POLITECNICO DI TORINO

Master Degree in Engineering and Management

Master’s Degree Thesis

Endoprostheses and esoprostheses: an economic analysis of the adoption of 3D printing in the Italian orthopaedic manufacturing sector

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Abstract

The entire history of mankind, since prehistoric times, has been characterized by a continuous process of technology development related to discovery, transformation and utilization of materials. The degree of evolution of the society is commensurate to the ability of man to convert raw materials into utensils, indeed we talk about *Stone Age, Bronze Age, Iron Age.* Nevertheless, it is hard to identify a class of material which characterizes modern man; only in the XX century new materials such as polymers, alloys and composites have revolutionized the entire scenario. After the advent of new materials, it is the development of new technologies which makes possible to obtain products, also functionally different, starting from a limited series of materials. The technological ability to transform raw materials in order to obtain an artefact with its own function, is of crucial importance.

One of the more powerful and revolutionary technology of the last years is represented by 3D printing, which belongs to the wider field of Additive Manufacturing (AM). It will, and is already, change the way in which products are manufactured, from simple objects to medical devices.

In this thesis, we will analyse the economic impact of 3D printing technology in the Italian orthopaedic manufacturing sector.

Initially, in the first and second chapter, we deal with the history of prostheses: we start from the history of biomechanics which is the mechanical study of human body and then we will describe what a prosthetic implant is and its general features.

The third chapter is concerned about the traditional manufacturing process of orthopaedic prostheses both for endoprostheses and esoprosthesis. The use of materials and the general manufacturing process will be described.

In the four chapter we move attention to Additive Manufacturing, describing its history and the technologies that have been developed. Then, we deal with the widen horizon of Additive Manufacturing looking at its diffusion process and, then, analysing the implications of this technology under an Intellectual Property aspect.

The five chapter deals with the 3D printing process for producing prosthetic implants. We will examine the related technologies and then the impact of 3D printing process on the existing manufacturing models.

In the last chapters we will examine in depth the market of medical devices and what is the effect that Additive Manufacturing has had on it. By performing a sector study our ultimate goal is the understanding of the impact of AM on the Italian orthopaedic manufacturing sector.

Contents

List of figures

Chapter 1

1. Biomechanics: the science of prostheses

A prothesis is a medical device consisting of an artificial implant of a part of the body, which substitutes an organ or a tissue such as a tooth, a bone or a limb. The term comes from the Ancient Greek prostheses, and it means "addition, application, attachment". A prostheses, in fact, has the function of replacing a missing body part, which may be lost through trauma, disease, congenital disease or to integrate an injured one in order to restore the normal function of the body.

The human body can be roughly described as a set of rigid segments (bones) and joints (joints) with different degrees of freedom. The whole system is driven by forces that have the insertion of the muscle into the bone as point of application and the line which connects the two ends of the active muscle as direction. The muscle however can only contracting, this means that the muscular forces act only in a direction parallel to the axis of the muscle and directed toward the centre of the muscle itself. When these simple forces

1.1 Biomechanics

"Biomechanics is the study of the structure, function and motion of the mechanical aspects of biological systems, at any level from whole organisms to organs, cells and cell organelles, using the methods of mechanics." (Biomechanincs s.d.)

1.1.1 History of biomechanics

The dawn of the biomechanics can be traced back to the protohistoric times of the fertile crescent civilization, particularly Egyptian and Sumerian civilization. The tradition indicates Imhotep, a high priest, architect and sculptor as founder of Egyptian medical science; later in times he will be deified as "God of Medicine". The findings, discovered during archaeological excavations near from Cairo (Egypt) and dated to around 3.000 BC, suggest that the Egyptian civilization had surprisingly advanced knowledge of anatomy and mechanics for the time, as showed in the figure below.

Figure 1 Egyptian prosthetic limb, 3.000 BC (Dr. Andrea Loprieno-Gnirs s.d.)

The artificial limb is a woman's first toe and it is made of wood and leather. The prostheses presents signs of wear and both with the way in which it is assembled allowing to be bent they suggest that it really helped its mistress to walk.

It is in the ancient Greeks that we can identify the birth of the *ars medica antiqua.* In particular we consider Hippocrates (460 BC) as the founder of medicine; he introduced the inductive method (a method similar to the scientific one of Galileo Galileo) and as scrupulous researcher and keen observer, he renewed the concept of medicine linking injuries and health of a person no more to divine intervention but only to human circumstances of the person himself. He invented the idea of medical record and introduced for the first time the concept of diagnosis and prognosis. With Hippocrates, Aristoteles (350 BC) and Archimedes (250 BC) the medicine is going through a flourishing period; many testimonies of the use of prostheses can be found also in the Roman civilization. The Roman scholar Pliny the Elder (AD 23-79) wrote of a Roman general in the Second Punic War (218-210 BC) who had an amputated right arm. He had an iron hand which allowed him to hold his shield and was thus able to return to fight.

Biomechanics suffers a severe set-back during the Middle Ages, in which people had a rough awareness of his own anatomy. This condition is the consequence of religious taboos which prevent dissection of corpses that is fundamental to increase anatomical knowledge.

Most prostheses of the time were made to hide deformities or injuries suffered in battle, with little attention to functionality.

Figure 2 - Middle Ages hand prostheses (Pietro s.d.)

It is in the humanistic period that the first attempts to give a mechanical justification to the behaviour of the human body occurred; the first major historical testimony in this field comes from Leonardo da Vinci (1452-1519). He first turned his interest to the study of head and brain, then he studied the proportions of the human body, investigated the skeleton and the musculature by drawing bony elements seen from each side and in section.

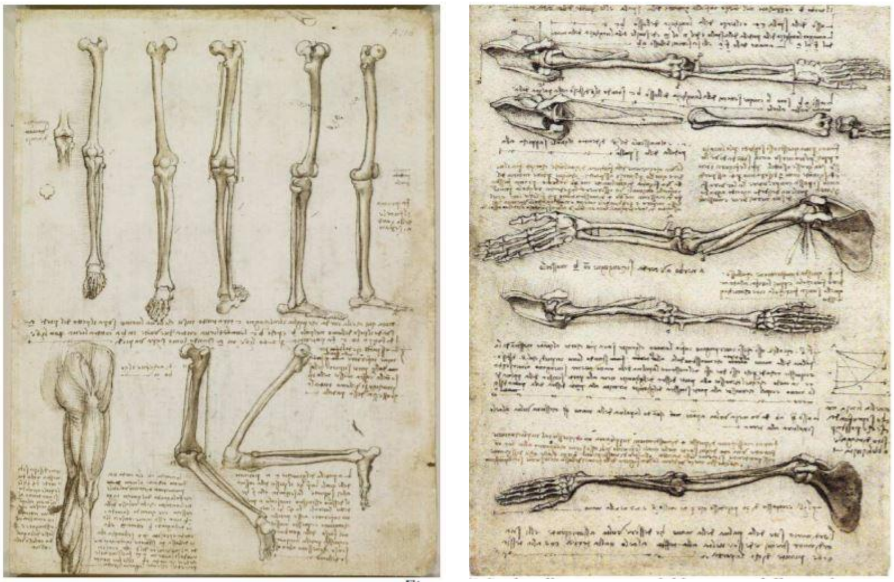

Figure 3 - Studies on harm and leg mechanics (Kevle s.d.)

