and some facts on the result of the research on the literature of the performance of each stent.

Table 2.1 Benchmarking FDA approved Esophageal Stents used for RYGBP complications Technical vs Medical data.
*All the technical data were extracted from their respective companies' web pages. *Not approved by FDA*
NC= Non-covered, PC=Partially covered, FC=Fully Covered. Some Products are not specified the total time of the placement of the stent.

Technical Data							Medical Data					
Name	**Company**	**Material**	**Length (mm)**	**Diameter (mm)**	**Cover/ Coating**	**Product**	**No. Patient**	**Clinical success**	**Migration Rate**	**Complication Rate**	**Time**	**Use**
WallFlex[20]	Boston Scientific	Platinum Nitinol	40-100	8-10	NC/PC/FC Silicone		23	67%	33%	35%	3 months	Leaks
Evolution[20]	Cook Medical	Nitinol	18-20	8-15	PC/FC Silicone		*-					
Polyflex[4]	Boston Scientific	Polyester	90-150	16-21	PC Silicone		3	66%	33%	66%	-	Leaks
BonaStent Esophageal[20]	Endo Choice Inc.	Nitinol	40-100	18	FC Silicone		10	100%	33%	40%	3 months	Leaks
EndoMAXX[16]	Merit Medical Systems	Nitinol	70-150	19-23	Silicone		35	100%	14%	11%	3 months	Leaks
***Hanarostent**[12]	Mendo Medikal	Nitinol	180-240	24-28	Silicone		15	93%	33%	23%	1 month	Leaks

Table 2.2 Benchmarking FDA approved Esophageal Stents Used for cancer complications, technical and medical data.
*All the technical data were extracted from their respective companies' web pages. *Not approved by FDA*
NC= Non-covered, PC=Partially covered, FC=Fully Covered. Some Products are not specified the total time of the placement of the stent.

Technical Data							Medical Data					
Name	**Company**	**Material**	**Length (mm)**	**Diameter (mm)**	**Cover/ Coating**	**Product**	**No. Patient**	**Clinical success**	**Migration Rate**	**Complication Rate**	**Time**	**Use**
Ultraflex[18]	Boston Scientific	Platinum Nitinol	20-80	8-20	NC/PC/FC Silicone		19	82%	0%	21%	2 months	Cancer
Alimaxx-ES[15]	Merit Medical Systems	Nitinol	70-120	12-22	FC Silicone		45	11%	36%	20%	1 month	Cancer
Niti-S stent[25]	TeaWoong Medical	Nitinol	60-150	18-20	PC/FC Silicone		42	95%	7%	12%	-	Cancer
***BD Sx-ELLA**[21]	CS ELLA	Poly-p-dioxanone	60-135	18-25	NC		23	76%	4%	17%	-	Cancer

After the compilation of our base data on the benchmarking, we can proceed to use it on a methodology of design as the Quality Functional Deployment (QFD), in the.

To be approved, these products needed to pass strict standard postulated by the FDA. To apply for the approval of the FDA they have a document of recommendations, below we will list this requirements as our own for to propose an integral design and a relevant alternative of product. All this info were subtracted from the *Guidance for Content of Premarket Notification for Esophageal and tracheal prostheses*[26].

I. Device Name
II. Manufacturer Information
III. Device Classification
IV. Device description
V. Comparison with predicate device
VI. Changes or modifications
VII. Device materials and biocompatibility
VIII. Performance testing
    A. Deployment testing
    B. Expansion force testing
    C. Compression force testing
    D. Dimensional Testing
    E. Corrosion testing
    F. Tensile strength tests
IX. Performance testing Animal and Clinical
X. Performance standards/ Special controls
XI. Sterility
XII. Proposed labeling
XIII. Summary or Statement
XIV. Certification of Truthfulness and Accuracy
XV. Indications for use

These requirements need to already pass lab tests, they are for putting the product in the market already and have accomplished some other standards, for example, the section of device materials and biocompatibility, the materials need to qualify for *the ISO-10993 Biological Evaluation of Medical Devices Part1: Evaluation and Testing.* All this specifications can be consulted for further information on the official document, *Guidance for Content of Premarket Notification for Esophageal and tracheal prostheses*[26].

These listed requirements are important, but will focus on the VII, VIII as the relevant for our project. Because of the restrictions of time and monetary topics we will make lab tests and mechanical simulation to accomplish these requirements, also we will collect relevant data form the literature to justify each decision on our design methodology. We will continue this part on the Chapter 2, 4 and 5.

2.5. Bio-materials

After reviewing the data collected for the develop of the Table 2.1 and Table 2.2 in the section 2.4 Benchmarking and the QFD house at the 5.1 Design Methodology "QFD" and "TRIZ" we conclude that materials known as biomaterials are relevant for our design because of their attribute of being able to be degradable in the organism.

Bio materials are the ones whom degraded in organic environments. To understands the concept of biodegradable and the differences between other concepts that are alike. On the article *Physicochemical characterization of degrading polycaprolactone scaffolds by* Bosworth et al. in 2010 [27], its explained the terminology and their definitions of these materials in Table 2.3.

Table 2.3 Terminology and definitions of biomaterials [27].

Terminology	Definition
Biodegradable	At macromolecular breakdown with dispersion in vivo, but without proof of its elimination. (excludes biodegradation by environmental, fungi or bacterial means.
Bioresorbable	It degrades whilst in vivo and are further resorbed by natural metabolism for total elimination.
Bioabsorbable	It dissolves in the presence of bodily fluids without chain cleavage and changes in molecular mass.
Bioerodible	Experience degradation on its material surface.

Following this terminology, polymers that can behave this way like PLA and PCL are "Bioresorbable", but both materials can undergo with two different ways of degradation in certain circumstances, can either be Bioresorbable or Bioerodible.

It's been well established the term of "biodegradable" in the literature to refer to a material that can degrade in the organism, but after introducing this practical and more specific and accurate terminology, we´ll continue to refer to materials that present this property in general as biomaterial.

Its shown in the Chapter 5, the main issues in the use of available products SEMS or SEPS, presented limitations like, occlusion of stenosis or migration of the prosthesis and complications at the extraction of the prosthesis. The development of prosthesis of biomaterials, which are completely absorbed by the body once the medical disease has been heals, are the main advantage.

The most popular biomaterials in the literature for develop of new prothesis are, polylactide acid (PLLA), poly-l-lactic acid (PLA), poly-caprolactone (PCL), poly(butylene adipate terephthalate) (PBAT), polyglycolic (PGA) and polyhydroxy butyrate (PHB) for biopolymers,[27]–[33] and magnesium alloys (MG) and zinc (Zn) alloys [28], [34]–[42].

Even of all the available and well documented of biopolymers, PLA and PCL are more popular on the research groups because of their acceptance by the Food and Drug Administration (FDA) for biomaterials applications [28] for this reason we will focus in PLA.

In the topic of the “bio metals”, Magnesium (Mg) and zinc (Zn) stand out. The Mg alloys possess a elastic modulus (41-45 GPa) closer of the natural bone, also when it degrade, most of the Mg alloys present a pitting corrosion, allowing the grow of the bone tissue [38]. For this reason, will be focused on this metal to homogenizes the degradation tests of both materials and will be presented later in the chapter 4 Characterizations of materials.

2.5.1. Bio polymers PLA

The usage of polymers in the industry have been well establish, but until the 1980s, research groups and companies star to research into natural fibers. Because of an environmental concern. The excess usage of petroleum derived plastics and their durability and non-environment friendly issue, government regulations in Asian and European countries focus on bio-derived polymers for recyclable and reusable products for packing field [29].

Will be discuss about these properties of the PLA and how it's been improved it in the literature. Many research groups have focus on how improve the kinetics of the material, so it can present a greater performance on different environments PLA is a bio polymer accepted for the FDA, for its excellent process ability, and biocompatibility [28].

It's well know that the PLA and their hydrophilic property, make this polymer not completely suitable for the food packaging and its mechanical properties are affected with the presence of humidity and moisture[29].

In the Table 2.4 Thermal Properties of PLA. Its shown the glass temperature, melting temperature and the processing temperature of the PLA that is, 60°C, 153°C and 188°C to 210°C respectively [30].

Table 2.4Thermal Properties of PLA.

Thermal Properties (°C)	PLA
Glass transition temperature (°C)	60
Melting Temperature (°C)	153
Processing temperature (°C)	188-210

Some procedures have been used to improve the stability of the thermal properties in PLA to obtain more stable behaviors to different types of processing. The Table 2.5 Mechanical Properties of PLA shows the values of the tensile yield strength (MPa), tensile modulus (GPa), tensile elongation (%), notches izod impact (J/m), 48-110, 3.5-3.8, 2.5-100 and 13 respectively [30].

Table 2.5 Mechanical Properties of PLA

Mechanical Properties	PLA
Tensile Yield Strength (MPa)	48-110
Tensile Modulus (GPa)	3.5-3.8
Tensile elongation (%)	2.5-100
Notched Izod Impact, 23°C (J/m)	13

The reinforce of mechanical properties have been used by adding composites with Kenaf derived cellulose of thermally grafted aminosilane, this composite have been used because of its well attachment to the PLA an also to contra rest the water absorption of the PLA to make this polymer-composite reinforced more stable to degradation actions[29].

The degradation process is the most important attribute of the PLA, but it's well known that this process take a long time, considering that the life time of the products made of this polymer trend to be between 8 to 16 weeks [12], [15]–[21], [25], [26], [43]. For this case the alternative for instead of just accelerate the degradation process of the polymer, make that the polymer increase the regeneration process of the lesion (bone), this have been study by adding hydroxyapatite (HA) to the PLA [32]. The best relation between PLA and HA it's to add 80 wt.% to maintain the mechanical properties like the bone to improve the recovery of the tissue, more research is needed to secure the improvement of this procedure.

As we see, the reinforcement of the PLA it's been taken serious for the research groups, but also the way to process the polymer. Poly lactic acid (PLA) possess numerous attributes that make it a suitable alternative for biodegradable products, its thermal stability, process ability, low environmental impact, good mechanical properties, but the thermal stability gets affected with the presence of humidity [30]. Because of its property of degradation, all these attributes get affected as the degradation occurs.

It's well known that the PLA is easy to process, have been reported in numerous reports that the way of how the polymer it´s processed has as consequence different behavior of it properties[29]–[31], [33], [41], [44]. For example, if the polymer is processed in injection molding or extrusion, the sample, even if it has the same geometrical dimensions, will present different mechanical behavior[30].

The post processing of the polymer it's also an issue, once the polymer its crystalized, re process the product present a change of crystal structure and as consequence, a change in its mechanical properties. By saying this we can conclude that the polymer as it is, is very easy to process and manipulate, but each process and how its process has an effect on the behavior of the material, at Ding, W., et al. in 2015 [44] this issue its well explained.

The usage of laser cutting on bio polymer have presented a change in the degradation rate of the polymers, the effect of heat has a change of the morphology of the material, having as consequence an accelerated rate of degradation [33]. This means that the product may fail faster in its environment of placement, but also can be treated as a control of the life time of the product, but more research is needed to sustain this theory.

As conclusion, the PLA is a bio polymer (derivate of natural components), is biodegradable (degrades in vivo environments) and is also bio compatible to the human organism (nontoxic), has the approval of the FDA, it's easy to process and thermos stable, but present different behavior to different ways to processes. Different manufacture processes present differences to its mechanical properties. The PLA is a hydrophilic polymer (absorbs humidity) and this attribute make the polymer not suitable to packing products, but really good alternative for biomedical devices.

2.5.2. Bio metals Mg alloys (AZ31)

The use of conventional metallic alloys for implants and prothesis have the problem of the removal or retention dilemma [34]. In some cases, the patient must live with the prothesis all his life, because once of the fixation of the bone, this new tissue has grown and keep the device fixed, making impossible to remove without make any damage to the healed area. And in some other cases, the device is provisional, but has as inconvenience the new surgery or intervention to remove this device. Bio medical implants like screws, pins, plates, and in our case, stents, its desirable to use materials that can degrade in the physiological environment [38].

Magnesium (Mg), is degradable in physiological environments through corrosion, is non-toxic, and the excess of Mg in the body can be easy excreted in the urine [34]. Magnesium is considered the fourth of the abundant cations in the human body and the 50-65 wt.% of this amount is located in the bones [37].

Another main reason of why Mg alloys are very attractive to substitute the usage of conventional metallic alloys for biomedical devices, it's the more likely to bone mechanical properties, stainless steel (189-205 GPa), titanium (110-117 GPa) and cobalt alloys (230 GPa) [38],possess greater elastic modulus than bone (3-20 GPa) [36], the elastic modulus of Mg alloys (45 GPa) [38] present less difference and for this reason it will expect a better performance.

The conventional metallic alloys for biomedical devices, for their well know manufacture process, are cheaper that bio polymers.

One of the main reason of why the Mg alloys are very popular in the research field to consolidate it as a biomedical device, it's because of its high degradation rate in physiological environments, and its hydrogen gas release during this process and increase the alkalinity of body fluids, all of which its clinical applicability [37].

Mg alloys with Al, present a resistance in simulated body fluids in compassion with the pure Mg tests. It's also know that high concentrations of Al can be dangerous to osteoblasts and neurons, and in some cases, this high concentrations its considered cause of dementia and Alzheimer´s disease [38].

The composition of the AZ31 Mg alloy is describe in Table 2.6 Chemical composition of AZ31 alloy. The weight percentage (%wt.) of Al is 2.83, Zn 0.80, Mn 0.37, Cu 0.002, present in the alloy of AZ31 [45].

Table 2.6 Chemical composition of AZ31 alloy.

Chemical composition of AZ31 alloy.	
Al	2.83 %wt.
Zn	0.80 %wt.
Mn	0.37 %wt.
Cu	0.002 %wt.
Mg	bal.

Many research and implementations had been tested to improve these disadvantages of Mg alloys to be use for biomedical devices, some of these research are: the use of polymer or bio-ceramic coatings, new Mg alloys, chemical treatments to the alloys and the combination with substances to improve the bioactivity [34]–[37], [40], [42].

Some of the treatments for he Mg alloys it's to extend the life time of the product by retarding the degradation process by chemical or heat treatments. Soaking the Mg in hydrofluoric acid (HC) makes a fluoride conversion coating that improves the corrosion resistance [34], even that the difference it's not much, it can be employed as a pretreatment procedure for subsequent process.

Another method to increase the corrosion resistance of Mg it's the addition of a Calcium Phosphate (CaP) coating by anodization using electrolyte with ZrO_2NPs. Calcium phosphate, during in vivo tests, have presented bio compatibility with bone tissue and is also bio degradable, for these reasons its used as research matter and present a light increase of the corrosion resistance of the Mg alloys, by acting as a coating [37]. This coating has a lower corrosion rate than Mg, that's why it can be used as active to prolong the life time of the product.

The mechanical properties of the Mg alloy AZ31 listed are elastic modulus (44.8 GPa), Poisson's ratio (.35), shear modulus (176 GPa), mass density (1.77 g/cm3), tensile strength (260 MPa), yield strength (172 MPa) and compressive strength (97 MPa) in the Table 2.7 Mechanical Properties of Mg alloy AZ31 showed below.

Table 2.7 Mechanical Properties of Mg alloy AZ31

Mechanical Properties of Mg alloy AZ31	
Elastic Modulus (GPa)	44.8
Poisson´s Ratio	.35
Shear Modulus (GPa)	176
Mass Density (g/cm3)	1.77
Tensile Strength (MPa)	260
Yield Strength (MPa)	172
Compressive Strength (MPa)	97

The thermal properties are listed in the Table 2.8 Thermal Properties of Mg alloy AZ31, that contains the thermal expansion coefficient (26 26µm/m°C) and thermal conductivity (96 W/mk).

Table 2.8 Thermal Properties of Mg alloy AZ31

Thermal Properties of Mg alloy AZ31	
Thermal Expansion Coefficient	26µm/m°C
Thermal Conductivity	96 W/mk

The mechanical properties show us that as the literature said, these properties are more alike to the long bone properties[36]. As it passes the time in the physiological environment, these properties of the AZ31 starts to increase, and it's very important to maintain them as close possible until the patient has healed. The AZ31 as it is, cannot maintain its properties long enough for do the task for what's was design. Here is where the coatings start been attractive to prolong the life time of the

Mg alloys. Even when Al family Mg alloys have a better performance in the life time issue, high concentrations of Al can be dangerous for the new growth of tissue and for the neurological system.

Polymer and bio ceramic coatings, their main purpose is to improve corrosion rate of Mg alloys, some coatings, even when theoretically look promising, in some cases, the attachment between the Mg alloy and the coating it's not favorable and the performance decreased [40].

Coatings are promising when the application of the prosthesis involve growth of bone tissue. This to ensure that the release of hydrogen gas of the Mg alloy, dose not interfere with the new tissue, also to maintain the mechanical properties of the Mg alloy during the healing process.

The most popular coatings of bio polymers involve the use of PLA and PCL, both have presented good attachment to the Mg alloy and the improve to the resistance to corrosion [41], [42]. Many ways to process the materials may vary, dip coating, aerosol are the most common ones.

In the coating process by spray, the materials and the process was fixed, but the porosity pf the coating was the variable factor. the concentration of polymer in the solvent to produce the solution to be used on the spraying device to apply the coating, determinate the properties of the product.