Da Vinci used his knowledge of anatomy and mechanics to deepen the mechanics of walking, of sitting and getting up from a chair, of jumping.

He was therefore concerned with describing form and function and his studies do not only investigate anatomy but go further, from the study of the motion of the limbs up to the nature of pain and trauma. In his anatomy notes there are references to traumas, especially those caused by what he referred to as *percussione* (impact trauma). In his deep interest in human anatomy, Da Vinci, at the end of the fifteenth century, wondered if the joints of the body were deputies to absorb impacts. Noting that the pain caused in landing on the heels after a jump it is remarkable but becomes small if the landing is carried out on the tips, he also deduced that "what it offers the most resistance to a blow suffers the most damage ". This introduces the modern concept of shock attenuation (like the body absorbs energy), and more generally anticipates contemporary studies on foot-ground reaction forces and how the body absorbs impacts, and which ones damage these impacts can cause over time.

Just a few years later Leonardo da Vinci, in the XVI century, we can find the founder of biomechanics: Galileo Galilei for his contributions given in applying mechanics to biological problems. He studied the size of the bones in relation to their resistance and the floating position of the human body.

Each of these figures contributed to the development of knowledge in this field, but the reference point for biomechanics goes back to the Iatromechanical School (Padua Medical School) which deserve credit for considering human organism subject to immutable physical laws.

Santorio Santorio (1561-1630), Gian Alfonso Borelli (1608-1679) and Giorgio Baglivi (1688-1707) are regarded as the leading figures of Iatromechanical School. Each one of them had a relevant role, however, Baglivi with the maximization of Borelli's mechanical conception of human body, conceives the "human machine", thinking of it as constituted by a large number of smaller machines. Baglivi's "human machine" is a foretaste of the bionic man.

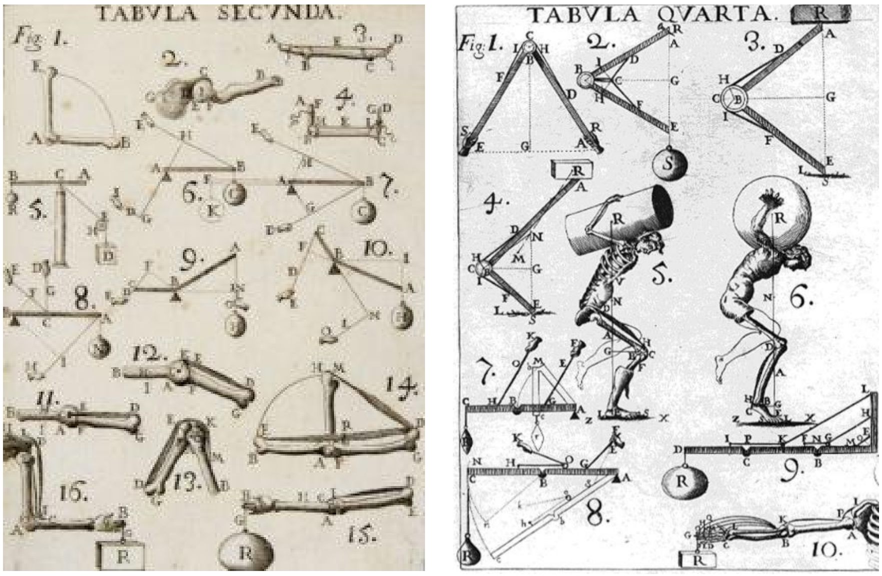

Figure 4 - Iatromechanical School studies (Maldonato s.d.)

In the same years, the French army surgeon Ambroise Parè built lower limb prostheses. Nevertheless some devices, regarding hands and legs, were too sophisticated for the times and they failed because of the inadequacy of the technology of the time.

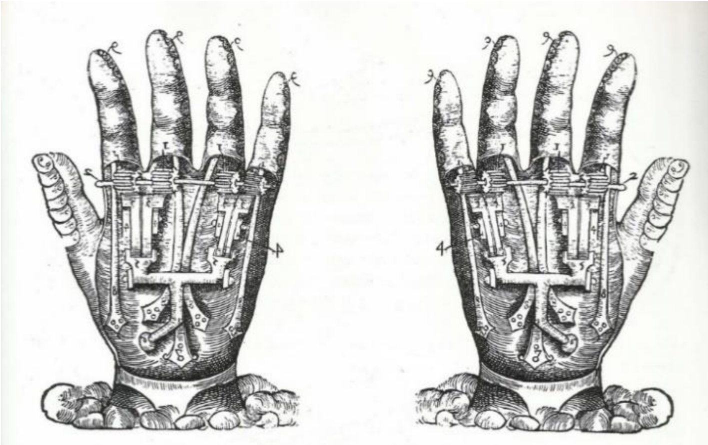

Figure 5 - Parè's atrificial hand

The attempt to implant metals in various parts of the human body dates back to very ancient times, but in the times preceding Pasteur, the onset of gangrene nullified clinical advantages.

After humanism, the eighteenth century is considered another important phase of convergence between science and technology through the re-evaluation of the technique. It is in this period that Pieter Verduyn developed the first knee joint prostheses, which would later become the model for current devices.

The iatromechanical research, by introducing the quantitative method in medicine, is a milestone in the development of biomechanics, albeit primitive. The American Civil War created an astronomically high number of amputations, thus forcing Americans to enter the field of prostheses. Events of this kind, which affect entire nations, helped in transforming and advancing the prosthetic field with their refinements in the mechanisms and materials of the devices.

Figure 6 - Steel and brass hand developed for a war amputee (Group s.d.)

Unlike the civil war, the First World War did not favour the advancement of prosthetic development, but it is following the Second World War that the current meaning of biomechanics originates from the technological progress that comes after it. The biomechanics that

characterizes the transition from qualitative to quantitative is reborn for humanitarian purposes for health care and not as a cultural exercise.

Figure 7 - Heavy wooden leg from the first half of the 1900s (Group s.d.)

1.1.2 Application

The word biomechanics and the related biomechanical, as the Oxford English Dictionary explains, come from the Ancient Greek βίος bios "life" and μηχανική, mēchanikē "mechanics", to refer to the study of the mechanical principles of living organisms, particularly their movement and structure. (Biomechanics 2012)

The fields of application are a big variety, and among the most important we mention:

- Biofluid mechanics: the study of both liquid and gas in and around biological system, for example the study of blood circulation in human cardiovascular system. It is also called biological fluid mechanics;
- Biotribology: is a study of friction, wear and lubrication of biological systems especially human joints such as hips and knees. (Davim 2013)
- Comparative biomechanics: it is the study of mechanics in biological but non human organism, strongly related with ecology, palaeontology and neurobiology;
- Computational biomechanics: the study of the mechanics of biological system through the application of engineering computational tools, such as the finite element method.
- Continuum biomechanics: the mechanical analysis of biomaterial and biofluids, that is fundamental in order to avoid issues in the reaction of the organism to the external materials plant.

Nowadays biomechanics boasts "sister" sciences like biomedical engineering, tissue engineering, kinesiology and orthoprostheses with whom he works in synergy in order to be able to understand, in the smallest details, how our body moves. Once the analysis of the movement could only take place using sketches designed by skilled artists; today is the computer the one which provides an indispensable contribution.

The fascinating collaboration between engineering, medical science and information technology will allow the creation of more and more useful prostheses in the coming years, with the ultimate goal of improving the life of people.

Chapter 2

2. Orthopaedic Prostheses

2.1 Introduction on orthopaedic prostheses

The prostheses - as has previously been said - are medical devices that, applied to the body, replace in part or totally missing parts recovering the structure and the lost function (i.e. upper or lower limb in the amputee or hip replacement). Some applications require full implantability, this means that the device must be used completely within the body, other ones, instead, are completely external to the body even in direct contact with the body.

In the orthopaedic sector, generally, we talk about prostheses with reference to two types of artificial devices esoprostheses or prosthetic limb and endoprostheses or artificial joint:

- Esoprostheses or artificial limbs are prostheses that completely replace a limb or a missing part of it and they have functional roles, but also aesthetic purposes. Their interface with the organism is with the skin surface and they can be can be worn and removed.

Figure 8 - Lower limb prostheses (Ortopedia Somp s.d.)

- <u>Endoprostheses or artificial joints</u> are medical devices which substitute, partially or totally, a joint that no longer works adequately due to degenerative or traumatic pathologies. They are systems permanently implantable inside the body surface where they play their role in direct contact with the tissues of the host organism.

Figure 9 - Joint replacements (Shockey s.d.)

The joints of interest for the replacement with prostheses are mobile articulations or diarthrosis.

2.2 A general background on skeletal system

The skeletal system is composed by bones, joints and associated tissues (cartilage and ligaments) and it accounts for 18% of body weight.

The bone elements are about 206 mineralized tissues with the main function of transmitting and enduring strength. They are classified in five categories: long bones, short bones, flat bones, irregular bones and sesamoid bones. In the long bones it is possible to recognize a long and cylindrical central part, the diaphysis, which is crossed by a wide canal and formed by compact or cortical bone tissue and two wider extremities, the epiphyses constituted by spongy or trabecular bone tissue. The function of the single bone element exerts a decisive influence on the internal conformation of the bone and consequently also on the external configuration. (Pietrabissa s.d.)

In engineering and designing a prostheses it is of crucial importance the knowledge of anatomy and physiology and in this sense the study on the dynamic osteogenesis. The analysis on dynamic bone behaviour have been conducted with two objectives: evaluation of bone mechanical properties through both *in vitro* or *in vivo* experiments and theoretically predicting the response of bone elements to the actual dynamic conditions. (Stanfield 2012)

The culmination of these studies is represented by the so called Walff's law, which states that *"Under load and as a result of pathological alterations of the external form of the bone elements, the transformation of the bone architecture follows mathematical laws"*.

There are three distinct processes in which a clear correlation is observed between mechanical actions and structural organization of bone tissue:

- Bone healing: morphological and structural reorganization of the bone tissue that is observed around the fracture gap;
- Bone modelling: the shape of the bones appears to be optimized with respect to the mechanical function to which they are in charge; during skeletal maturation the local morphology of the supporting bones is also defined by the physiological load history;
- Bone turnover: under the action of the load history the bone is subjected to a continuous process of replacement of its extracellular matrix in order to guarantee the calcium homeostasis in the blood and the structural integrity of the skeleton. This process occurs through an osteoclastic reabsorption sequence followed by a phase of osteoblastic deposition and subsequent mineralization of the newly formed collagen matrix.

These laws are the pillars for designing and developing medical devices with the role of replacing bones morphology and function.

2.3 Artificial joints

Orthopaedic surgery has various endoprostheses available designed to replace different skeletal components, each of which reflects as much as possible the morphology and above all the functionality of the part it will replace.

The main joints of human body and consequently the ones replaced with prostheses more frequently are the hip, the knee and the shoulder.

2.3.1 Hip replacement

The hip replacement is the most used in orthopaedic surgery due to different reasons:

1. hip is the joint that has to withstand highest loads and therefore more easily undergoes mechanical failures;
2. pathologies that limit the functionalities of the hip are very disabling;
3. hip replacement is surgically easy;
4. hip kinematics is easily reproducible with artificial spherical joint.

During the years, from the first documented attempt of replacing hip with an artificial one in 1890, several prostheses models have been developed and the evolution of design, materials, implantation and anchoring methods has almost always been dictated by the result of clinical experience.

Over the years different kind of prostheses have been developed: prostheses that only covered the head of the femur restoring the articular surface, other ones which only covered the head of the femur and were fixed inside the medullary canal of the femur, prostheses which provided also for the replacement of the acetabulum, and finally the ones that are more used today are the ones made by two components: the femoral components and the acetabular component (the so called THA).

There are two possible solution to solve a malfunctioning hip:

- Total hip arthroplasty (THA), the proximal portion of the femur and the acetabular bone is removed with appropriate surgical techniques, then replacing these components with two different endoprostheses (femoral and cotyloid)
- Endoprostheses, either the femoral part or the cotyloid part is surgically replaced with a prosthetic component that will interface with the natural component.

THA is composed by 4 elements:

1. a metallic femoral stem fixed in the medullary canal of the femur;
2. a spherical metal head;
3. an acetabular articular element, generally polymeric, the shell;
4. metal back of the acetabular element that binds it to the bones of the pelvis.

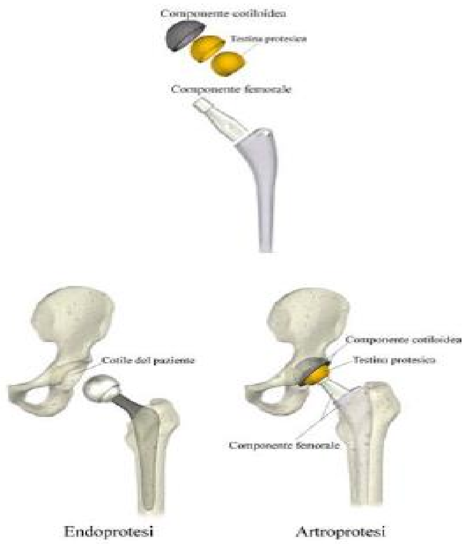

Figure 10 - Comparison between endoprostheses and arthroprostheses (F.Biggi, et al. s.d.)