Wong et al. 2010, used AZ91, is ta Mg alloy with different concentrations of Al and Zn (9% and 1% respectively), were coated with PCL at two saturations of porosity in the coating, and it presented results that prove that the amount and dimensions of the porosity, if it close pack pores, the performance of the Mg alloy at compressive tests, were better[42]. As well, the use of dip coating, AZ31 and PLA as materials, also have proven the resistance to corrosion of the Mg alloy [41].

As conclusion, the addition of diverse materials and composites to improve properties that make the product more functional is very important to the companies and research institutes. One big attribute of the bio polymers it's that they are easier to manipulate and combine them to reinforce their weakness, water absorption, mechanical performance, degradation rate, flexibility.

2.6. Conclusions of the literature review

As conclusion of the section 2 Literature review, has been exposed the context of the term "Obesity", the impact in the society, causes and consequences of this alimentary disorder. The obesity and overweight are more common on industrialized countries like Unites States, Mexico and New Zealand have a percentage of overweight bigger that 30% and its expecting to grow. And this disorder can be cured by changing the habits and routines through exercise and healthy ingest of food.

The medical procedures to treat the overweight disorder are called Bariatric Surgeries and the main purpose is to reduce the digestion of calories by malabsorption or restrictive procedures. The restrictive procedures are to reduce volume capacity of the stomach to be filled with less amount of food. The malabsorption procedure consists in the invasive shortening of the digestive system to make a non-completed digestion of the income food to absorb less calories.

The most common bariatric surgery is the gastric bypass Roux-en-Y, is one of the most effective ones but has some inconvenient, this procedure present, foregut leaks and stenosis as the more common complications. These complications have been treated with the use of medical devices, designed for tracheal stenosis for cancer, but have demonstrate been a successful treatment for RYGBP complications.

There were analyzed the most popular commercial stents approved by the FDA, and the requirements of this institution to approve those products. Those requirements of the FDA were the start point for the product design goals and there will be stipulate them on the house of QFD in the chapter 5.1 Design Methodology "QFD" and "TRIZ".

Following the comments of the physicians on the study cases analyzed on the benchmarking, a research on biomaterials were made, concluding that the PLA as polymer and the AZ31 as Mg alloy were the most promising materials for biomedical prosthesis and implants, because of their attribute of being able to be absorbed in vivo and their bio compatibility.

Both materials have their pros and cons and they're not suitable to been used as biomedical devices, no until tests in vitro and in vivo can ensure their proper performance expected to be a functional product. Bio polymers are a reliable alternative for low load bearing bio devices. Magnesium alloys are friendlier to bone growth treatment.

The PLA and AZ31 have been tested in different mediums to estimate their corrosion rate (degradation rate), but a standardized and more reliable in vitro test is needed to collect more alike in vivo data to predict the life-time of the materials. For this reason, in the next chapter, 4 Characterizations of materials, a protocol of a degradation test for both (polymer and metallic) materials will be propose and carried out to estimate the degradation rate of both materials on a more alike medium (simulated body fluid).

3. Materials and Methods/Methodology

In this chapter will be explain the concepts selected as relevant to the development of a new prothesis as a post treatment of a RYGBP. The data collected at the Chapter 2 Literature review will start to take form to fill all the topics needed to the development of a new product of biomedical use.

3.1. Product Requirements

As was said in the section 2.4 Benchmarking, the FDA has standard requirements for the medical devices available in the market and, as organization, they give an approval of safe and quality products. Following these requirements, they were selected as relevant for our first stage of product design, that is, materials proposal, design proposal and justification of materials and design proposals. The requirements of the FDA that are relate to this first stage of product design are the stipulated as:

FDA Requirements

VII. Device materials and biocompatibility
VIII. Performance testing
- A. Deployment testing
- B. Expansion force testing
- C. Compression force testing
- D. Dimensional Testing
- E. Corrosion testing
- F. Tensile strength tests

These requirements represent the essential attribute of the product, the materials of what they will be made, the function ability and the usage, that in this case, is the deployment procedure, if the product can accomplish this three statements, can pass to the next stage, that is the performance test in vitro/in vivo, talk about this last in the final chapter 6 Conclusions and future work.

The direct translation of these FDA requirements to the process that we are going to take in this project are, (1) the selection of the materials by their mechanical properties and as was explained in the benchmarking, the degradation rate by the section VII of the FDA requirements, (2) the geometrical design of the product to accomplish the deploy procedure and the compression force needed to be qualified as a functional design, and (3) the FEA simulations of to prove those designs.

By the section VII of the FDA requirement, the selection of the material will be into detail in the chapter 0

Characterizations of materials, where the materials will be analyzed and selected for this usage, mechanical properties, and behavior in physiological environments, as everything that goes with the characterization of degradability of a biomaterial, process of the material, selection of the degradation tests, immersion medium, and protocol design.

In the section of the VIII FDA requirement, the analyze of the benchmarking and physician's points of view and declarations relevant for a new product proposal will be taken care in this part of the project in the chapter 5, a design methodology, a deeper analysis of the benchmarking and geometrical design proposals by 3D modeling.

As its described by the FDA, the sections A and C are part of the chapter VIII, this is because these two statements are very related, for the same reason they will be documented in the same chapter. The FEA simulations will represent the environment where the product will be placed, to test its function ability and the manipulation to be placed into the patient, statements, assumptions and analysis need to develop this part of the chapter were based on the literature and software tools, SolidWorks™ were used to the modeling and the simulations.

The image Figure 3.1 its graphically explained how the FDA requirements were translated into the methodology of the project.

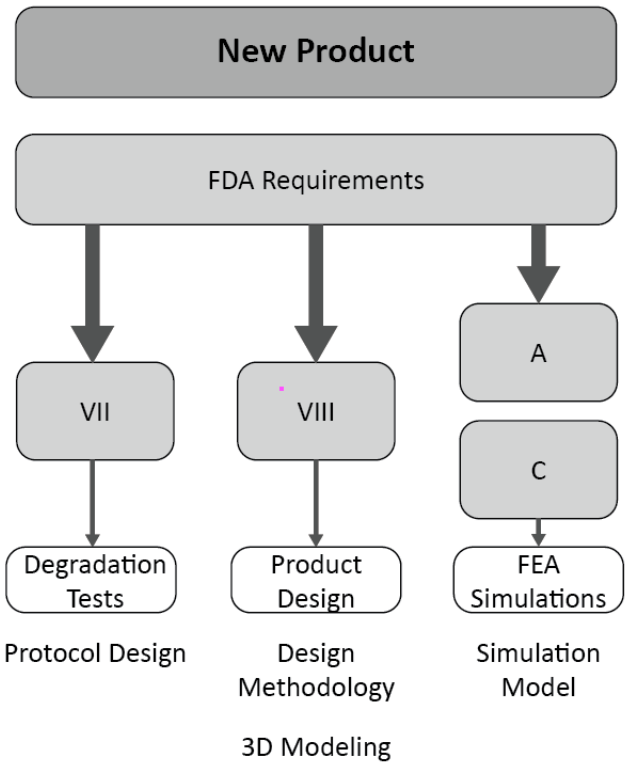


Figure 3.1Translation of FDA requirements into the Methodology of the project
The FDA requirement VII is now turn into a Degradation test, the FDA requirement VIII is the product design and all that involve in a proposal of a new product, the sections A and C are the ones that the product will be tested on with a FEA simulations.

By first stage of a product design three concepts need to be taken care of, selection of materials, the design and the performance of the product. The main properties of the materials are the degradation rate and their mechanical properties. The mechanical properties and the degradation rate have a direct impact to the performance and the function ability of the product. The performance of the product is driven by the geometrical design and the materials selected. And the function ability of the product is driven by the properties of the material and the performance of the design with those materials. This correlation of properties of the product is represented by the Figure 3.2.

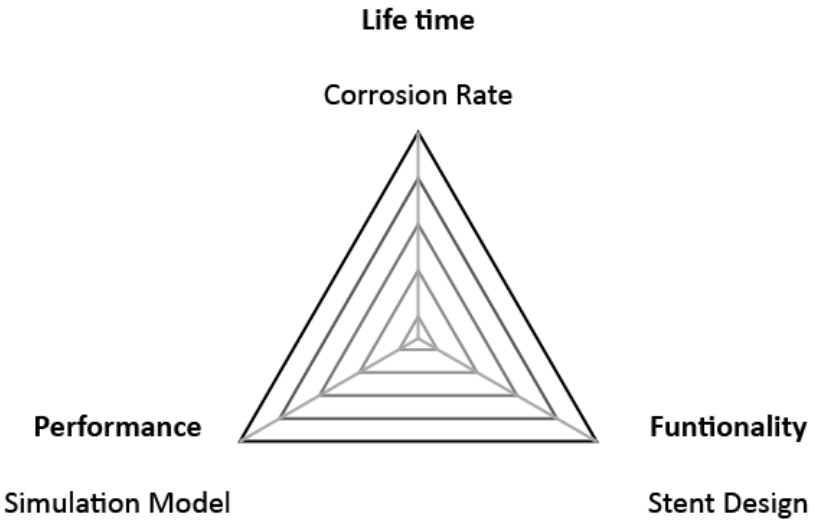


Figure 3.2 Correlation of attributes of the Design

In the project, these three topics will be discussed, the life time of the materials to select the suitable for each stent design proposed and how this proposal design behave in the FEA simulation to be taken as an alternative for prothesis design. The corrosion rate will affect to the function ability and the performance of the product, the stent design, will change the performance and the life time of the stent and finally the performance is driven by the functionality and the life time of the material, and will be tested by FEA simulations.

4. Characterizations of materials

To provide alternatives of design of product, its needed to select the materials that these products will be made of. These materials need to accomplish some requirements. Following the requirements of the FDA as product design approval, in the topic of materials, they must be, biocompatible with the human physiological environment, non-toxic, cytocompatibility and even more, following the medical case studies of the section 2.2.3 Areas of opportunity and 2.4 Benchmarking, research has made of materials that have the attribute of been biodegradables. For the functional performance needed for this specific task that is, prevent foregut leaks, stent migration, and been easy to place, literature of bio materials has been review in the section 2.5 Bio-materials to select the materials more suitable to perform this task in the product design.

4.1. Selection of materials

Even of all the available and well documented of biopolymers, PLA and PCL are more popular on the research groups because of their acceptance by the Food and Drug Administration (FDA) for biomaterials applications [28].

The metal that is more alike to the mechanical properties of the bone that is also biodegradable is the Mg, and most of all the Mg alloys, for this reason is why this material is a popular research topic for the materials for biomedical prosthesis and implants [38].

Both materials have their pros and cons, they are not the perfect material to substitute the conventional materials for biomedical devices, but also, these materials, stainless steel, titanium and cobalt, are either the perfect materials for these tasks. The main goal of the private sector and the research institutes is the development of materials non-toxic, resistant, biodegradable and even to be able to improve the healing process, by realizing antibiotics, vitamins, or whatever substance that can improve the cell regeneration trough the degradation process.

The PLA and the Mg alloys are the most close and promising materials for the biomedical devices for their bio compatibility, easy absorption by the physiological environment, manufacturability and mechanical properties. Further info and characteristics about these materials can be found in the chapter 2.5 Bio-materials.

The specific material to be used are PLA form Nature Works Ingeo^{TM} Biopolymer 3251D, designed for injection molding. Even though, Nature Works don't recommend this polymer for been in contact whit human body fluids or been used for any medical device, this was the product affordable by the research institute, and the similarity with the medical grade polymer is very close.

For the Mg alloy, AZ31 where the material selected for its industrial propose and availability, the mechanical properties and its low level of Al compound.

4.2. Selection of immersion solutions

In vivo corrosion/degradation is drive by the corresponding flow present at the placement of the device, as well as the composition of the body fluids to which the devices is exposed. In vitro tests environmental conditions are defined by the solutions selected, and factors like temperature and surrounding ions and others factors, alter the degradations ratio [39].

Before start mention desirable solutions to make the degradation tests, it's important to know how is the environment in vivo, some of the ions in the body fluids are Na, K, Ca, Mg, HCO_3, Cl, HPO_4 and SO_4, and the concentrations may vary of each part of the body.

The PLA is a more neutral material, that experiment degradation to almost any saline solution. The degradation process of the PLA its dived by temperature and exposure to humidity. And is also proved that when the polymer its exposed to constant flux of water or any saline solution, the degradation rate increase [29]. For this reason, we will focus on determinate the accurate medium to a in vivo environment.

To the date, in vivo and in vitro rates have and existence of lack of correlation of the Mg and Mg alloys corrosion rates, even more to correlate also these rates with other materials like bio polymers. The main propose to this test is to propose a new simulated body fluid (SBF) as similar possible to in vivo physiological environment to tests both materials, polymer and metals, further research its needed to standardize this proposal.

Is well known that some parameters will change the degradation rate of the materials, for example different kind of solutions will impact different to different materials, this is for the chemical compositions in one of each of those materials, and, for the ions present in those solutions. For example, the addition of Al to the Mg alloy increase the corrosion resistance but also, when the alloy its exposed to SBF (simulated body fluid) the corrosion resistance decrease to high levels of Al [38].

Is well know that in some Mg alloys the inorganic ions like HCO_3 and HPO_4, in some alloys can increase the corrosion rate and in some others may retard this ratio [38], for this reason, the solution selected is Hank´s Solution, for having a presence of this ions but not at high levels. The in vivo environment may have this high presence of these ions, but the place of the body where the prosthesis will be placed its considered as a factor for the degradation tests, a more neutral in vitro environment looks more attractive, and a continuous new batch to replace the consume medium and to simulate the production of new ions, just like the organism works.

In the Figure 4.1 Hank´s Solution by CTR Scientific shows the product used, and Table 4.1, its shown the compositions of each inorganic ions the solution. As the table shows, the levels of HCO_3 and HPO_4, are 4.2 and 0.8 mmol $^{L-1}$ respectively, when other solutions have values of 27 and 0.3 for SBF and 26 and 0.4 for MEM.

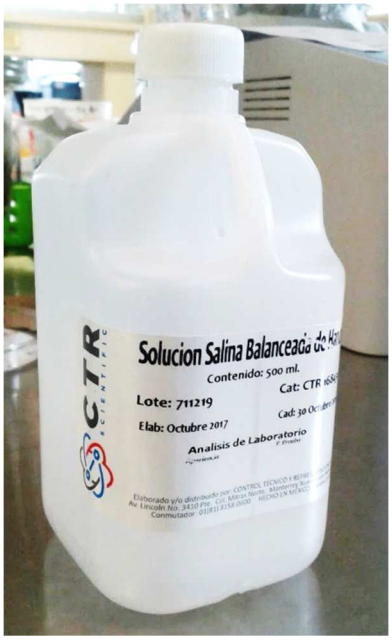


Figure 4.1 Hank´s Solution by CTR Scientific

Table 4.1 Ion concentration in Hank´s Solution

Ion concentration in Hank´s Solution	
Na^+	142 mmol L^{-1}
K^+	5.9 mmol L^{-1}
Ca^{2+}	1.3 mmol L^{-1}
Mg^{2+}	0.8 mmol L^{-1}
HCO_3^{2-}	4.2 mmol L^{-1}
Cl^-	145 mmol L^{-1}
HPO_4^{2-}	0.8 mmol L^{-1}
SO_4^{2-}	0.8 mmol L^{-1}
Glucose	1 mmol L^{-1}

We propose a constant change of medium to renew the active ions in the corrosion process. As the addition of proteins, fetal bovine serum (FBS), to simulate regeneration process with the presence of proteins, and regeneration cells. The addition of this serum will impact in the degradation rate, it's been proven that this addition will decrease the corrosion rate [39]. The protein used for our degradation test is fetal bovine serum by ATCC shown below in Figure 4.2.

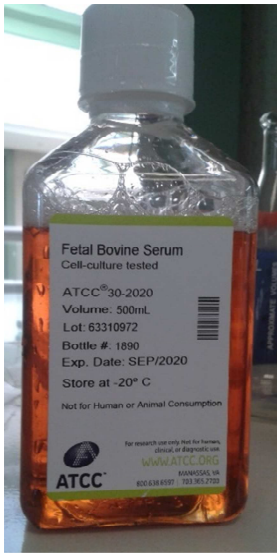


Figure 4.2 Fetal bovine serum form 30-2020 by ATCC

Some other parameters have influence in the process of the degradation rate like, the relation between superficial area exposed and volume of the medium (cm^2:ml). in the nest section 4.3 Degradation test, will be describe the process of the sample fabrication, the selection of the parameters and the procedures required to make our degradation tests of PLA as bio polymer and AZ31 as bio metal.

4.3. Degradation test of PLA and AZ31

In this section of the Chapter 4, all the procedures to fabricate the sample will be explained and why these procedures were selected. All the summary of the research of materials and immersion solutions will collide at this point to the proposal of a standard protocol of degradation test for metals and polymers for biomedical usages. The brands, models and pictures of the equipment used for the degradation test and for the sample fabrication are at Appendix A Instruments.

4.3.1. Samples fabrication

The material to be used are PLA form Nature Works Ingeo™ Biopolymer 3251D, designed for injection molding purchased in pellets. The Mg alloy purchased were an AZ31 in cylindrical bar of 3/4" inch (19.05 mm) of diameter and 2 meters long.