Both the solution are valid, and the more suitable one is chosen on a case by case basis. In designing, realizing and implanting a prosthetic device the following issues shall be taken into consideration:

1. designing of a structure that re-establishes the kinematic conditions typical of the natural joint and which withstands the loads to which it will be subjected;
2. realization of a joint interface in which friction and wear are minimised;
3. ability to absorb shocks at the joint;
4. biocompatibility of materials and its wear waste, this means that they must not produce undesired alterations or responses in the host tissues;
5. study of the implant shape as its stiffness and the type of resection it requires determine a bone reaction that may or may not adapt to the new tensional situation;
6. study of bone-prostheses interface which means study of the surfaces and coatings of the prostheses as they determine a bone reaction, such as bone modelling.

In order to obtain minimum friction, low wear and ability to absorb shocks the materials used are basically three: metal (alloy of Chrome, Cobalt and Molybdenum), Ultra High Molecular Weight Poly-Ethylene (UHMWPE) and ceramic. The most used joint couplings are metal – metal, and metal – UHMWPE due to the fact that the coupling with ceramic are more fragile even if they allow minimum friction. The first one is classified as *hard-on-hard,* instead the second one as *hard-on-soft,* and it's positive aspect is characterized by the low wear; on the other hand the wear leads to the release of metal ions inside the body that result be quite toxic thus reducing the biocompatibility of these prostheses.

The first total hip arthroplasty were non-cemented and their anchorage to the bone was due to the simple mechanical anchorage between the femoral stem and the smaller sized canal created in the femur. Later on, cemented prostheses for which the anchorage is obtained through an acrylic resin, that polymerizing and hardening, determines the stability of the interface have been developed.

Nowadays both cemented and non-cemented hip prostheses are used; the first ones are most common in the US and in older patients, the second ones instead are the most used in Europe.

Figure 11 - Non-cemented hip prostheses (Manzini s.d.)

According to the Agency for Healthcare Research and Quality, more than 300,000 total hip replacements are performed each year in the

United States. Also in Europe the number is high and similar to the one of the United States, what instead is really different is the cost with which the hip replacement is performed within them being significantly lower in Europe.

2.3.2 Knee replacement

The second joint for number of surgical substitution with prosthetic implant is the knee joint.

Knee kinematics is much more complex than that of the hip but the transmitted loads are lower; knee movement is defined by ligamentous structures that constrain the relative positions of tibia and femur and allow only movements within the physiological range. Movements knee are not only in the sagittal plan, but also allow rotation, stabilized by ligaments, on other planes. The range of allowed movements and degree of freedom are some of the causes of the difficulty in implanting a good knee prostheses.

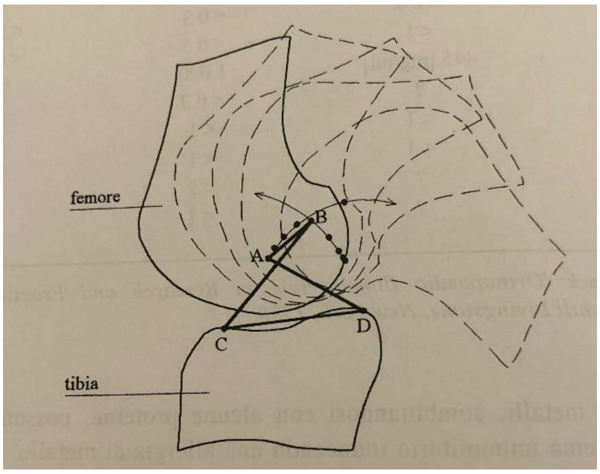

Figure 12 - Knee kinematics on the sagittal plan (Pietrabissa s.d.)

The main types of knee arthroplasty are (Knee replacement surgery s.d.):

3 total knee replacement, it involves replacing the joint surface at the end of the thigh bone (femur) and the joint surface at the top of the shin bone (tibia) and it is possible that also the patella must be substituted. The components are cemented in place or, f not cemented the surface of the component facing the bone is textured or coated to encourage bone to grow onto it, forming a natural bond;

4 unicompartmental (partial) knee replacement, it is the less invasive procedure and it offers the opportunity to preserve more bone, which is helpful if you need revision surgery at a later stage; however partial knee replacement isn't suitable for everyone because of the need of strong and healthy ligaments within the knee;

5 kneecap replacement or patellofemoral arthroplasty involves replacing just the under-surface of the kneecap and its groove (the trochlea) but it has a higher rate of failure than total knee replacement;

6 complex or revision knee replacement, it usually has longer stem in order to be more securely fixed into the bone cavity and it may obtain greater stability by interlocking the components in the centre of the knee.

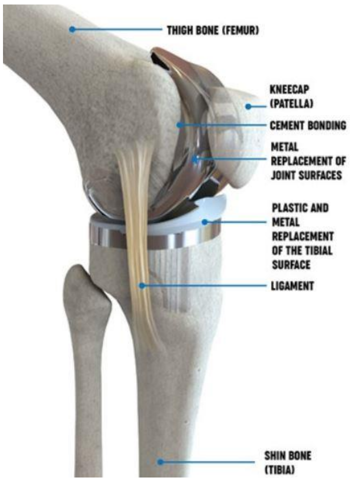

Figure 14 - Total knee replacement (Knee replacement surgery s.d.)

Figure 13 - Unicompartimental partial knee replacement (Knee replacement surgery s.d.)

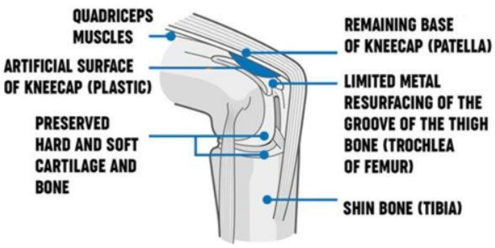

Figure 8 - Patellofemoral arthroplasty (Knee replacement surgery s.d.)

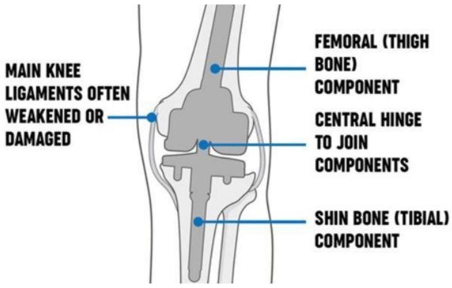

Figure 9 - Complex or revision knee replacement (Knee replacement surgery s.d.)

For the production of knee replacement are used material similar to hip replacement, because both joint replacements should met almost the same requirement. For this reason knee arthroplasty is made by metal condyloid component (Co-Cr-Mo) and a polymeric component of UHMWPE, usually supported by a titanium metallic basis.

According to the Agency for Healthcare Research and Quality, almost 500,000 primary knee replacements are performed each year in the United States. In Italy the data are not so exhaustive, but we know that more than 60,000 per year knee replacement have been performed in the last years.

2.3.3 Failure of orthopaedic prostheses

The causes of failure of a joint replacement can be different but they can by grouped together in 3 main family:

1. Mobilisations and dislocations
2. Usury and breakup
3. Infections

Despite the search for new materials, the friction of the articular surfaces, that is the rubbing against one another, still today wear the surfaces of the implant creating tiny particles. These particles accumulate around the joint in a process called aseptic or uninfected mobilization the bonds of the prostheses to the bone are destroyed by the body's attempts to digest the particles produced by this wear, causing the failure of the prosthetic implant. When the prostheses is mobilized (loosens), the patient may experience pain or instability. Furthermore, in this process of digestion of wear particles, the body also digests bone (a phenomenon called lysis). This can weaken or even fracture the bone and compromise the success of future revision surgery. In this case, in fact, surgery will also have to face the problem derived from the presence of bone gaps. Aseptic loosening is the most common mode of failure of hip and knee prostheses.

Dislocation is another cause of failure of a joint replacement. Dislocation is a sudden leap or migration of the prostheses from its normal position. It is commonly a problem of hip replacement rather than knee replacement. The percentage of dislocation after a hip prostheses from literature ranges from zero to 10%, but on average this complication occurs approximately in one patient out of 50. The dislocation can be caused by the mobilization of the implant, by inadequate soft tissues, by a scar in the bone or tissues, by the incorrect position of the prosthetic components, by neurological factors (such as some neuropathies or Parkinsonism), or by movements that do not conform to the implant implemented by the patient himself due to trauma.

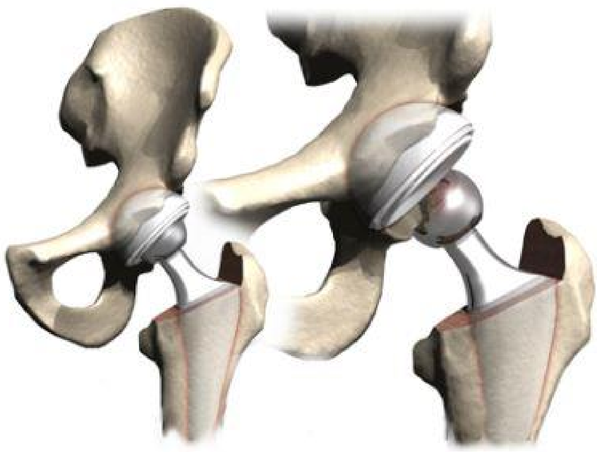

Figure 15 - Hip replacement dislocation

The joint replacement is a surgical procedure which intrinsically is subjected to the risk of infection, moreover in this case the implant of an artificial device inside human body makes the risk higher. Prosthetic infections can be classified according to the time of onset of symptoms after implantation into:

- Early infections with onset time < 4-6 weeks to 3 months. It is deemed that they are acquired during surgery due to dispersion of microbial material on the operating field.
- Late infections with onset time within 3 to 24 months from the positioning of the arthroplasty. They are considered by exogenous acquisition. The cause is the dispersion of microbial material on the operating field and the solution is represented by a combined medical-surgical approach that foresees the removal of the arthroplasty with spacer cement placement and repositioning of the arthroplasty once the eradication of the infection has been ascertained.
- Delayed infections with onset time > 24 months. They are considered by hematogenous pathogenesis, from remote infection sites. The approach is conservative and analogue to the one adopted for late infections, when it is possible.

The European Center for Disease Prevention and Control reports that in 2014 for 329,749 hip replacements (HPRO) 3,553 (1.1%) surgical site infections were reported one year after surgery.

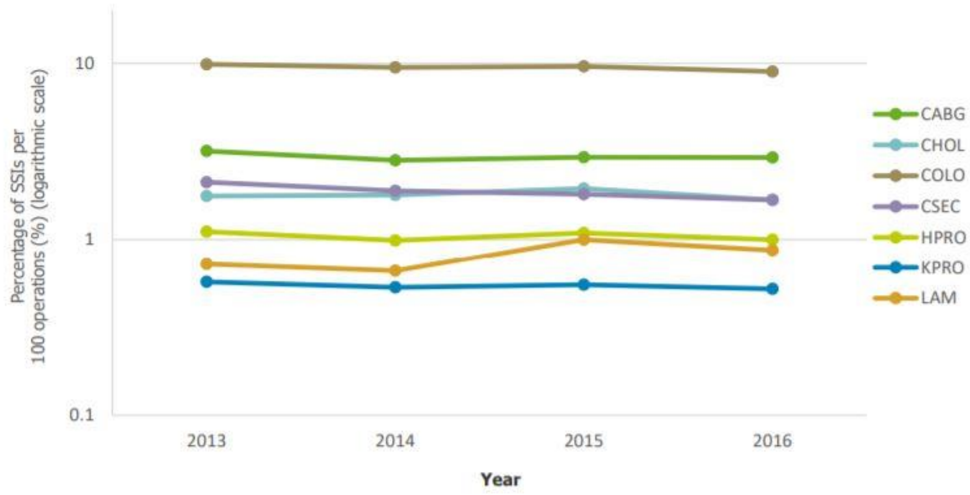

Figure 16 - Trends of percentage of SSIs by year and type of surgical procedure, EU/EEA, 2013–2016

The graph shows that HPRO, hip prostheses surgery, and KPRO, knee prostheses surgery, have lower percentage of SSI surgical site infection in respect to other common surgical procedures.

In Italy the cumulative incidence of surgical site infections (number of SSI x 100 / total number of operations) for HPRO hip replacements one year after hip replacement surgery is substantially in line with that of other countries.

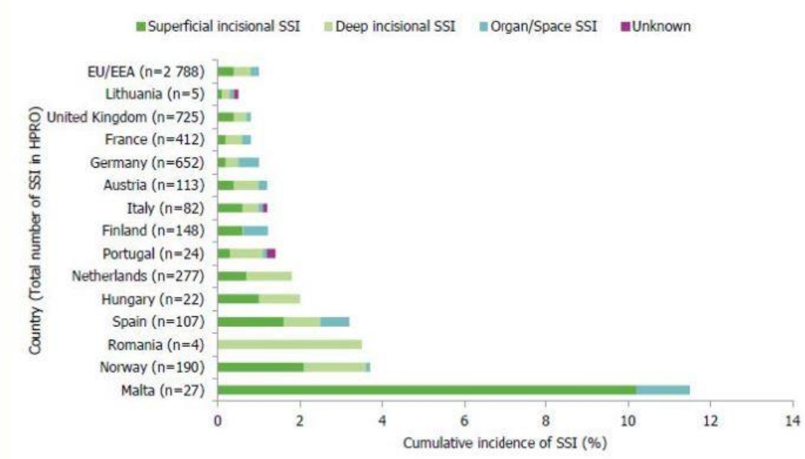

Figure 17 - Cumulative incidence of SSI for HPRO. Data source: ECD, HAI-Net SSI patient-based and unit-based data 2010-2011

2.4 Esoprostheses or artificial limbs

Esoprostheses are medical devices, custom-made with artisan technologies and CAD/CAM systems with the aim of replacing the morphology and, in part, the functionality of an amputated limb.