The material used was an Mg alloy, AZ31, it's an alloy in in the Mg-Al-Zn family. The raw material it was a solid bar of 19.05mm (0.75 in.) x 2 meters long (78.74 in). We needed at least 15 discs of 19.0mm of diameter x 2mm thick. To get this samples we used a robust tool to control the surface quality of the samples and its dimensions. The machine used was a conventional Lathe machine

EMCO, Maximat Super 11. With a section tool of 0.187in to cut the samples. Then se samples were polished with 800 to 1600 grind to obtain smooth surface on the apparatus STRUERS LaboPol-21.

For the polymer process, the pellets were dried at 100 °C on a Thermo Scientific Heratherm Oven, for 3 hours to remove the humidity off the pellets. The pellets were put on a cavity plates to produce a sheet of 18 cm (7.08 in) x 18 cm (7.08 in) x 2 mm thick (0.078 in). This cavity plates were put on a hot press at 25 tons at 200°C for 2 minutes. The Hot press were a Craver Model 4128 heated press, and another same model of press for a cooling process. The cooling process were carried put on this another press at 25 tons with the press at 25°C for 7 minutes until the cavity plates cool down. As were explained in the chapter 2 Literature review, PLA experience changes in its properties when its processed by heat as laser cut CNC machines. To cut samples of 19.05mm (0.75 in.), a waterjet cutting machine were used. The Flow Waterjet Mach2 1313b were used to cut 15 samples of PLA of a sheet of 18 cm (7.08 in) x 18 cm (7.08 in) x 2 mm thick (0.078 in). More info about the polymer process can be found in the Appendix A Instruments.

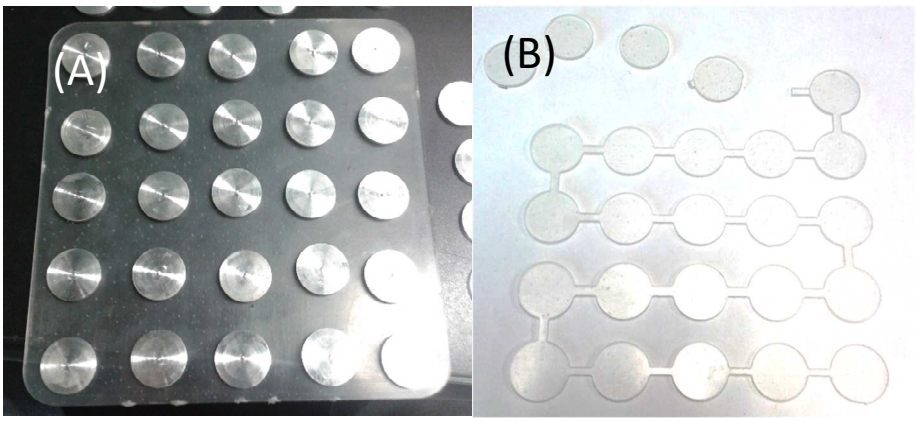


Figure 4.3 Samples for the Degradation Test.

(A) Samples of AZ31 after being machined at the Lathe machine, (B) Samples of PLA after being cut with the Waterjet CNC machine.

In the Figure 4.3 Samples for the Degradation Test, are shown the samples used for the degradation test, that will be explain below.

4.3.2. Protocol of degradation tests

In this section it will be described all the procedures, usages of instrumental and apparatus, the propose of this apparatus and all the requirements of the protocol designed for this tests as a proposal of a standard protocol for degradation test for polymers and metals bio degradable.

The Protocol this divided on six sections, apparatus, test specimen, test conditions, cleaning specimens after immersion test, measurements, and a detail description of the whole procedure.

- 1.- Apparatus

To perform the test, containers meeting the following characteristics are required:

- The recipient must have a capacity of at least 100 ml, the flasks used were of 125 ml.
- The recipient must fit in the machine/apparatus where the temperature and atmosphere will be controlled. The apparatus used was Shaker incubator Figure A.11 Shaker MaxQ 400 by Thermo Scientific.

All the manipulations of the samples and the medium were carried on a safety cabin BIOBASE Biological Safety Cabinet, with each flask, instrument, recipient, etc., cleaned with alcohol before putting them into the cabinet. Each new flask was previously exposed at UV light before been used. (Flask with FBS cannot be exposed at UV light, either the samples).

- 2.- Test Specimen

Three specimens were exposed at each period. All the specimens were a disc with 19.05mm (3/4 in.) of diameter and 2mm of thickness (.787 in.) All specimens were with the same dimensions with a tolerance of +/- 0.1mm

The surface treatment of the samples was by a mechanical polish (600-2000 grit) for the metallic samples and cleaned ultrasonically apparatus, Branson 2510 Ultrasonic Cleaner by Marshall Scientific in 20 ml of acetone for 10 min before the test with, then washed in distillated water and dry at room temperature or warm air before putting them on the flasks with the medium [35], [42].

The samples of polymer were washed with distilled water and dry with a clean cloth, before to be placed into the flasks with the medium for the immersion test [31]. All the samples must be handled with gloves.

- 3.- Test conditions

Three specimens were exposed for each period of time: 1, 3, 7, 14, 28 d.

Each sample was immersed in Hank's Solution with a surface area to volume ratio of 1:15 cm2/ml, with a protein concentration of 8% of fetal bovine serum (FBS). The medium must be maintained at a pH of 7.2 - 7.4 during the test and each 48 hrs. the medium were replaced with a new batch[35], [38], [39].

All the samples were placed in a Shaker incubator at 37°C and 120 rpm during all the test[35], [38], [39].

- 4.- Cleaning samples after test

The samples were washed with distillated water to remove impurities from the immersion test. All the samples were placed on vacuum capsules for 4 to 6 days to remove humidity at room temperature, before the final measurements[29].

- 5.- Measurements

The weight loss measurements were taken using an AL204 Analytical Balance by Mettler Toledo to get the mass loss. The corrosion rate will be described with the equation of corrosion rate CR shown below (1), where CR= corrosion rate, 8.76 is the constant of years by hours, ΔW is the mass loss (initial weight subtracts final weight), α is the surface area of the sample, d is the density of the material and t is the period at what the sample was exposed by hours [37]–[39].

$$CR = \frac{8.76x10^4 * \Delta W}{\alpha * d * t} \quad (1)$$

- 6.- Procedure

A. Pre-immersion phase

1. To test each material (Magnesium alloy AZ31 and PLA), a batch of 15 specimen is required. Each batch is divided in 5 groups (1,3,7,14,28 d); each having 3 specimens. The 3 specimens corresponding to a specific group of a batch are labeled as A, B, and C.
2. The magnesium batch is ultrasonically cleaned with acetone for 10 min at 40 kHz, whereas the PLA batches are cleaned with distillated water and a dry cloth. From this point, specimens should be handled with gloves.
3. Each specimen is labeled, weighed and documented on the Table 4.2 Binnacle of weight measurements shown below. Each sample is placed on a 125ml container/flask with lid, properly labeled.

Table 4.2 Binnacle of weight measurements

			Monitoring periods													
			1d			3d			7d			14d			28d		
Magnesium	Specimen ID		A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
	Mass Weighting	Initial															
		Final															
			Monitoring periods													
			1d			3d			7d			14d			28d		
PLA	Specimen ID		A	B	C	A	B	C	A	B	C	A	B	C	A	B	C
	Mass Weighting	Initial															
		Final															

4. Each flask is places at the safety cabin exposed with UV light for 10 minutes to keep the environment sterile.
5. The FBS (Fetal bovine serum) require to be storage at -20°C. Before starting the preparation of the SBF, its required to defrost the FBS at controlled temperature, a water bath heated can be used if it's possible. In case of having the apparatus, it need to set the temperature at 37°C for 2-2:30 hours to unfreeze the serum.

B. Immersion test

1. Preparation of immersion solution
   The Simulated Body Fluid (SBF) to be used as immersion solution is prepared according to the set parameters and conditions. The SBF is composed by 92% Hank's solution and 8% Fetal Bovine Serum (FBS).

   As shown in the Table 4.3, 100 ml of SBF are required per specimen. The preparation of this amount of SBF solution consist in the mechanical mixture of 92 ml of Hank's solution and 8 ml of FBS.

Table 4.3 Relation of exposed surface and volume of medium with concentrations of Hank´s solution and FBS

Sample features				**Immersion medium**			
Disc diameter (cm)	Disc thickness (cm)	Surface area (cm^2)	Volume of disc (0.57 cm^3)	Surface area to medium volume (cm^2:ml)	Total medium per specimen (ml)	Composition of SBF per sample	
						Hank´s Solution volume 92% (ml)	FBS volume 8% (ml)
1.905	0.20	6.897	0.57	1:15	100	92	8

Once the SBF is prepared, before its addition to the containers storing the specimens, a reading of pH level is done. The range of acceptable pH level is 7.2-7.4 (physiological level). If the solution is out of this range, a buffer solution must be added to fit it.

2. The corresponding amount of SBF solution (100 ml) is added to each container storing the specimen, and the pH level is measured again. If the solution within the specimen is out of the physiological range, a buffer solution must be added to fit it. From this moment, the pH is monitored each 24 hrs. to ensure a physiological level. If the solution within the specimen is out of this range, a buffer solution must be added to fit the acceptable range.
3. The specimens are placed in a shaker incubator, which is set at 37 ºC and 120 rpm
4. The SBF solution is replaced each 48 h.
5. When a group in a batch completes its study period, either 1, 3, 7, 14, 28 d; the specimens are taken from their containers to be washed with distilled water and sterilize.

C. Post immersion phase

1. When the specimen is taken out of the container, must be carefully treated. The PLA samples must be washed with distillated water and the Mg samples must be cleaned with acetone for 5 minutes. Then both materials are placed on an open recipient, previously labeled, this recipient its put into a vacuum capsule at room temperature for 4 or 6 days to ensure drying.
2. Once dried, specimens are weighed and the measurements documented in the control chart.
3. The collected data is processed by the equation 1 to give a degradation ratio for each material.

4.4. Results of degradation tests

In this section will be shown and discussed the results from the degradation tests. The selection of the materials more promising for the usage for biomedical devices were analyzed and selected. A selection of an optimal production process where selected to produce the samples of these materials. The immersion medium to put on test these materials were studied to select the suitable solution with more similarity to the in vivo environment. A degradation test protocol was developing to standardize the processes and procedures to carry out the test and the result were the following.

The physical appearances after each immersion period are shown in the Figure 4.4.

Figure 4.4 Samples of PLA and AZ31 after each immersion period of thedegradation test
The images are shown by cronological period, first the samples after 1 day of immersion, the second one,after 3 days of immersion, the third one of 7 days after immersino, the 4th one after 14 days and the 5th one after 28 days of immersion. In the samples of AZ31 in the first period, the samples presented a change of color similar of any steel alloy corrosion and opaque apparence at the adges, the second and third ones presented a total covered of this oppace apparance and rough surface.
The PLA samples turn opaque after each period with the apparance of grains in the structure getting fuzzy and blurry more each time.

The corrosion in the AZ31 samples is very notorious by the pass of time of exposure, the surface and edges changed, became porous and irregular, until the samples start to lose parts stating by the edges. The PLA samples, on the other hand, start to change color and to exposed contrast between transparency and opaque areas, until the piece turn almost white, but never lose part of its own, always remain as a disc through all the test.

In the Table 4.4 Weight of PLA AZ31 form the degradation test Table 4.4 is shown the data collected from the weighing of each period, identifying each sample with a unique label. The values were collected with a balance describe in the appendix A.10 Balance of precision.

Table 4.4 Weight of PLA AZ31 form the degradation test

AZ31		Periods														
		24			72			178			336			672		
	Sample ID	AZ-A1	AZ-B1	AZ-A3	AZ-A3	AZ-B3	AZ-C3	AZ-A7	AZ-B7	AZ-C7	AZ-A14	AZ-B14	AZ-C14	AZ-A28	AZ-B28	AZ-C28
	Initial	1.108	0.958	0.991	0.947	0.974	0.943	1.088	0.981	0.897	1.079	0.927	0.953	0.978	0.961	0.927
	Final	1.108	0.958	0.991	0.940	0.972	0.938	1.078	0.971	0.889	1.056	0.907	0.927	0.913	0.897	0.872

PLA		Periods														
		24			72			178			336			672		
	Sample ID	PL-A1	PL-B1	PL-C1	PL-A3	PL-B3	PL-C3	PL-A7	PL-B7	PL-C7	PL-A14	PL-B14	PL-C14	PL-A28	PL-B28	PL-C28
	Initial	0.637	0.653	0.649	0.679	0.677	0.640	0.685	0.702	0.640	0.683	0.649	0.656	0.667	0.645	0.643
	Final	0.636	0.652	0.648	0.678	0.677	0.640	0.684	0.701	0.639	0.683	0.648	0.655	0.666	0.644	0.642

After collect the data from all the samples, the mass loss of each sample is shown in the chart below in the Figure 4.5, were the differences of weight versus the immersed time show a possible tendency. The variability of the values its supposed the its caused by the differences in the dimensions of the samples, the change of surface exposed its well known in the literature that affects the degradation of a sample, and for this statement, it cannot just take the values of mass loss to design products of biomaterials.

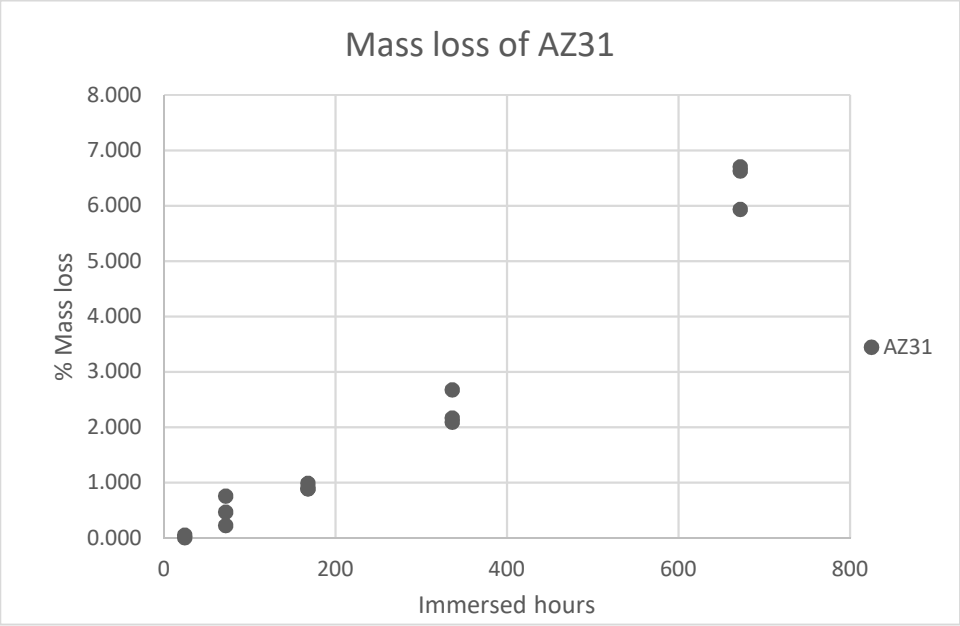


Figure 4.5 Mass loss of the AZ31 samples after degradation test

These values cannot be taken as degradation rate because other parameters must be taken for assure it degradation. The equation of Corrosion rate (1) used the time immersed and the density of the material and the area exposed to normalize the values. The values of the corrosion rate of each sample at the different exposure times in the medium its shown in the Figure 4.6.

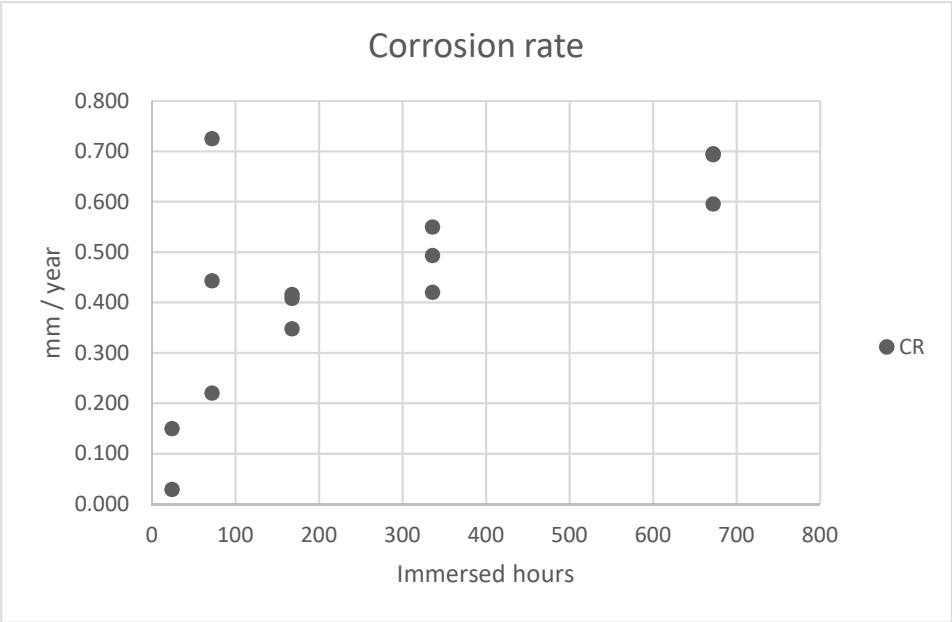


Figure 4.6 Corrosion rate of AZ31 samples

The corrosion rate of the samples trend to increase through the time and each sample has variability of its rate, but the assumption of that this variability is caused by the differences of the surface exposed its eliminated, by taken the surface area exposed, density in the equation. The values studied in the literature in compassion with these ones collected form our tests, show lower rates, this was expected by the usage of a lower ion concentration medium and the FBS as a protein.