The need for lower limb amputees to have a prostheses has been felt since ancient times. In fact, the loss of autonomy resulting from the amputation of a leg is certainly greater than the one due to the amputation of an arm. For this reason lower limb prostheses have been the subject of continuous research to improve their functionality. It was Otto Bock who, in 1919, created a type of prostheses that consisted of single prefabricated elements introducing the idea of modularity. This idea, still valid today, has paved the way for the production of prefabricated components (feet, knee joints) on industrial basis. These components, assembled together, with the utmost respect for the patient's anatomy and static standards, are connected to the custom built socket.

Human gait, apparently so spontaneous and natural, is actually the harmonious result of a complex set of movements and the prosthetic technology is inspired by this perfect model for the research and development of new components.

The needs and requirements of each individual amputee based on the level of amputation, age, general physical conditions and the physical and social environment must find satisfaction. In this sense it is useful the so-called classification matrix, which helps in identifying the correct prosthetic solution for the amputee by analysing structural and functional classes.

The components of a prostheses can be distinguished in functional components (feet, knees, hip joints), structural components (connection modules) and potholes. Lower limb prostheses in recent years have had considerable and substantial improvements thanks to the technologies and materials that have involved all its parts.

On the basis of the type of construction and composition, two systems of prostheses are today distinguished:

- Exoskeletal traditional prostheses, which are composed by a rigid structure;
- Exoskeletal modular prostheses, which better replicates the skeleton due to several elements constituting it: socket, joint, knee, cosmetic coating, modular tube and foot.

The exoskeletal modular prostheses are the most used due to greater alignment ductility and in this kind of prostheses the load-bearing function is guaranteed by a tubular structure that can be in aluminium, steel, carbon or titanium and must be chosen based on the weight of the person. The external appearance is given by a soft foam covering.

Figure 19 - Exoskeletal traditional prostheses

Figure 18 - Exoskeletal modular prostheses

Chapter 3

3. Orthopaedics prostheses production process

3.1 Introduction

After having discussed about what an orthopaedic prostheses is, what is the intended purpose and what are their peculiarities it's now time to move to the production processes through which they are realized.

Our focus will be on both endoprostheses and endoprostheses and, in particular, we will analyse the production processes for all different materials which compose a prosthetic implant.

3.2 Artificial limb

As already mentioned the history of artificial limb is really old and, during times, materials and procedures have changed following the advances in technology.

The twentieth century have seen the greatest advances in technology related to prosthetic limbs. Modern materials, such as plastic, have yielded prosthetic implants to be more strong and lightweight than earlier devices in iron and wood and the new sophisticated procedures makes possible to have fairly realistic-looking skin.

The new technology are responsible for the development of myoelectric artificial limb, which use the myoelectric signals from patient’s muscles in order to move the prosthetic limb. This technology will not be analysed in this thesis, because we focus on the prostheses physical structure and on its production process.

First of all, for the amputee, the requirements that the artificial limb has to fil are: lightweight and physical appearance.

In order to fulfil the first requirement the devices are made from plastic; the socket is made from polypropylene and the pylon from alloys of titanium and aluminium, even if the newest development is the use of carbon fiber. Urethan foam with a wooden inner keel are used for feet, instead socks are made from cotton or synthetic materials.

The majority of pylons (endoskeletal prostheses) are covered with a polyurethane foam with shape and skin colour the more similar to the ones of the amputee, in order to obtain a satisfying physical appearance.

3.2.1 Artificial limb: how are they made?

Artificial limb are not mass-produced to be sold in store, nevertheless many components such as feet and pylons are manufactured in a factory and then assembled together with the custom-made parts (the socket for instance). Only few facilities allow to produce an entire custom-made prosthetic limb.

The entire process of manufacturing a prosthetic limb can be divided in three main phases:

- Measuring and casting
- Making the socket
- Fabrication of the prostheses

In the first phase of measuring and casting the prosthetist is the figure responsible for the evaluation of the amputee. He takes impression or a digital reading of the residual limb and, after that, together with the measurements he makes a plaster cast of the stump. It this way, an exact duplicate of the stump is obtained (positive model), the positive mould.

Next, in the second phase, the mould is wrapped in a thermoplastic heated sheet in a vacuum chamber; the air between the mould and

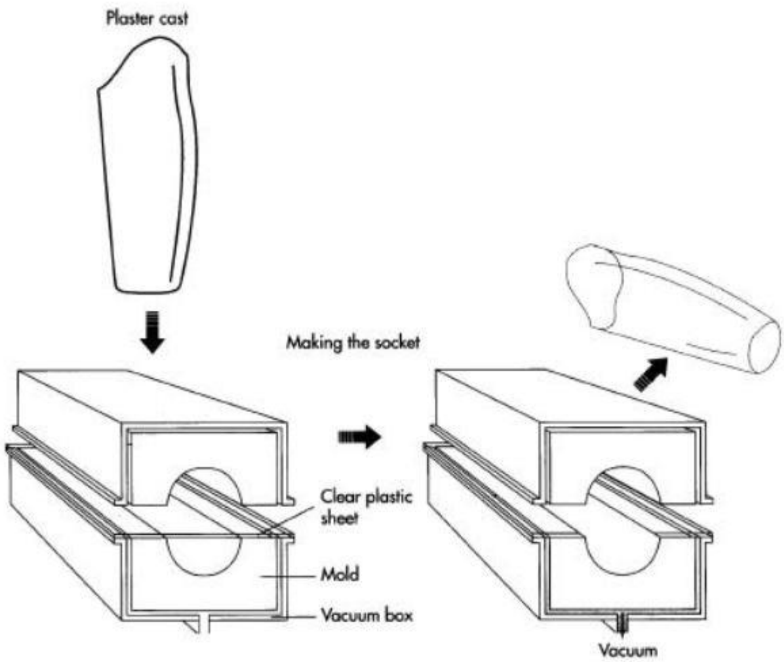

Figure 20 - Socket production (Artificial Limb s.d.)

the sheet is sucked out, collapsing the sheet around the mould and obtaining the exact shape of the mould. Usually it is transparent so that it is possible to check the fit. Then, before the permanent socket is made, the amputee is asked for some test in order to ensure that the socket fits properly; due to the thermoplastic behaviour of the sheet it is possible to reheated it adjusting the shape. After that, the permanent socket is formed as the same way of the test one.

The other parts of the prosthetic limb are manufactured in different ways, related to the material of the single component:

- plastic components are made using vacuum-forming, injecting moulding and extruding;
- endoskeletal prostheses, pylons are die-cast. In this process the metal (titanium or aluminium) are forced into a steel die of the proper shape;
- wooden pieces can be planed, sawed and drilled.

At the end of the manufacturing of each component, all of them are put together by a prosthetist's technician using such tools as a torque wrench and screwdriver. After that, the final adjustment on the custom-made limb are then made. (Artificial Limb s.d.)

3.3 Endoprosthetic implants

Endoprosthetic implants are of fundamental importance in improving the quality of human life. In the last decades the demand for endoprostheses is rapidly increasing due to the fact of an aging population and associated issues of osteoporosis and osteoarthritis.

The manufacturing of these bioimplants requires both knowledge of mechanical and biological engineering and also the integration of multiple processes related to the selection of the material itself and the actual production.

3.3.1 The manufacturing process

The increasing number of endoprosthetic devices required and the related expansion of the market has brought new challenges to the product quality and manufacturing efficiency. Also the requirements regarding precision and complexity of the structure are becoming more stringent and this makes appear the limitations of conventional fabrication process. For these reason, today, for the whole manufacturing chain, which involves the integration of multiple process, each process has equal importance.

The process involved in the manufacturing of an Endoprosthetic implant are essentially four: material selection, forming processing, surface finishing and evaluation of finished products.

3.3.1.1 Material selection

The first stage in the manufacturing of a bioimplant is the selection of the material. In biomedical application, more than other field of application, this choice is critical both for the long-term success of the implant and for the health of the patient.

Materials are considered acceptable if they met the following requirements:

- first of all biocompatibility, non-toxic for the patient;
- the implant must be able to resist at corrosion and wear, taking into consideration also the chemical and physical conditions in which it operates;
- the bioimplant needs suitable mechanical properties in order to have the right fatigue resistance;
- the manufacturing process should be economically suitable, from an industrial point of view.

Materials such as ceramics, metallic alloy (titanium-based and cobalt-based alloy) and polymers have been analysed and they are considered acceptable; each one of them presents some criticalities and some strengths that have been already mentioned in chapter 2.

3.3.1.2 Forming processing

After having selected the right material for the bioimplant, the second stage consist of the fabrication itself. We can classified the fabrication techniques in pre-fabrication of forming and post-fabrication of surface finishing. At present, there are several processes for forming orthopaedic implants which are capable of precise controllability, the most common ones are: wrought, cast and powder metallurgy.

Wrought technique accounts for the 70% of the market of titanium alloys because it is capable of realizing products with high purity by

Cobalt-base alloys	Ti&Ti-base alloys
Designation	
ASTM F-75	ASTM F-75 (ISO 5932/II)
ASTM F-799	ASTM F-136 (ISO 5832/II)
ASTM F-1537 (cast and wrought)	ASTM F-1295 (cast and wrought)
Principal alloying elements\% (mass fraction)	
Co(bal.)	Ti(bal.)
Cr(19–30)	Al(6)
Mo(0–10)	V(4)
Ni(0–37)	Nb(7)
Advantages	
Wear resistance	Biocompatibility
Corrosion resistance	Corrosion
Fatigue strength	Minimum modulus
	Fatigue strength
Disadvantages	
High modulus	Power wear resistance
Biocompatibility	Low shear strength
Primary utilizations	
Dentistry castings	Used in THRs with modular (CoCrMo or ceramic) femoral heads
Prostheses stems	Long-term, permanent devices (nails, pacemakers)
Load-bearing components in TJR (wrought alloys)	

Table 1- Characteristics of orthopaedic metallic implant materials (Kang s.d.)

eliminating hydrogen and other volatilities through carrying out several melt cycles. Thermomechanical treating bestow the final shape to the wrought bioimplant. This process is widely used for making stem of prostheses for load-bearing joints, such as hip and knee.

Casting technique is widely used for the production of Co-Cr-Mo (Cobalt, Chrome, Molybdenum) components and it takes shorter working period. Lin et al. revealed that the casting technique is the primary cause of the fatigue crack.

Powder metallurgy (PM) is one of the type of rapid solidification process, it can be used in the realization of bioimplants because it allows fine microstructure and isotropic mechanical properties. It results particular interesting in the production of orthopaedic prostheses because it is able to conjugate both small and large pores in the product by adjusting processing parameters such as powder size, temperature and pressure, an important characteristic because it promotes bone growth.

The disadvantages of wrought and cast techniques are both economical and mechanical. From an economic point of view both of them are time-expensive and require long and complex post-treatment. Moreover the bioimplants produced with wrought and cast are not enough porous and present the issue of the *stress shielding*. Research focuses the attention on powder metallurgy technique, which can solve both these reason. On the other hand it has some issues regarding the dimension of the target to powder and also the pre-treatment to which the powder should be subjected.

3.3.1.3 Surface finishing processes

When the raw bioimplant is completed it is of crucial importance that the surface of the implant is of really high quality. It is obtained by consecutive finishing steps which levelled roughness peaks and polishing prostheses surface. Precision grinding and polishing processes are more difficult every time in which the surface of the implant is not regular, such as is the knee implant which presents partly freeform surface and complex geometry. Due to this complexity it is estimated that this phase of the process typically accounts for 10%-15% of the total manufacturing cost.

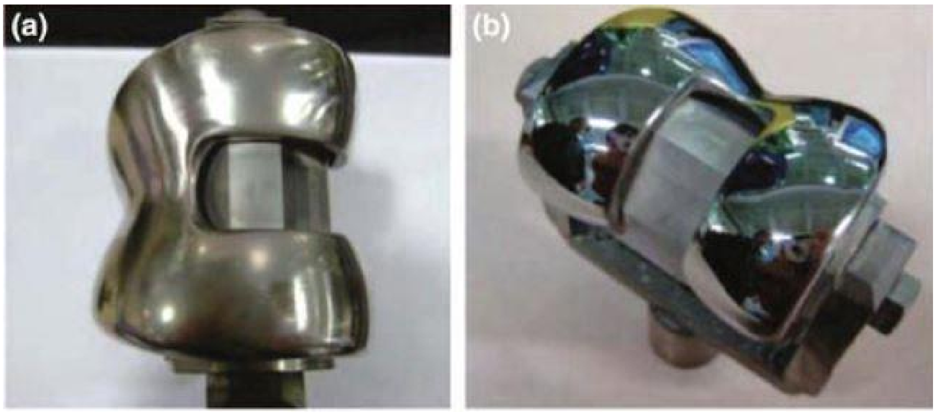

Figure 21 – Surface knee prostheses before (a) and after (b) polishing (Cheung C s.d.)

3.3.1.4 Precision measurement

The last stage of bioimplant production is the evaluation of finished product both for providing information in case of failure and for the predicting future performance. The measure of interests are: the metrology of implant surface, which is crucial in the process of integration with the bone, and the contact and non-contact measure because it is relevant for the lifespan of the implant and the mechanics of the patient.