The Figure 4.7 shows the behavior of the weight loss of the PLA during the degradation test.

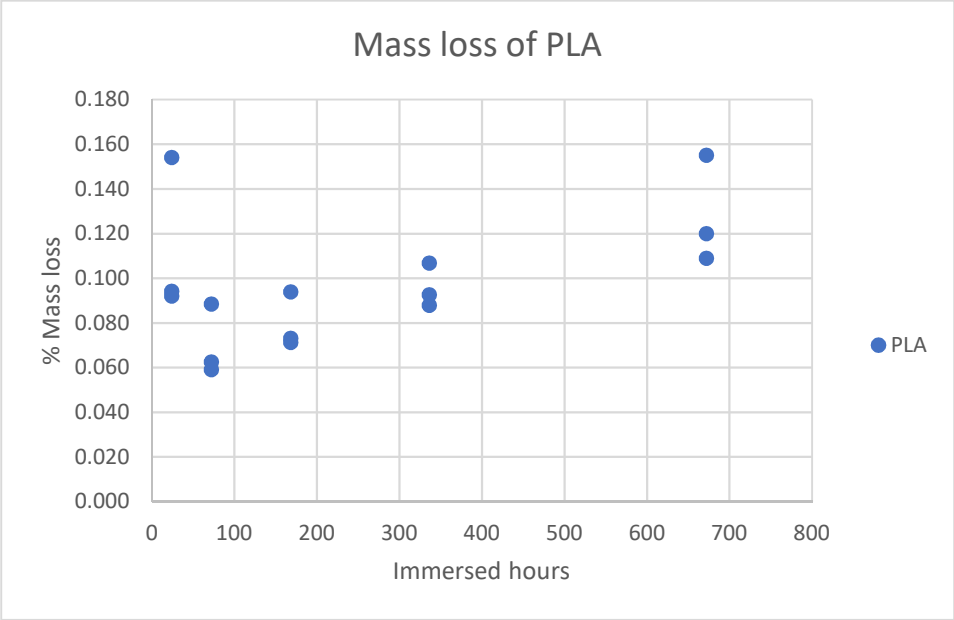


Figure 4.7 Mass loss of PLA samples after degradation test

The differences of the mass of the PLA are lower that the AZ31, just like is documented in the literature, but the values collected from our test show an even lower values in comparison with PLA in contact with other mediums, like Kirkland`s bio-corrosion media (KBM) [31]. This behavior requires a deeper research to prove if the FBS also decrease the degradation rate of PLA as it does to AZ31.

The corrosion rate of each sample of PLA is shown in the Figure 4.8. Its shown an expected behavior of a decreasing tendency, because of it low mass loss and the hours exposed to the medium, the equation decreases the CR value, making the chart show a decreasing tendency, even when the mass loss is increasing in each period, but at low amounts.

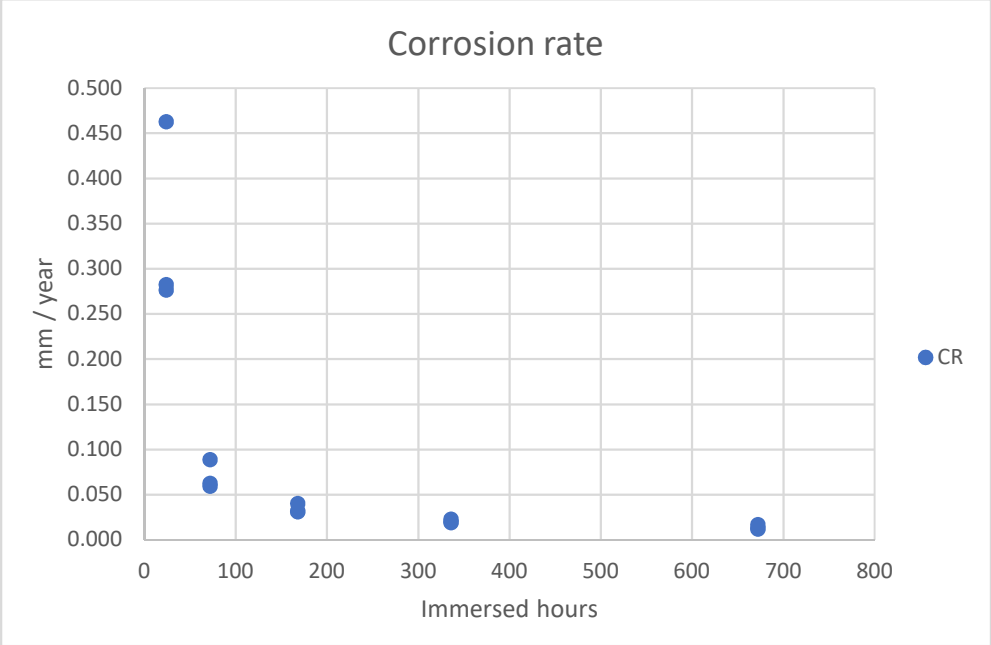


Figure 4.8 Corrosion rate of PLA samples

To have a value of CR of each material, an average of weight of samples, and average of final weight of each sample were made, the differences of these two values were obtain and put in the Eq. of corrosion rate (1), and average of time exposure was also made to calculate these values. The CR resultant is 1.249 and 0.043 for AZ31 and PLA respectively shown in the Figure 4.9.

Corrosion rate values are lower that the documented in the literature for AZ31 and PLA. In the case of AZ31b this tendency was expected by the usage of a non-aggressive medium like Hank`s solution, by been a solution of neutral concentration of ions like other medium used in the literature. Also, the usage of FBS decrease the CR value of AZ31, another expectation proved in this test that were documented in the literature. It's well known that the PLA has a lower CR value, but it's not well establish that how much in comparison with AZ31 by using the same sample dimensions, same conditions of the test and same parameters in a well design protocol, to homogenizes the test and produce a comparable data between PLA and Mg alloys, in this case, AZ31. In case of PLA the degradation rates were expected also to be lower that the documented in the literature but without knowing the level of impact of the usage of this medium. A deeper research in this topic must be done, also more runs of this protocol designed to prove reliability of the procedures.

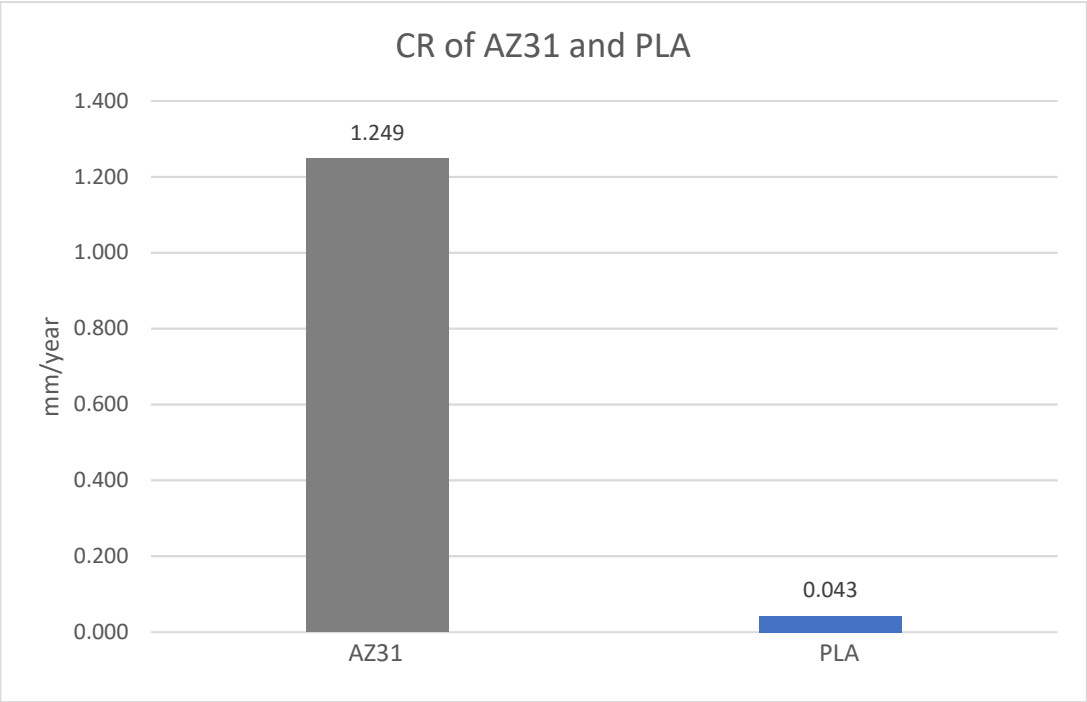


Figure 4.9 Corrosion Rate of AZ31 and PLA

5. Product Design

In the process to develop a new product, we must know the characteristics of this new design. The recommendations and the data collected form the benchmarking and the guidance for industry for esophageal and tracheal prosthesis as start point to our stent design. We will follow design methodologies and inventive methodologies to propose the new stent.

5.1. Design Methodology “QFD” and “TRIZ”

A design methodology that can represent a wide point of views from different people involve in the interaction of a medical device, from patients, physicians, engineers, biologists, chemistry and designers, the Quality function deployment (QFD) as a tool, can integrate, advices, suggestions, requirements, similar products, goals, inventive contradictions to process all this info to create relevant data to make a design proposal. Also, the Theory of inventive problem solving (TRIZ), as a tool for stimulate the creative problem solving with inventive, based on 1.5 million patents analyzed, will help us to make that design proposal an innovative proposal.

The QFD were deploy in Japan in the 1960´s as a systematic process that help in the development of new products, using as a main tool, the analyzing and understanding of the necessities and requirements of the customer or situation[46]. The QFD is a graphic tool that summarizes the info on a big matrix of data, each section of this graphic represents a relevant source of the necessities or requirements of the new product or the new version of an existing product. They are QFD templates on open-source to public usage, one of those templates were used to this project.

The sections in the QDF graphic named by appearance order are:

1. Customer Requirements (WHAT´S)

This section is filled with the data collected form the customer or the people involved in the usage of the product, in our case, physicians. All the Requirements listed need to be typed on a basic idea sentence or concept easy to read and understand.

2. Importance Rating

Each requirement will be ranked with an importance level, this level is our priority order to track the main issue or the aspect that we need to focus on. This section is also given bay the field research.

3. Functional Requirements (HOW´S)

In this section is work of the designer to translate the What´s into measurable parameters, in the same order as the list of What´s. This parameter also named HOW´S, need to be controllable by the material selection, function, geometrical design, physical principle or whatever tangible medium quantifiable.

4. Target Values

The parameters listed on the HOW´S section, need to be written down on this section as value to reach, value to not pass or value to overcome. These values need to be congruent to the parameters listed.

5. Relation Matrix of WHAT´S and HOW´S

In this section the What's and How´s collide, each requirement must be analyzed to see if affect or is affected by another parameter listed in the HOW´S section. The relation between each Colum and row can be a strong relation, moderate weak o non-relation.

6. Correlation Matrix

The section of correlation matrix is composed of two stages, is a task for the designer to, first the parameters that has more impact on the requirement section takin care of the importance rating, determine if the parameter of the HOW´S section need to be improve, decrease or keep as it is, to reach the target values at the section 4. After doing this, the parameter that need to move (increase or decrease) must probably will affect another parameter, this impact can be positive or negative, each scenario must be represented with a graphic icon to know which parameter relay on another and how is the behavior of the parameters through each other.

7. Competitor Ratings

The competitor rating helps to evaluate if our problem is being already taken care of by another company or institution, or if a secondary issue has been solved by one of them, also helps to make a study of advantages and disadvantages of the competition and to be more prepared to propose a more viable and attractive product. This analysis is by rank each requirement of the WHAT´S list for each competitor, and our design expected.

In the Figure 5.1 QFD Graphic divided by sections and numbered on order of the methodology its shown how the QFD graphic is filled to fully understand the data collected on the benchmarking and the produced by the project team.

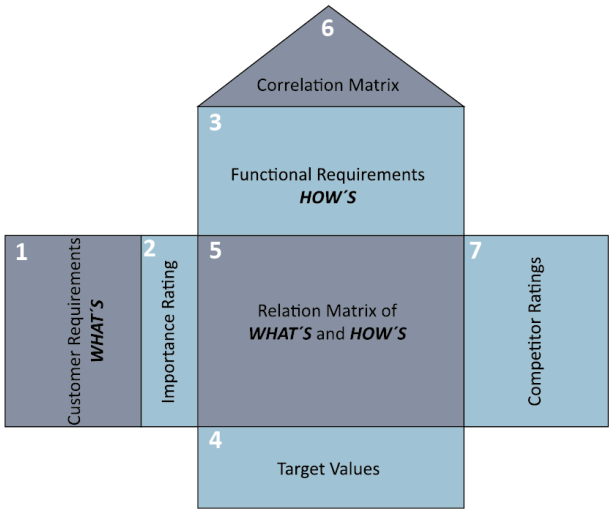


Figure 5.1 QFD Graphic divided by sections and numbered on order of the methodology

After making all this analysis, we already understand better the concepts involved in the project, positive and negative and how these concepts behave one with the other, but more important, how can we manipulate these concepts to create a design of value. This product of value relay on the creative manipulation of the contradictions on section 6, also known as the roof of the QFD. At this point is where the TRIZ methodology comes in.

TRIZ is an algorithm based on a high level of inventive and creativity to solve design problems based on science and technology as a result of analysis of more than 1.5 million patents. When a technical system has reach the optimal performance, and need to be improve, somehow will interfere with another part, this conflict we can see them in the roof of the QFD.

The methodology consists in translate the parameters in the section 6 into one of the 39 parameters of TRIZ, these parameters must be listed into two columns, the parameter that need to be improve and the parameter that decrease. After match the contradictive parameters, we place them into the matrix of TRIZ, , column for parameter to improve and row for parameter that decrease, the matched cell contains inventive principles, these principles must be taken by true and start the design process for all of them to exercise the creativity until reach a viable design[46].

5.2. Design proposal

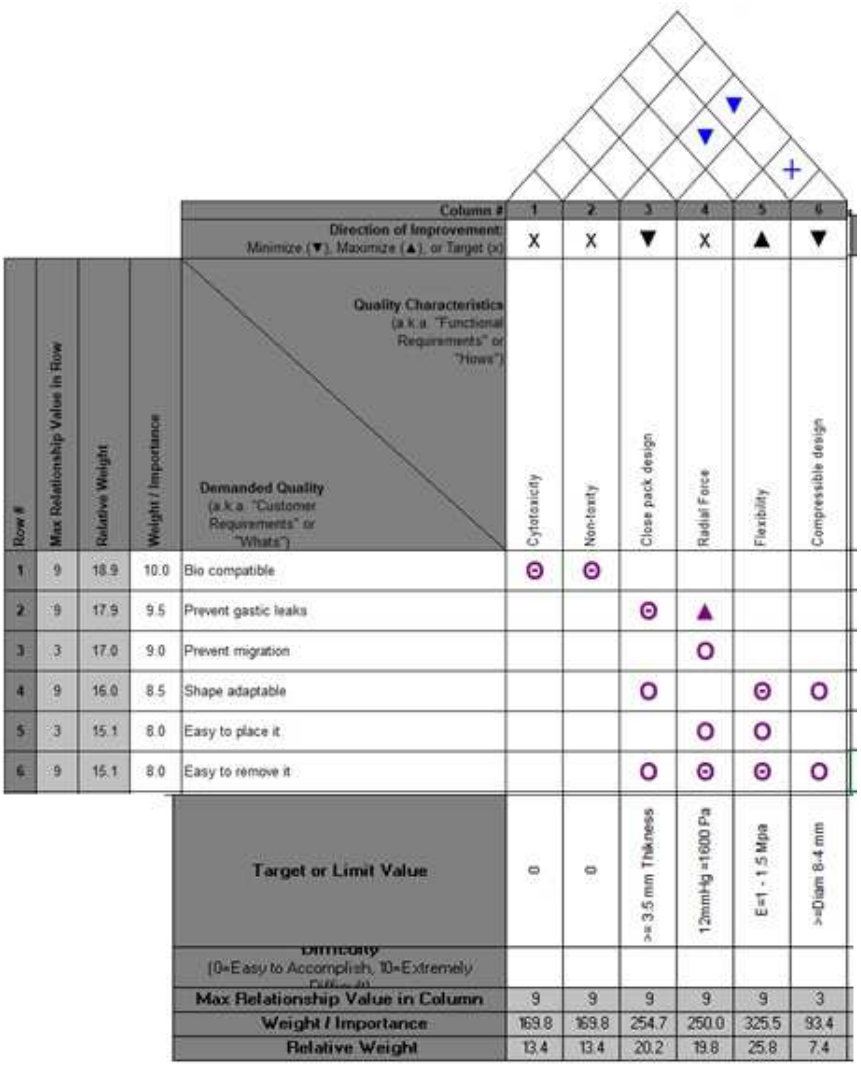
As was explained in the latest section 5.1 Design Methodology “QFD” and “TRIZ”, we started with the methodology of QFD, we translate all the data collected form the Benchmarking form the chapter 2. Following the same steps of each section, the info collected form the benchmarking will be analyzed. The requirements of the FDA are taking form in this section of the project,

1. Customer Requirements (WHAT´S)

Following the recommendation of each case study form the usage of each different commercial stent, the concepts were, that of whatever material that can be used for the stent, this material must be biocompatible with the physiological environment, and cannot be harmful to the new cells production. The product must be functional and indeed, seal the leak when its presented, also must have enough axial force and been easy to fix into the gastric tube to reduce the probability of migration, this geometry must be flexible to adapt into the gastric tube, to prevent discomfort and complications during the healing process. And finally, the product must be friendly to the manipulation, which mean, the product must me simple and easy to use, to reduce the complications during the placement and the removal after the healing process had done.

2. Importance Rating

To rank these statements, we are following the guidance requirements for industry of the FDA [26], as a pass or not pass, form the most essential requirement of the product to be considered as functional, given the rank as its shown in the Figure 5.2, the statements were, Biocompatibility, leak sealing, prevent migration, shape adaptable, easy to place it and easy to remove in that order.



Row #	Max Relationship Value in Row	Relative Weight	Weight / Importance	Demanded Quality (a.k.a. "Customer Requirements" or "Whats")	Cytotoxicity	Non-toxity	Close pack design	Radial Force	Flexibility	Compressible design
				Column #	1	2	3	4	5	6
				Direction of Improvement: Minimize (▼), Maximize (▲), or Target (x)	X	X	▼	X	▲	▼
1	9	18.9	10.0	Bio compatible	⊙	⊙				
2	9	17.9	9.5	Prevent gastic leaks			⊙	▲		
3	3	17.0	9.0	Prevent migration				O		
4	9	16.0	8.5	Shape adaptable			O		⊙	O
5	3	15.1	8.0	Easy to place it				O	O	
6	9	15.1	8.0	Easy to remove it			O	⊙	⊙	O
				Target or Limit Value	0	0	>= 3.5 mm Thikness	12mmHg =1600 Pa	E=1 - 1.5 Mpa	>=Diam 8-4 mm
				Difficulty (0=Easy to Accomplish, 10=Extremely Difficult)						
				Max Relationship Value in Column	9	9	9	9	9	3
				Weight / Importance	169.8	169.8	254.7	250.0	325.5	93.4
				Relative Weight	13.4	13.4	20.2	19.8	25.8	7.4

Figure 5.2 QFD graph with the sections 1, 2, 3, 4, 5 and 6 filled with the data relevant for our project

3. Functional Requirements (HOW´S)

The statements form the section 1 of the QFD were translated in to quantifiable parameters. For a material to be considered for usage of biomedical prosthesis, the biocompatibility can be referred to a non-cytotoxicity, to not interfere with the grow of new cells, and non-toxic for the organism that refer to the biocompatibility. To seal the leaks, the geometric design of the stent must be closed-packed to eliminate the leak when is presented, the shape adaptability, the migration and the placement of the stent, relay on the radial force of the product, as well for the geometric design to make it flexible and a compressible design, so the stent can be placed in the easily and be mechanically functional.

4. Target Values

The target values go respectively to the parameters of the section 3, these parameters must be measurable, and in this section, we need to put on the graphic those values. The cytotoxicity and the non-toxicity are values of pass or not pass on the material, so in these parameters we put 0,

even though we can measure, this parameter relay on the properties of the material. The close pack design is a 3.5 mm of thickness that is the first station of the foregut leak. The radial force and the flexibility relay on the mechanical properties of the material, and this material must have an elastic modulus of at very leas of 1.5 MPa [46], [47].

5. Relation Matrix of WHAT´S and HOW´S

In this section its analyzed all the statements form section 1 and the parameters form section 3 to see how interact all the attributes involved in the product, and we can notice that must of the functional requirements relay on the mechanical properties of the material, and with geometrical design we can modified and try to achieve the optimal design to have the best performance possible, taking in account the requirements of the FDA seen on the Chapter 2.

6. Correlation Matrix

All the sections are very important, but this section it's the culmination of all the data, after we fully understand the product is when we can propose a new design to accomplish all the requirements. This new design must solve or find a balance between the negative correlation between the parameters listed in the section 3. In this section the close pack design interfere whit the flexibility of the design and the compressibility, when the robustness of the design increases those other two attributes decrease, is here where the new design must fix this issues with a creative geometrical solution.

7. Competitor Ratings

In this section, each statement is ranked with values from 5 to 1 to each competitor, and our goal of the new design. Wallflex, Bonastent, EndmoMAXX, Hanarostent and BD Sx-ELLA were the product evaluated in this section for its popularity in the medical field, must of them have an acceptable performance, the results are shown in the Figure 5.3. All the products are bio compatible, the Wallflex is the product with less point on the preventing the gastric leak with 3, according with the Table 2.1, must of the product have presented migration with at least 25% of the time, that's why must of the product were ranked with 2, the design of the stent, just the Endomaxx is the product designed for high flexibility but not to functional, ranked with 3, must of every stent are easy to place it and all the products were ranked with 4 and 5, and all the stent are also easy to remove with exception of Hanarostent because of its longitude. Our product will try to accomplish every statement listed in the QFD with the priority of flexibility and radial force.

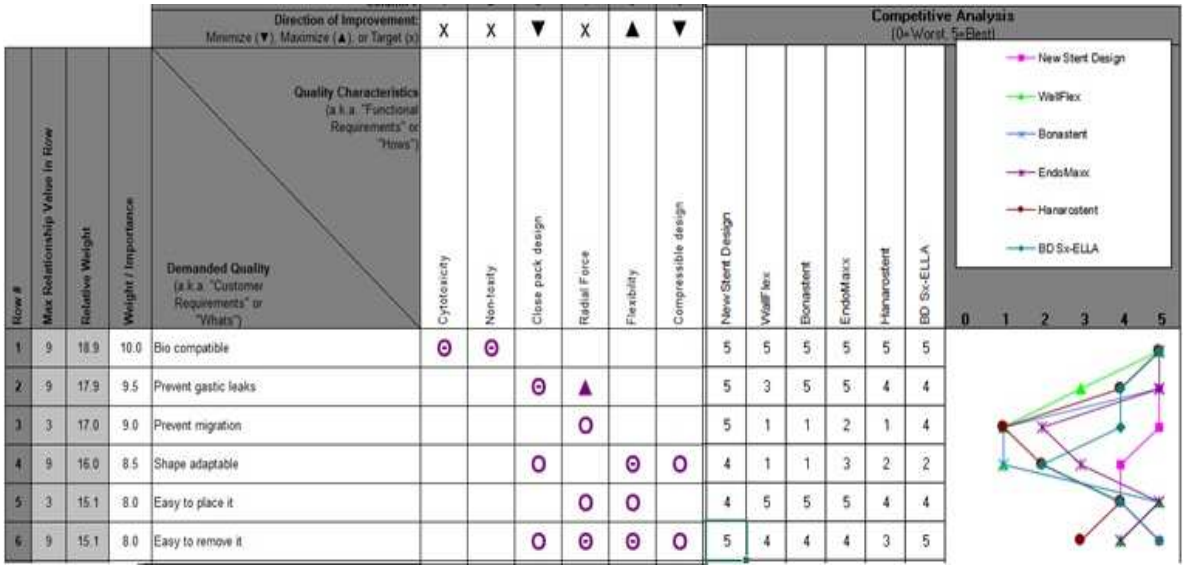


Figure 5.3 QFD Graph of the Section 7 Competitors evaluation

After fulfilling the QFD graph, we can continue with the TRIZ methodology, first we going to list all the parameters from the section 6 that may affect other ones and try to translate them as accurate possible form the list of parameters of the TRIZ list as is shown in the Table 5.1, those parameters are Close packed design, flexibility, and compressible design.

Table 5.1 Translation between the QFD parameters to TRIZ parameters

QFD parameter	TRIZ parameter
Close packed design	8 - Volume of a static object 12 - Shape 36 - Complexity of a mechanism
Radial Force	10 – Force
Flexibility	12 – Shape 35 - Adaptability 36 - Complexity of a mechanism
Compressible design	8 - Volume of a static object 12 – Shape 35 - Adaptability 36 - Complexity of a mechanism

Then we going to make pairs of TRIZ parameters of improve parameter versus decreasing parameter in for of matrix, the resultant matrix is shown in the Table 5.2. Must of the combinations result on a big repeatability of the inventive concepts.

Table 5.2 TRIZ Matrix of the parameters translated form the QFD roof

Inventive Matrix TRIZ	10. Force	12. Shape	36. Complexity of a mechanism
8. Volume of a static object	• Nesting (levels, layers) • Extraction • Thermal expansion	• Extraction • Vibration • Transformation of physical and chemical states	…
35. Adaptability	• Dynamicity • Mobility	• Dynamicity • Thermal expansion • Segmentation • Counterweight	• Dynamicity • Change of mechanism • Thermal expansion

As we can see, the inventive concept “Thermal Expansion” is named a few times, and must of the SEMS are made of nitinol, a material that can expand in the exposure of heat, this is a good sign that our matrix has relevant info for our design stage.

To conclude our section of design methodology, the inventive concepts like, adaptability, extraction, extraction are the concepts that are mentioned more times and dynamicity and mobility are, also heavy weight on our project.

5.2.1. Geometric design

In this section it will be proposed the geometric designs of our stent for RYGBP complications, all the modeling was made in SolidWorks™ by Dassault Systems Corporation.

One of the main issues of the stent design is the manufacturability, but in this project the manufacture process will not be taken in count, to no limit the creative process and innovative proposals of design.

Design Proposal - Stent-01

By taking the concepts of TRIZ, “extraction”, “mobility”, and “segmentation”, this design is separating the patron in steps, linked by a curve diagonal shown in the Figure 5.4, to let the design adapt and rotate when its collapsed. These assumptions are theoretical and will be putted on tests later in this chapter.

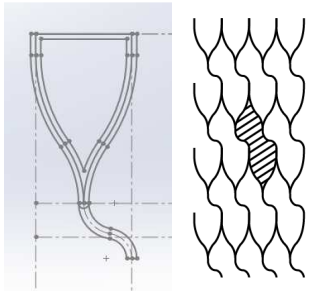


Figure 5.4 Pattern of the Design proposal STENT-01
The inventive concepts of TRIZ used to create this design were segmentation and extraction, giving to the design more adaptability and keeping its compression resistance. The (left) base of the pattern is a shape of a pin, and a connector of a diagonal curve to link to the next module. The pattern (right) marked it’s the open area leaving in the design to ensure its compressibility to the deploy process of the stent.

Design Proposal - Stent-02

By taking the concepts of TRIZ, “counterweight” and “dynamicity”, this design made by a group of a shape of “tweezers”, shown in the Figure 5.5, to let the design adapt and giving a high compression resistance. These assumptions are theoretical and will be putted on tests later in this chapter

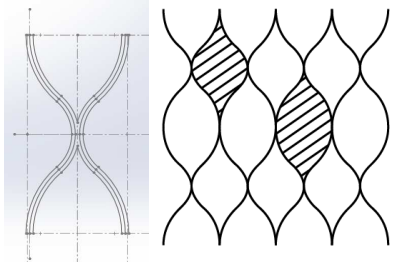


Figure 5.5 Pattern of the Design proposal STENT-02
The inventive concepts of TRIZ used for this design proposal were, “counterweight” and “dynamicity”, the (left) shape of double pin or “scissors” made of this design, a very resistant to compression and has a good adaptability by been made of modulus. The patters marked shows the space available to compression.

Design Proposal - Stent-03

By taking the concepts of TRIZ, “counterweight” and “dynamicity”, “mobility” and “segmentation” this design made by a group of a shape of “mirrored tweezers”, shown in the Figure 5.6, to let the design adapt and giving a high compression resistance. The curve links substituting straight lines and giving more mobility and adaptability to the design. These assumptions are theoretical and will be putted on tests later in this chapter

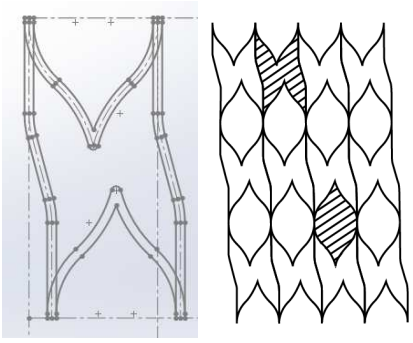


Figure 5.6 Pattern of the Design proposal STENT-03
The inventive concepts of TRIZ for the design of this proposal we, “segmentation”, “counterweight”, “mobility”. (Right) The modulus of this design is a mirrored scissor and a non-linear connector between modulus to improve adaptability. (left) The marked areas give the notion of high compressibility to the deploy proses.

In the Figure 5.7 are shown the 3D models form SolidWorks™.

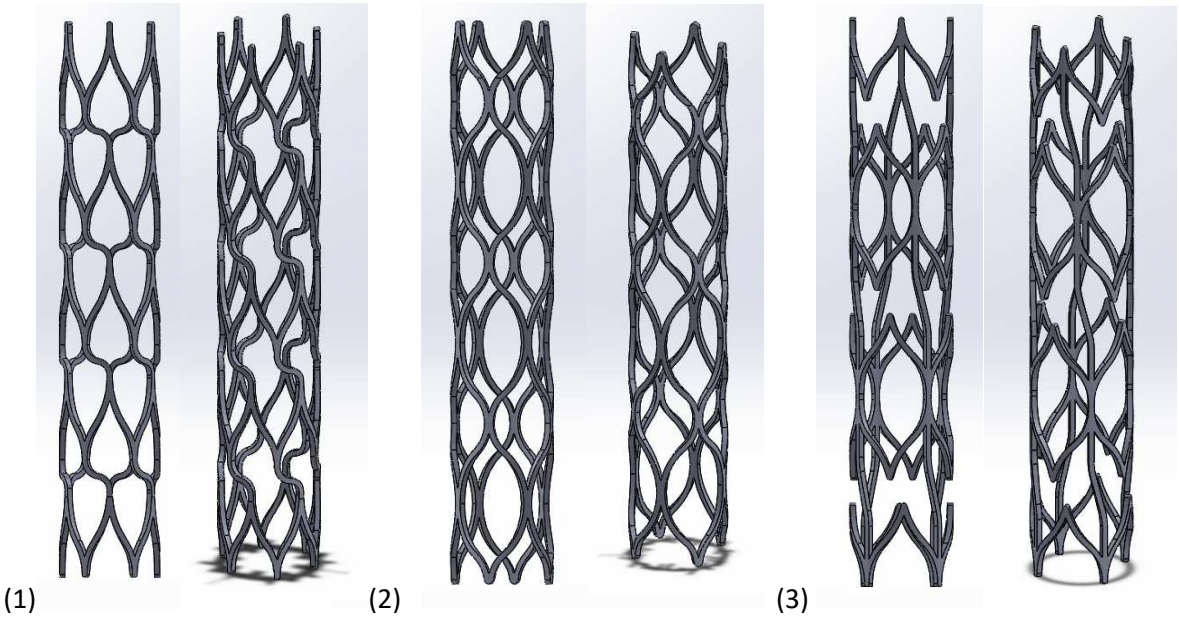


Figure 5.7 3D Models of the Three Design Proposals
(1) The design proposal Stent-01, (2) the design proposal Stent-02, and (3) the design proposal Stent-03. All the proposals are shown with a front view(left) and an isometric view(right). All the stents were modeled by 1 mm thickness square profile wire.

5.3. Environment of the product

As it was shown in the Figure 2.5, the result of the surgery is part esophagus, part stomach and depends of le length of the stent, can be also intestine, for this reason is hard to measure the forces involved in the new directive system, but is well know that the esophagus is the one that apply more force in comparison with the other two parts[46], this is why well will focused on cover the forces in the esophagus with the assumption of, if the stent can support the forces of the esophagus, it will support the forces of the digestive system after the RYGBP.

Some of the relevant data to understand how it's the environment where our product will be placed, is the average diameter of the esophagus, the length and the peristaltic velocity. This info its described in the Table 5.3 [48].

Table 5.3 Parameters of the esophagus before surgery

Parameter	Value
Esophagus inner diameter	15 mm
Esophagus length	30 cm
Peristaltic wave velocity	3 cm/s

In the model made by M. Garbey et al. 2016, was reproduced the peristaltic movement to simulate the contraction of the esophagus on different segments of the tube, to measure the pressures present in the esophagus. This study has no quantitatively validated versus a clinical data, but its assume a high reliability of the model. This study has present an average of 20 mm Hg that are about 133.3 Pa each mm Hg. With this data we can use it to apply some simulations to test the adaptability, radial force resistance, and compressibility to the placement procedure [46]–[49].

Other studies reveal that the contractions of the circumferential stress are about 0.7 MPa, the half form another mathematical models studied, all these studies reveal that the data its need to be confirmed with more research, for practical proposes we going to use the highest value detected from the collected data that it a pressure about 12 mm Hg that represent about 1600 Pascals [46]–[49].

Acids, textures, secretions, soft muscle and another specific parameter Will be discarded for the model to simplify the simulation, with the propose to test the behavior of the stent on pure mechanical forces and to put on test the differences of the geometrical design under those forces and see the differences on the performance of the stent.

5.4. Simulation model

In section it will be documented all the parameters, assumptions and results expected and how to analyze the result form the simulation models. To do this on a structural way, we are going to section this chapter in four, parameters, assumptions, results expected and reading of simulations results.

- Parameters
    - Stent

According with the benchmarking, the commercial stents vary on diameters and length, to cover a group of patients, we will postulate our designs and simulations models to an average of those dimensions, leaving the diameter on 18 mm and the length on 100 mm like its shown in Figure 5.8.

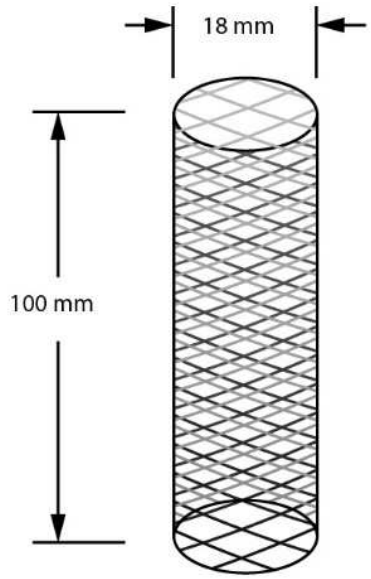


Figure 5.8 General dimensions of Simplified Stent

- Environment

Once the surgery has done, the new digestive tube is part esophagus, a section of stomach and intestine. This new digestive tube will behave differently in its different sections. After the research have been proved that the esophagus is the one that will apply more stress to the stent, and for that reason it will be take the new digestive tube as an esophagus with the assumption of, if resist that pressure, it will resist the behave of the whole new digestive tube. The pressure measured were of 12 mm Hg that is equivalent to around 1600 MPa as a uniform force of compression to the stent. A simplified description of the model its shown in the Figure 5.9.

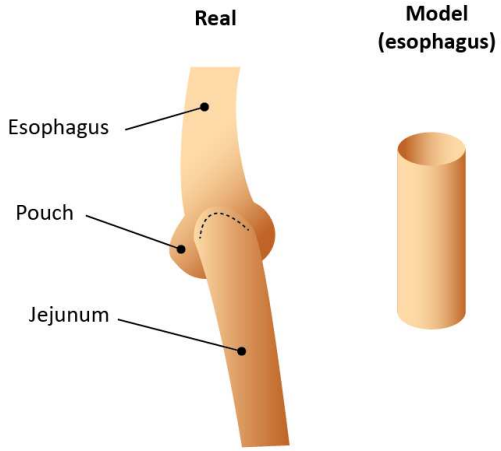


Figure 5.9 Simplified model of the environment for the simulation model.
Real is how the digestive system ends after the surgery, and the model is considered as a simplify shape as a cylinder with a uniform force applied to the stent.

- In the usage of the stent

The stent will be fixed form the upper part to the digestive tube, so we will assume that the stent will not experiment deformations in that area, to put on test the adaptability of a compressive force on the rest of the product. These fixation points will be showed at the simulation images.

The stent will be tested at compression forces to see the behavior of the stent at the forces mentioned in the section above. Also, the stent will be tested at it compress force needed to deform the stent to be able to reduce the diameter of the stent without tear the part apart or present a plastic deformation, those 1600 Pa present in the 100 mm of digestive tube model equal to 9.2 N, 10N will be used for our FEA studies. A graphic description of the performance test its shown in the Figure 5.10 to understand the parameters used and how will interact in the simulation.

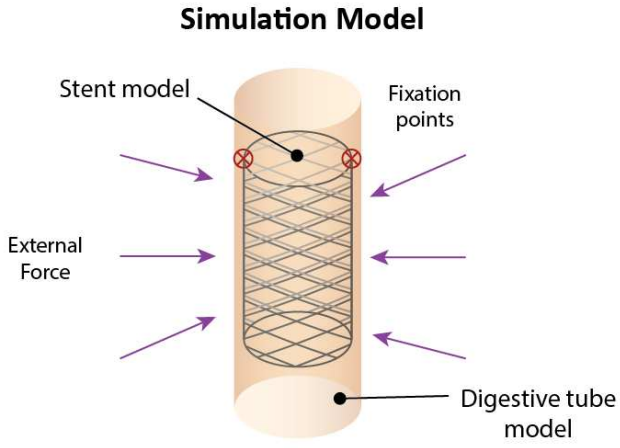


Figure 5.10 Simulation Model to Performance Test
A uniform radial force is applied to the stent to test its compression resistance and adaptability to irregular shapes.

- Assumptions

The force apply is of the esophagus, that represent the biggest will be taken to make the simulation, the force will be uniform to the whole stent except for the fixed part, that is the upper part of the stent to test the adaptability of the product.

Just mechanical properties will be taken for the simulation, the pretense of degradation of the material, the presence of gastric acid that may reduce the mechanical properties will not be taken for the simulation.

- Simulation results

The data that the simulation will give us is a graphic illustration of the deformation of the product, a color scale of the areas that experience more stress that color scale, in each color will represent a value tension of Von Mises, a physical magnitude proportional to the deformations energy, to tests failure theories.

- Results expected

To analyze the results of the simulations, we will focus on three things, the Von Mises values, color patterns and the ability of compression. All the follow data are visually explained in the Figure 5.11.

  - Von Mises. The value of the yield strength of the design must be at least three times higher of Von Mises values resultant to ensure a partially long life-time of the product during the degradation processes.
  - Color patters. The color patterns of the resultant graph must be uniform and repetitive, to show and adaptability of the stent. The force is applied uniformly to the stent, and if the stent does not behave uniformly, the adaptability is not achieved. The Von Mises values must be following with the latest statement.
  - A second simulation will be run to prove the compressibility of the stent, this to test the colocation procedure and be able to be deploy by tracheotomy without reaching the plastic deformation according to the Von Mises values.

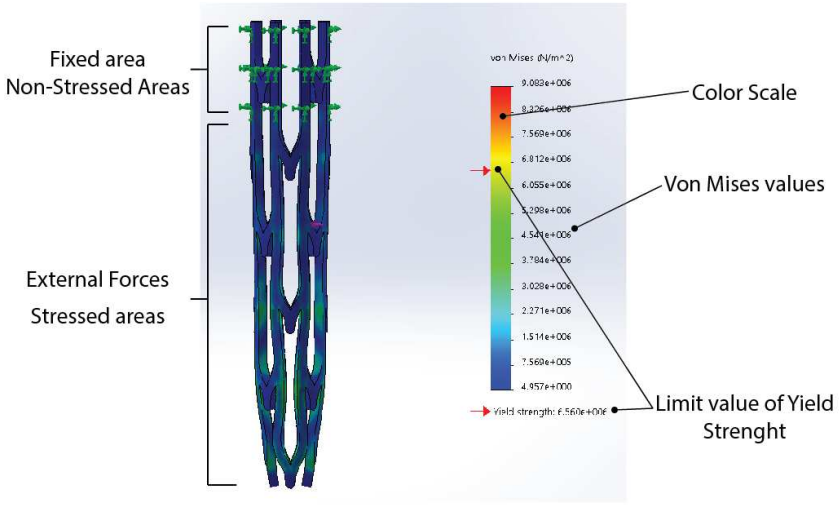


Figure 5.11 Example of the info given by the simulation by SolidWorks™

5.5. Results of FEA Simulation

In this section, the design proposals will be tested by the Simulation feature of SolidWorks™, according with the statements discussed in the sections 5.3 and 5.4 above in this chapter.

The simulations were run of two materials, AZ31 and PLA, with the mechanical properties described in the section 2.5 of this document.

Two simulations per design, per material were run, the first one is testing the compressive resistance which the stents are exposed in the environment named as “scenario 1”. The second one of the maximum force resisted to be compressed for the deployment procedure named as “scenario 2”.

Simulation - Stent-01 (PLA)

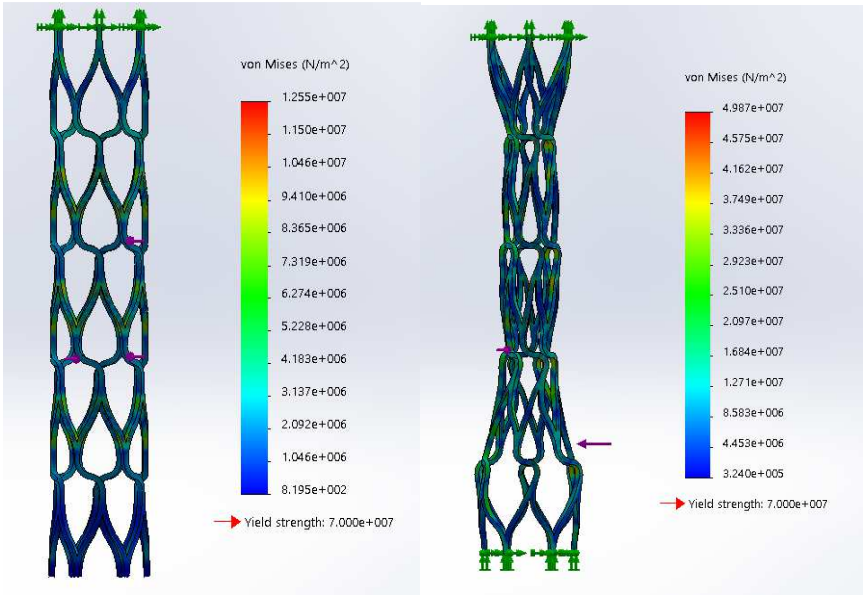


Figure 5.12 Simulation result of Stent-01 of PLA
Scenario 1(Right), shows a high resistance of compression at 10 Newtons (N) which represent at which the stent will be exposed at the physiological environment, the Yield Strength (YS) of the material is about 70 MPa (megapascals) and the limit shown in the von Mises graph is 10 MPa, with imperceptible deformation. Scenario 2 (Left) shows an exaggerated deformation of +8 times at the stent at 75N that the stent will reach a diameter of 10mm for its placement.

In the scenario 2, the bottom part of the stent was fixed too, to obtain a behavior of the stent more alike of the will happen to the stent under high level of compression force, by not doing this, the stent took a cone shape, opening in an exaggerated way the bottom part of the stent and having unreliable data. The natural behave of the stent is to rotate the bottom part and an elongation of the length of the stent and at the same time reducing the diameter. This simulation does not give a very reliable data but also give us a close idea of the limits of the stent to the compact state to the deploy process.

Simulation – Stent-01 (AZ31)

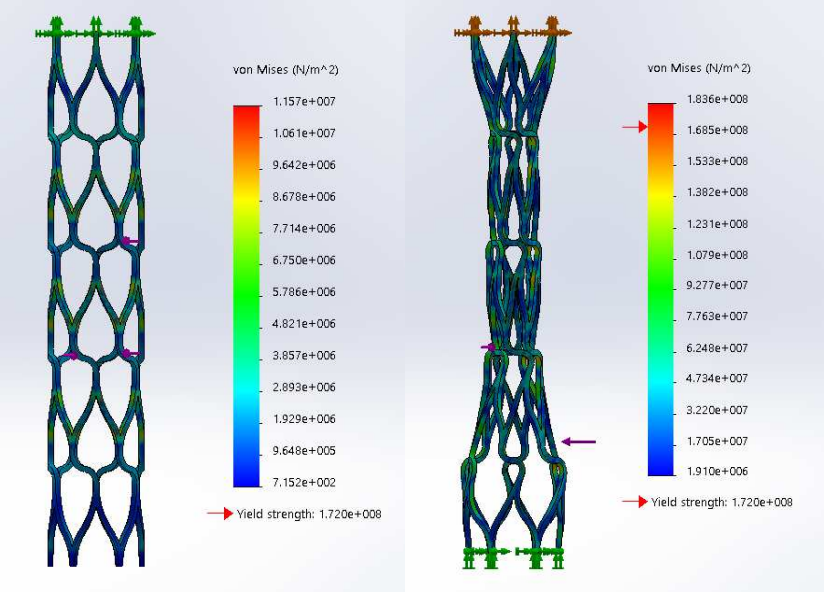


Figure 5.13 Simulation result of Stent-01 of AZ31

Scenario 1 (Right). Shows a high resistance of compression at 10 N that represent the force exerted by the environment, the YS of the material is 172 MPa and the limit value shown in the von Mises graph is about 10 MPa with an imperceptible deformation. Scenario 2 (left) shows an exaggerated deformation of +30 times at 300 N force at will the stent will reduce it diameter to 10 mm and almost reaching it plastically deformation state.

Simulation - Stent-02 (PLA)

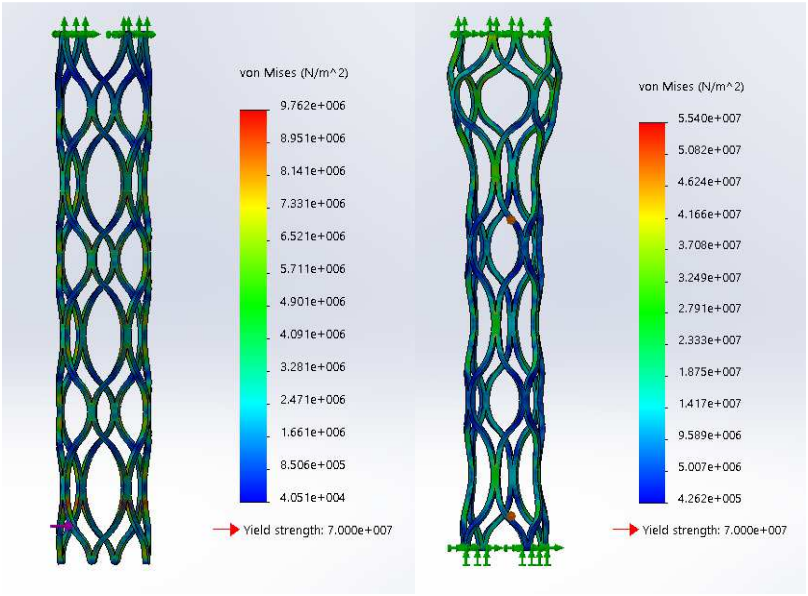


Figure 5.14 Simulation result of Stent-02 of PLA

Scenario 1(Right), shows a high resistance of compression at 10 N that represent at which the stent will be exposed at the physiological environment, the YS of the material is about 70 MPa and the limit shown in the von Mises graph is 9.7 MPa, with imperceptible deformation. Scenario 2 (Left) shows an exaggerated deformation of +5 times at the stent at 150 N that the stent will reach a diameter of 11 mm for its placement.

Simulation – Stent-02 of AZ31

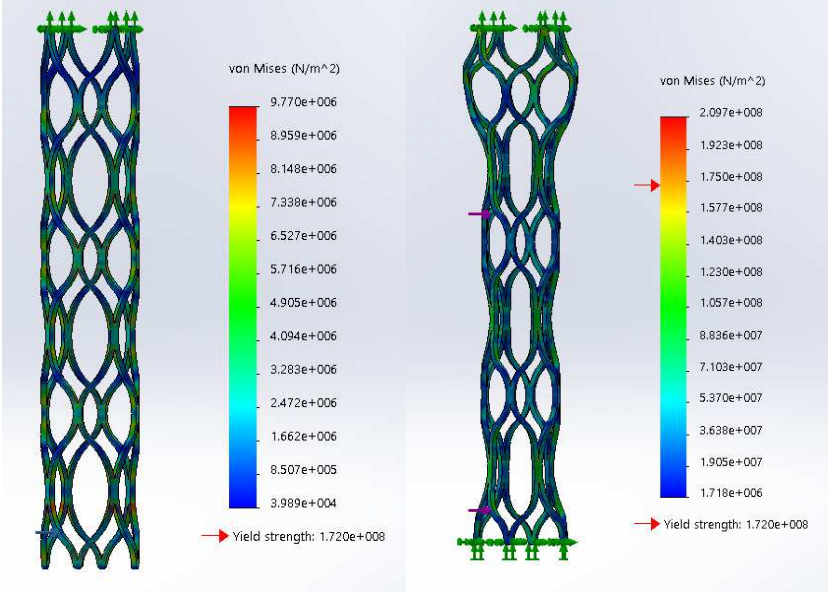


Figure 5.15 Simulation result of Stent-02 of AZ31

Scenario 1(Right), shows a high resistance of compression at 10 N that represent at which the stent will be exposed at the physiological environment, the YS of the material is about 172 MPa and the limit shown in the von Mises graph is 9.7 MPa, with imperceptible deformation. Scenario 2 (Left) shows an exaggerated deformation of +20 times at the stent at 700 N that the stent will reach a diameter of 11 mm for its placement.

Simulation - Stent-03 (PLA)

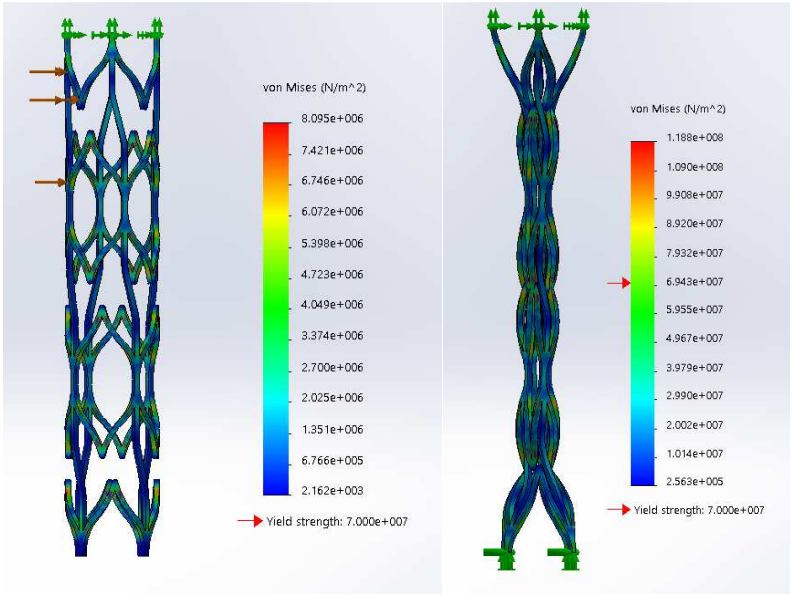


Figure 5.16 Simulation result of Stent-03 of PLA

Scenario 1(Right), shows a high resistance of compression at 10 N that represent at which the stent will be exposed at the physiological environment, the YS of the material is about 70 MPa and the limit shown in the von Mises graph is 8 MPa, with imperceptible deformation. Scenario 2 (Left) shows an exaggerated deformation of +4 times at the stent at 150 N that the stent will reach a diameter of 8 mm for its placement.

Simulation – Stent-03 AZ31

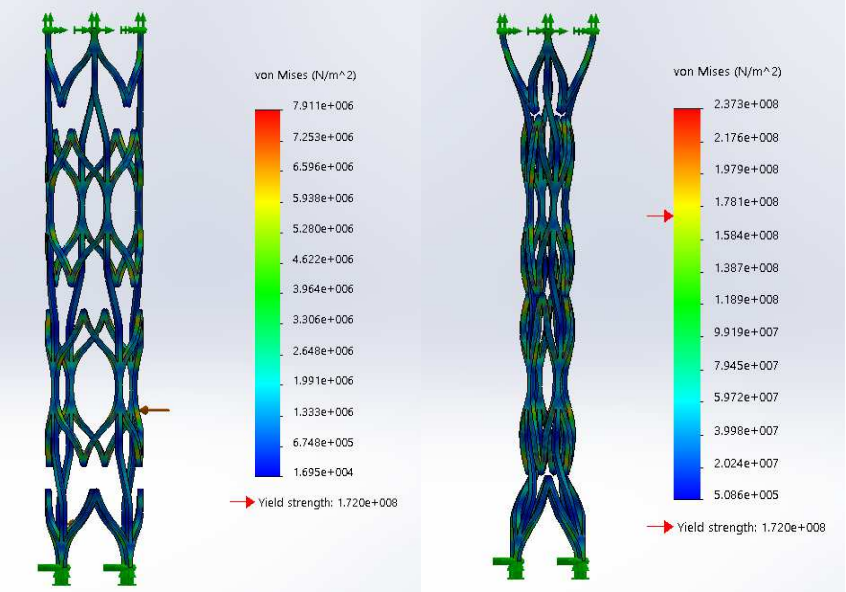


Figure 5.17 Simulation result of Stent-03 of AZ31
Scenario 1(Right), shows a high resistance of compression at 10 N that represent at which the stent will be exposed at the physiological environment, the YS of the material is about 172 MPa and the limit shown in the von Mises graph is 7.9 MPa, with imperceptible deformation. Scenario 2 (Left) shows an exaggerated deformation of +20 times at the stent at 300 N that the stent will reach a diameter of 8 mm for its placement.

The same issue was repeated in each simulation of the scenario 2, for both materials. In the Stent-01 and 02, a bugle is presented, this happened because of the nature of the geometrical design, those stents tend to elongate when the reduction of the diameter is done. In the Stent-03 this is not presented because of its design of mirrored scissors that allow it to compact in a uniform way.

A first run of the FEA simulations were run with 2 mm thickness but the results were of a compression resistance a lot bigger that the flexibility and compressibility of the stent was inexistent, a second run of simulations were run of the same pattern design of stent but now with 1 mm thick and the result of compression resistance and flexibility are more balanced.

In the Stent-01 for both materials demonstrate a more compactability for the deploy process of the stent and a good compression resistance, making it a friendly usage design.

The Stent-02 presented the highest mechanical resistance to compression and compactability but also the less compactable design, by just reaching 11 mm and using more force in compassion with the other two. This is not necessary a negative issue of the design, if the material degrades to quick, it will loss it mechanical properties faster, but if those mechanical properties are above the need it will be considered as functional for a larger period of time. Is also know that an exceeded design in topics of mechanical performance is counterproductive, for this reason, more research must be done in this issue.

The Stent-03 presented the best adaptability of all the three stents in both materials, and a good compression resistance and an easy compactable design for deployment, making a this design a good alternative of RYGBP prothesis.

In resume the Stent-01 is the easiest to be deploy by its compactable design, the Stent-02 is the more resistant to compression making it the strongest of the three, and the Stent-03 is the most adaptable of all making it the most comfortable design.

A resume of the result obtains form the FEA simulations are shown in the Table 5.4 and Table 5.5.

Table 5.4 Resume of Results of FEA simulations of PLA Stents

	Scenario 1	Scenario 2
	Resistance to compression Limit of elasticity 70 MPa	Compactability
Stent-01 PLA	10 MPa	75N to 10mm
Stent-02 PLA	9 MPa	150 N to 11mm
Stent-03 PLA	8 MPa	150 N to 8mm

Table 5.5 Resume of Results of FEA simulations of AZ31 Stents

	Scenario 1	Scenario 2
	Resistance to compression Limit of elasticity 172 MPa	Compactability
Stent-01 AZ31	10 MPa	300N to 10mm
Stent-02 AZ31	9 MPa	700 N to 11mm
Stent-03 AZ31	7 MPa	300 N to 8mm

A description chart of the performance result from the FEA simulations are shown in the Figure 5.18 and Figure 5.19, comparing the Compression resistance, Adaptability and Compactability of each stent in both materials.

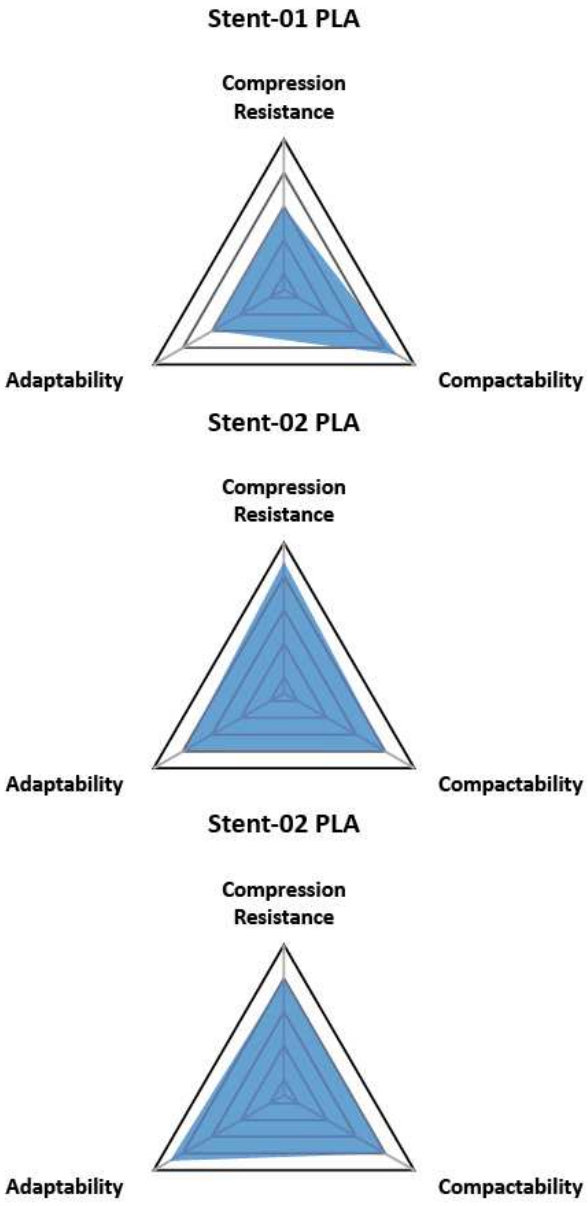


Figure 5.18 Performances of PLA Stents after FEA simulation

The resultant performance of the Stent was qualified by three concepts, compression resistance, adaptability and compactability. Compression resistance was analyzed by the lower measurement in the von Mises scale after 10 N force of the three stents. The adaptability is the color resultant in the stent after applying uniform force to the stent turn on a uniform color. The compactability is qualified by the minimum force required to deform the stent without plasticly transform it.

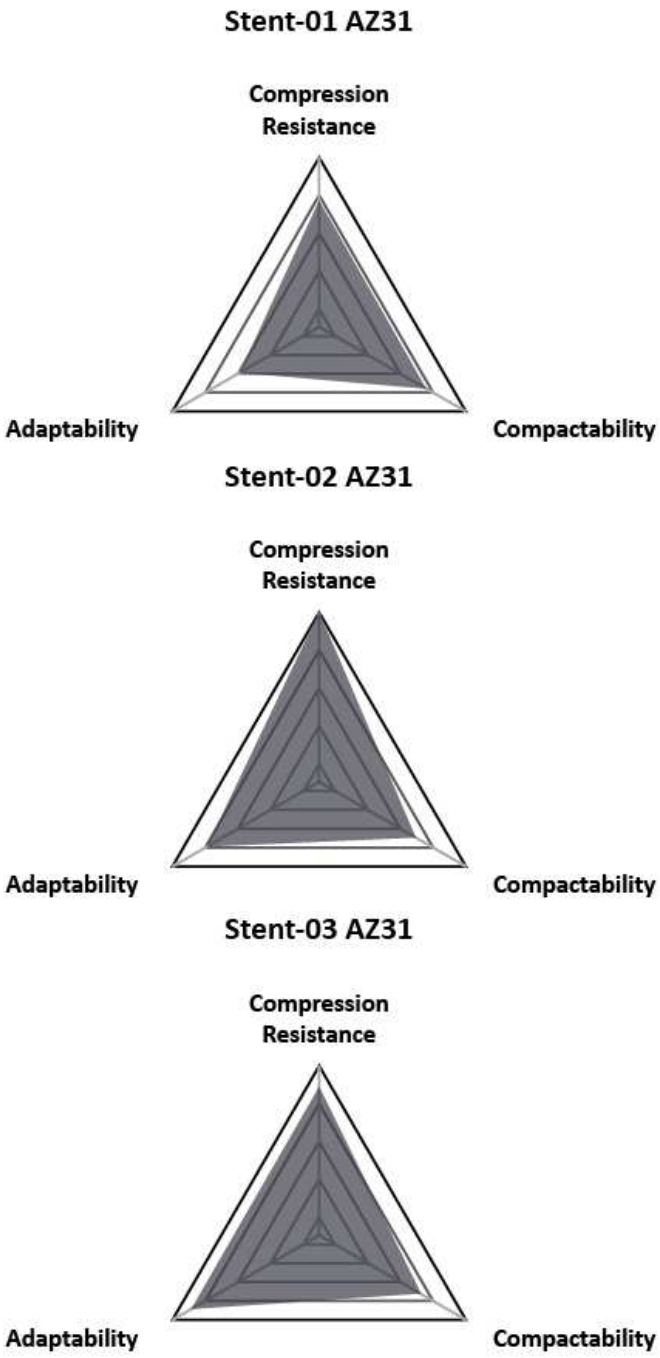


Figure 5.19 Performances of AZ31 Stents after FEA simulations
The resultant performance of the Stent was qualified by three concepts, compression resistance, adaptability and compactability. Compression resistance was analyzed by the lower measurement in the von Mises scale after 10 N force of the three stents. The adaptability is the color resultant in the stent after applying uniform force to the stent turn on a uniform color. The compactability is qualified by the minimum force required to deform the stent without plasticly transform it.

6. Conclusions and future work

The design process of new products is not an easy task, an exhaustive research must be done to propose an alternative of value. For the project of new prothesis development, a multidisciplinary group with knowledge and expertise of the medical, material engineering, product design and mechanical engineering fields are required because of its complexity. To provide a stent design for post treatment of RYGBP were analyzed studies cases of the usage of esophageal stents to treat RYGBP complications and a research of products available in the market approved by FDA. The case study consultation of the usage of different brands and types of stent point out in the latent need of the biodegradable prothesis.

A selection of biomaterials was made to propose a new product and a new protocol of degradation test was developing to standardize the test for Mg alloys and Bio polymers to produce comparable degradation rates of both materials. The results of this study result in similar values in comparison with the found in the literature, but with lower rates of corrosion in the both materials selected, PLA and AZ31.

After the implementation of the design methodologies, three requirements were needing to consider a stent design as functional, the compression resistance, the compactability and the life time of functionality of the biomaterial mechanical properties. Degradation test and FEA simulations were made to test these qualities of the design proposals, having as result three different alternatives with more focus of each requirements, one with more adaptability, other with more compression resistance and a last one with more compactability. A unique design to accomplish all the requirements did not achieve because of its complexity, but a good balance of the three requirements were obtained, making all the proposal a good alternative of product.

For future work, more runs of the protocol must be done to prove the reliability of the procedure. During preliminary tests, a variability of pH values of the medium of Hank´s and FBS must be analyzed the causes of this behavior. By the usage of FBS its provided a friendly environment to bacteria and spores or any other contamination, even when the procedures try to be as sterile possible, is probable that the samples could be contaminated, a deeper research must be done in this area and by making more runs of the protocol will improve the process.

Instead of comparing the results of our degradation test with the ones in the literature to predict the mechanical properties behavior, mechanical tests must be done to the samples used in the degradation test using the protocol proposed, to collect a homogenic data of using the same medium, parameters and considerations to both, polymeric and metallic materials, to calculate the corrosion rate and their mechanical proprieties, in a process controlled and standardized.

By collecting our own data of mass loss and mechanical properties, a better estimation of product performance can be achieved and selection of the suitable design will be needed to continue with the product process development, prototyping and in vitro studies of the stent selected, as well as the selection of the manufacture process, and if it’s the case, coating post processes for the stent, depending of the corrosion rates collected, to finally the final product to be tested in vivo.

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Appendixes

A. Instruments

In this section its shown the instrumentation, machines and apparatus used to processes the materials to produce the samples required and for the development of the degradation tests in this project.

A.1. Lathe Machine

The material used was a Mg allot, AZ31, it's an alloy in in the Mg-Al-Zn family. The raw material it was a solid bar of 19.05mm (0.75 in.) x 2 meters long (78.74 in). we needed at least 15 discs of 19.0mm of diameter x 2mm thick. To get this samples we used a robust tool to control the surface quality of the samples and its dimensions. The machine used was a conventional Lathe machine EMCO, Maximat Super 11. With a section tool of 0.187in to cut the samples.

Figure A.1 Lathe Machine EMCO Maxmat Super 11

A.2. Polisher of samples

Once the samples were cut into discs of 2mm thick, those samples were polished with 800 to 1600 grind to obtain smooth surface on the apparatus STRUERS LaboPol-21.

Figure A.2 Struers LaboPol-21

A.3. General Protocol Oven

The pellets of PLA were dried at 100°C for 3 hours to eliminate the presence of humidity, following the technical data of the material. This process was carried out in Thermo Scientific Heratherm Oven.

Figure A.3 Thermo Sientific Heratherm Oven

A.4. Hot Press

The pellets were put on a cavity plates to produce a sheet of 18 cm (7.08 in) x 18 cm (7.08 in) x 2 mm thick (0.078 in). this cavity plates were put on a hot press at 25 tons at 200°C for 2 minutes. The Hot press were a Craver Model 4128 heated press, and another same model of press for a cooling process. The cooling process were carried put on this another press at 25 tons with the press at 25°C for 7 minutes until the cavity plates cool down.

Figure A.4 Craver Model 4128

A.5. Refrigerated Bath Circulator

To control the temperature of the Cooling Press, a refrigerated bath circulator a LabTech Thermo-circulator were used.

Figure A.5 LabTech Thermo-circulator

A.6. Waterjet cutting machine

As were explained in the chapter 2 Literature review, PLA experience changes in its properties when its processed by heat as laser cut CNC machines. To cut samples of 19.05mm (0.75 in.), a waterjet cutting machine were used. The Flow Waterjet Mach2 1313b were used to cut 15 samples of PLA of a sheet of 18 cm (7.08 in) x 18 cm (7.08 in) x 2 mm thick (0.078 in).

Figure A.6 Flow Waterjet Mach2 1313b

A.7. Water bath

The Fetal Bovine Serum require to be storage at -20°C, and once we need to use this serum, we need to un frozen it with controlled temperature, Wisd WiseBath water bath increase the temperature gradually.

Figure A.7 Wisd WiseBath water bath

A.8. Safety Cabinet

The Biological Safety Cabinet were used to manipulate all the substances, to maintain sterile all the instruments and samples, because of the use of proteins. The equipment used was BIOBASE Biological Safety Cabinet.

Figure A.8 BIOBASE Biological Safety Cabinet

A.9. pH meter

The Mettler Toledo FiveEasy™ pH bench meter was used to monitor the behavior of the medium during the tests, we need to keep the samples in an environment physiological alike. (7.2-7.4).

Figure A.9 Mettler Toledo FiveEasy™ pH bench meter

A.10. Balance of precision

AL204 Analytical Balance by Mettler Toledo, was used to measure the differences of weight in the samples after the immersion tests. This apparatus of high precision has a definition of ten thousandths of a gram (0.000X gr).

Figure A.10 AL204 Analytical Balance by Mettler Toledo

A.11. Shaker incubator

Shaker MaxQ 400 by Thermo Scientific has the option to set controlled temperatures, controlled oscillations (RPM) and a timer to control the period of samples in the apparatus. When this timer goes off, it makes a sound to let us know that has already done, and the temperature stays on but the oscillations turn off.

Figure A.11 Shaker MaxQ 400 by Thermo Scientific

A.12. Ultrasonic cleaner

Branson 2510 Ultrasonic Cleaner by Marshall Scientific were used to clean the AZ31 samples before the immersion test on 20 ml of acetone for 10 min to remove impurities from the latest processes.

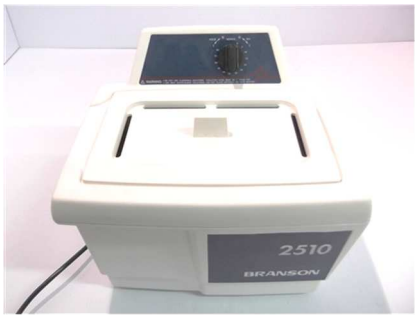

Figure A.12 Branson 2510 Ultrasonic Cleaner by Marshall Scientific

A.13. Electric sterilizer

25X QUART electric sterilizer by WAFCO, was used to sterilizer the flasks before been used to contain the medium during the degradation tests.

Figure A.13 25X QUART electric sterilizer by WAFCO

B. Preliminary degradation tests

In this section its shown the results of preliminary runs of the test to see the variability of the pH values of the medium in contact with the different materials. And the dry processes to select the optimal for both materials.

B.1. Ph Values of ratio of superficial area on medium volume

On this preliminary test the, al the stipulations on the protocol describe in the section 4.3.2 Protocol of degradation tests except for the exposure of UV light to the sterilized flasks, all the rest of the stipulations like relation between surface area exposed to volume of medium, concentrations of medium, temperature, oscillations were take care off.

B.1.1. Data collected of pH of cm2/ml variables

The data collected is described in the Table B.1 Data collected of preliminary run test Of PLA pH values, where the hour 0 shows the initial pH value of each of the three samples and the monitoring of every hour in the shaker with 37°C and 120 rpm.

Table B.1 Data collected of preliminary run test Of PLA pH values

Material	*Hour*	*Period*	*pH*	*Material*	*Hour*	*Period*	*pH*
PLA	0	1	6.89	*PLA*	14	11	6.78
	0		6.89		14		6.85
	0		6.89		14		6.74
	1	2	7.36		16	12	6.53
	1		7.34		16		6.59
	1		7.24		16		6.46
	3	3	7.44		18	13	6.2
	3		7.42		18		6.29
	3		7.37		18		6.08
	4	4	7.51		19	14	6.26
	4		7.49		19		6.28
	4		7.47		19		6.35
	6	5	7.58		20	15	6.35
	6		7.59		20		6.34
	6		7.51		20		6.37
	7	6	7.66		22	16	6.35
	7		7.6		22		6.34
	7		7.56		22		6.37
	8	7	7.7		23	17	6.79
	8		7.73		23		6.76
	8		7.58		23		6.74
	10	8	7.82		24	18	6.98
	10		7.75		24		6.88
	10		7.67		24		6.85
	11	9	7.69		48	19	7.68
	11		7.72		48		7.66
	11		7.57		48		7.63
	12	10	7.24				
	12		7.34				
	12		7.12				

In the Table B.2 shows the values of pH collected on a preliminary test to know how these values behave before running the final test.

Table B.2Data collected of preliminary run test of AZ31 pH values

Material	*Hour*	*Period*	*pH*	*Material*	*Hour*	*Period*	*pH*
AZ31	0	1	6.89	*AZ31*	14	11	7.36
	0		6.89		14		7.88
	0		6.89		14		6.93
	1	2	7.4		16	12	6.89
	1		7.33		16		7.39
	1		7.35		16		6.73
	3	3	7.58		18	13	6.55
	3		7.57		18		6.85
	3		7.54		18		6.32
	4	4	7.71		19	14	6.33
	4		7.75		19		6.65
	4		7.68		19		6.66
	6	5	7.75		20	15	6.66
	6		7.82		20		6.42
	6		7.77		20		6.67
	7	6	7.87		22	16	6.85
	7		7.9		22		6.84
	7		7.86		22		6.89
	8	7	7.89		23	17	6.97
	8		7.94		23		7.1
	8		7.9		23		7.04
	10	8	7.93		24	18	7.01
	10		8.01		24		7.2
	10		7.94		24		7.16
	11	9	7.96		48	19	7.67
	11		8.03		48		7.77
	11		7.92		48		7.91
	12	10	7.85				
	12		8.02				
	12		7.58				

From each material had 3 samples and were monitored for 24 hours during about one hour each.

B.1.2. Graphics of pH values

To analyze the data, form the pH values monitored for 24 hours, the graphs, show the behave of the pH values, and one measure at the 48th hour, giving the Figure B.1 and Figure B.2,

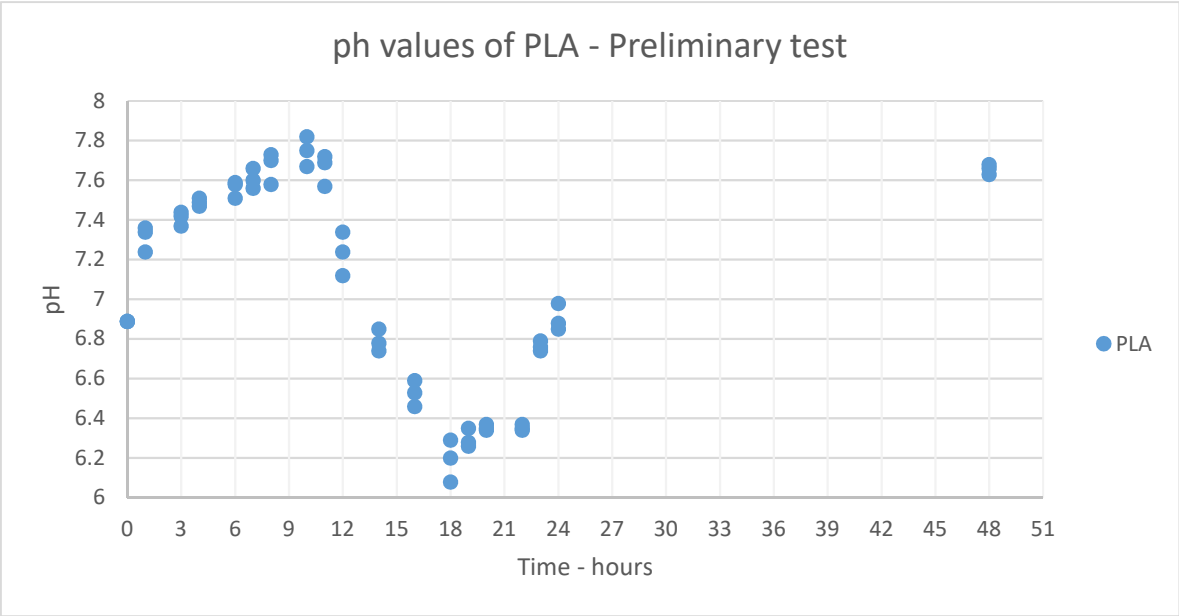

Figure B.1 Ph values of PLA

The start values when the Hank´s solution was combine with FBS, was about 6.9. with the pass of time, the value starts to increase until the 10th hour, then the pH decrees until reach values around, 6.1 at 18 hours after the start, and then start to increase again until reach neutral values of 7 at 24 hours after the immersion, and a final measure at the 48th hour to see that the value stabilized to reach 7.7.

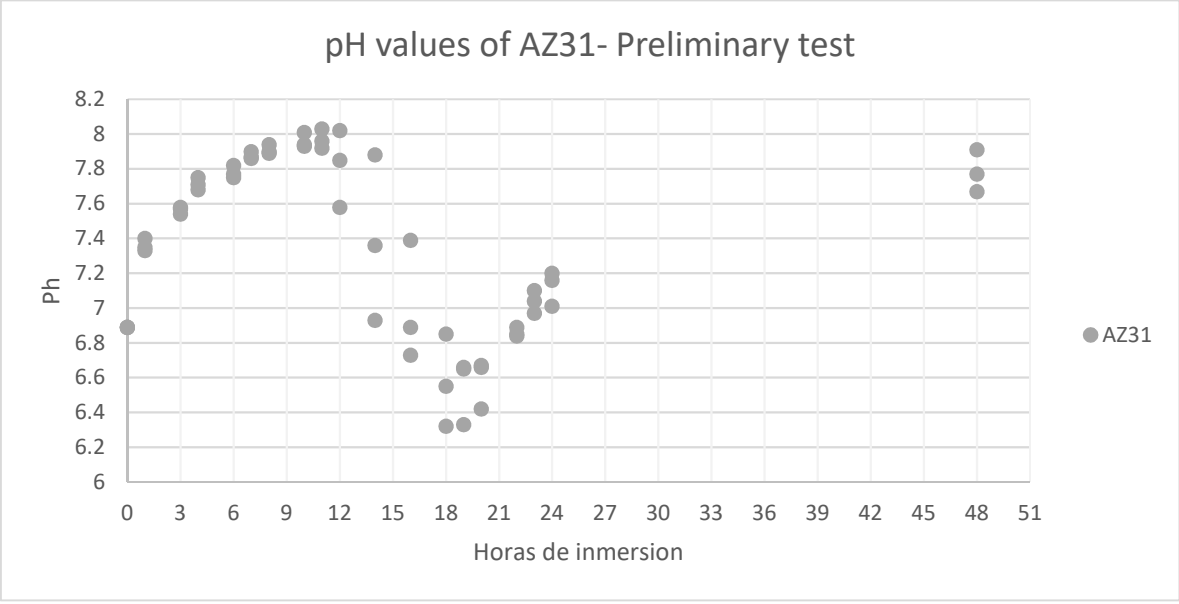

Figure B.2 Ph values of AZ31

The start values when the Hank´s solution was combine with FBS, was about 6.9. with the pass of time, the value starts to increase until the 12th hour and reach a value of 8, then the pH decrees until reach values around, 6.3 at 18 hours after the start, and then start to increase again until reach neutral values of 7.2 at 24 hours after the immersion, and a final measure at the 48th hour to see that the value stabilized to reach 7.9.

B.2. Dry tests

After having some problems to collect the weight loss of the PLA, and a lack of a standard protocol in the literature of how and for how long dry the PLA, a dry test was run for PLA and AZ31.

The test consisted on leave six samples of PLA and AZ31 on static 50 ml of water at room temperature for 24 hours to put on test if the samples absorbed humidity. Three samples of each material were dried at room temperature at vacuum in other three samples of each material were dried on an oven at 80°C.

Four measurements were made, the initial without been in contact with water, samples after 24 hours of been immerse in water, the weight after 24 hours of dry and a second weight at 48 hours of dry, the results are show below.

B.2.1. Data collected for dry tests

The data collected its show in the Table B.3 organized by material and the code that was assigned of each sample, there were four measures for each sample, the initial, after immersion, 24 hours of dry and 48 hours of dry. The samples from A to C were dried at vacuum and the samples from D to F were dried in an oven at 80°C, both procedures are identified by color to an easy read.

Table B.3 Dry test data of PLA and AZ31

Dry Test Data			
	AZ31	PLA	Sample
Initial	0.9254	0.6951	1A
	0.8159	0.6446	1B
	0.8881	0.6964	1C
	0.8924	0.7021	1D
	0.986	0.6622	1E
	0.9191	0.6693	1F
After immersion	0.9257	0.6965	1A
	0.8166	0.6464	1B
	0.8883	0.6984	1C
	0.8928	0.7038	1D
	0.986	0.6636	1E
	0.9188	0.6711	1F
24 hours of dry	0.9256	0.6938	1A
	0.8164	0.6437	1B
	0.888	0.6959	1C
	0.8924	0.6987	1D
	0.9861	0.6591	1E
	0.9192	0.6662	1F
48 hours of dry	0.9254	0.6932	1A
	0.8164	0.6435	1B
	0.8881	0.6953	1C
	0.8927	0.6989	1D
	0.986	0.6589	1E
	0.9191	0.6664	1F

B.2.2. Graphics of dry tests

Form the data collected, the graph shows in Figure B.3 shows that the AZ31 the data were transformed into percentage. The percentage of humidity gain on AZ31 is considered as non, because the values never reach a level of confusability, and it were to low. The values of PLA, compared with the literature, are very alike on the percentage of humidity gain and by reaching values above of 0.7%.

We assume that the sample had already some amount of humidity before starting the test, so the values taken of humidity gain, is the value of humidity loss after the dried process.

The values that reached highest percentages were the samples dried on the oven, but this procedure was not used on our protocol for degradation test because it causes a change of the morphology of the samples of PLA. The process used on the protocol were at vacuum at room temperature, even when its slower, it proves to be a safe and reasonable process to dry hydrophilic polymers.

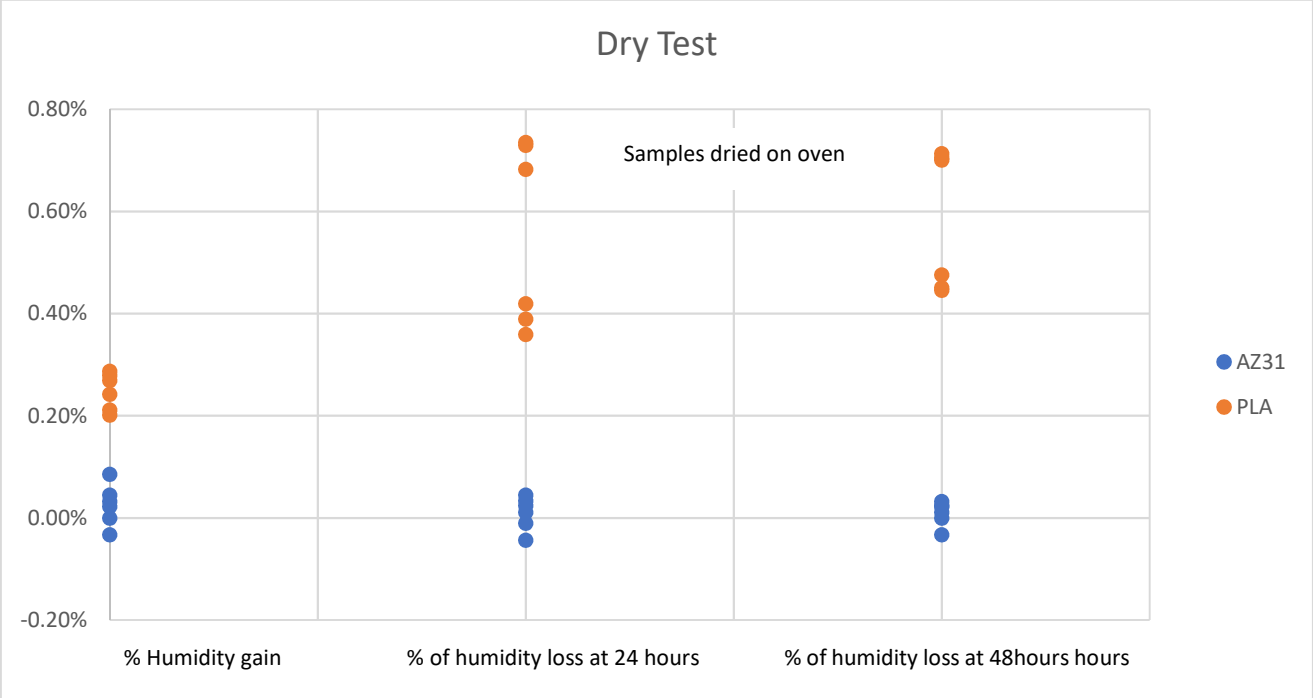

Figure B.3 Dry test of PLA and AZ31 by percentages
The % of humidity were made by the initial weight and the weight after the immersion, the % dried at 24 hours were made by the weight after the immersion and the weight after 24 hours dried, and the % dried at 48 hours were made by the weight after the immersion and the weight after 48 hours dried.

B.2.3. Samples result from the Dry test

After the dry test this are the samples resultant to be exposed 24 hours to water and 48 hours to dry processes. The Figure B.4 shows and describe the appearances of the samples after this test.

Figure B.4 Samples after Dry Test
(left) the samples were dried at vacuum at room temperature for 48 hours, the samples of PLA loss about 0.4% of weight, considered as humidity. (Right) samples were dried at 80°C in an oven for 48 hours and the PLA samples registered a 0.7% of weight loss considered as humidity. The appearance of the samples changes in the usage of the oven on the PLA samples. The AZ31 samples did not present absorption of humidity and not appearance change at the exposure of the oven.