The most common used techniques in this field are:

- conventional 2D imaging carried out through optical microscopy or scanning electron microscopy (SEM) with the limitation of analysing at only two-dimension;
- coordinate measuring machines (CMM) which is able to analyse free-form product, such as knee implants, thanks to a probing system. The CMM process consists of four sequential tasks of which the probing is the core;
- scanning probe microscopy (SPM), is uses a working principle similar to the one of CMM, with a sharp tip which having contact with the analysed area and can create damages on soft surface showing distorted images. This issue is solved with the non-contact mode which makes possible to observe restricted working area with high resolution;
- optical profiler uses a light beam to scan the workpiece, it has the good advantage of the non-contact with the surface and so it avoids possible damages, on the other hand it is not able to provide the same accuracy of the other methods. (Kang s.d.)

3.4 Conclusion

The manufacturing process of endoprostheses implant is challenging in all of its stages. It is necessary to interconnect mechanical engineering and biomedical engineering and also the knowledge of biomaterials. This interdisciplinary process requires important resources and continuous research.

As regard biomaterials the most promising ones are titanium and cobalt alloys, the privileged and most promising forming process is to powder metallurgy (even if nowadays processes based on additive manufacturing, which will be covered later, show enormous promises) and the surface finishing is moving to sub-micron precision and nanometre surface roughness.

Chapter 4

4. Additive manufacturing technology

4.1 Introduction

3D printing is the fabrication of three-dimensional objects through the deposition of a material by using a print head, nozzle, or another printer technology starting from a 3D digital model.

The term is often used synonymously with Additive Manufacturing (AM), even if it is just one of the several processes belonging to the field of AM, defined as a process of joining materials to make objects from 3D model data, usually layer upon layer, as opposed to subtractive manufacturing methodologies. Other synonyms are "Additive Fabrication", "Additive Processes", "Additive Techniques", "Additive Layer Manufacturing" and "Freeform Fabrication".

3D printing is today, within Industry 4.0, the most disruptive digital technology, able (potentially) to overturn traditional production paradigms. This is a real revolution, since production no longer takes place by removing material from a solid, but starts from a 3D (virtual) model and then "prints" layer by layer, exactly (or almost) as happens in the common ink printers that we have at home or in the office. A revolution that connects and integrates with the processes related to Smart Manufacturing and IoT.

Needless to say, Additive Manufacturing is definitively changing the way companies work, relying on it as a tool for rapid product development. After more than twenty years of research, development, testing and use, more and more industries are embracing AM technologies, and we expect they will keep growing in the future.

4.2 History of 3D printing

3D printing process is nowadays familiar to all, but the origins and the history of this technological revolution are unknown to the most.

The first man who contributed to the begin of this technology was the Japanese Doctor Hideo Kodama of Nagoya Municipal Industrial Research Institute; he invented the first single-beam laser curing approach. Doctor Kodama applied for a patent for his rapid prototyping system in 1981 in Japan: in his system UV light hardens a photopolymer material and build up the model layer by layer. His work brought him to conceive the ancestor of stereolithography (SLA), which was developed by Chuck Hull in the following years.

In the 80s Mr. Chuck Hull had been working as employee for a company that used UV light to put thin layers of plastic veneers on tabletops and furniture. He was upset to the fact that the production of small plastic parts could take up to two months, and it is a huge amount of time. Therefore, he suggested the company a different use of UV lamps: by overlapping thousands of thin layers of plastic on top of each other and then engraving the shape by using UV light, there would have been the possibility to form 3D objects. Through his work, Mr. Chuck Hull developed a system in which the light was shone into a vat of photopolymer (a material that turns from liquid into plastic-solid after being hit by light) and etched the shape of one level of the object, keeping it up this way until all the layers are printed. This technology was then patented with the name of "Apparatus for Production of Three-dimensional Objects by Stereolithography" in 1986. Later on, after the issuing of the patent, he founded his own company: the 3DSystems, a company still firmly at the top of the sector. They gave birth to the first commercial example of rapid prototyping, the SLA-1 in 1988, which gave an important shock among automotive, aerospace and medical companies. Nevertheless, it was the SLA-250 the first model to be sold to the public.

In the same years, an undergraduate at the University of Texas patented another 3D printing technology: the *Selective Laser Sintering* (SLS), a process similar to previous one, but with the substitution of the resin with the Nylon which is a liquid with a powder. As the powder is a solid, it does not need supports, so it has a number of practical advantages.

Carl Deckard called his machine Betsy; even though it was not able to produce objects with complex details and good quality, it was a success because its aim was to test the idea for the SLS. Its main feature consists of powder grains fused together locally by a laser. However, four years must pass before the startup DTM (today merged with 3D Systems), in 1992, produced the world's first SLS machine.

In the meantime, Scott Crump submitted a request for patenting the *fused deposition modelling* (FDM) in the US. This technology substituted the laser and the powder and used melted plastic to "spread" layer by layer depending on the object.

In 1989 he and his wife co-founded the Stratasys company, that is one of the market leaders for high precision 3D printers. The FDM is now the simplest and most common technology and, after the patent was issued in the 1992, the first industries to take on the technology was medicine.

In the 1993 it was the turn of the MIT – the Institute of Technology based in Boston. The technology developed allowed to print in colour, up to a maximum of 28 different colours. It was defined as "Three dimensional printing" and in addition to printing in colour, it was a useful and expensive technology for printing objects that are very faithful to reality.

Only in the 1995 comes the possibility of printing real solid objects, with high density that had little to envy to traditional industry. Thanks to the Germat of the Fraunhofer Institute and their *Selective Laser Melting* it was possible to melt metal powders and obtain objects with a density of 98%. The 99% of density was achieved is 2002 with the *Electronic beam melting,* or electronic beam fusion, which is a technology by which a high energy source, composed by an appropriately concentrated and accelerated electron beam, strikes a material in "micro granulometric" form causing its complete fusion.

The turning point comes in 2005 with the *RepRap Project*, which stands for *Replicating Rapid Prototyper*. It is worth mentioning because it is the first completely opensource project, free and downloadable from anyone. It is oriented to the development of cheap and Do-It-Yourself (DIY) solutions for the hobby and domestic 3D printing, by using a variation of FDM technique. This project is based on the idea of giving the printers the possibility to print their own parts necessary to make a working clone of the original printer, by trying their hand at rebuilding their 3D printer; this way of acting, makes potentially obsolete the economies of scale logic in the field of goods production.

Two years later, in 2007, a spinoff of the Dutch Royal Philips electronics was born: the *Shapeways*. It is a service which consists of a network of 3D printers, to which all printers can affiliate, with which the company guarantees a 3D printing and shipping service all over the world. Today, therefore, each person can make use of rapid prototyping using a 3D printer even if he does not possess a 3D printer; this is possible thanks to the Opensource ides that leads behind this service: with the RepRap project and thanks to the capillarity and development of the network, the frontiers have been completely opened up.

Another important year for the development of additive manufacturing technique was the 2009, the year in which the *MakerBot* was founded by Bre Pettis, Adam Mayer, e Zach "Hoeken" Smith. They started from RepRap and simplified it, they provide the service of open-source DIY 3D printer. The result they reached was the first printer that could be purchased in an assembly box and a built with the hand of the owner at an affordable cost. This was the exact moment in which 3D printers became accessible to the general public.

In 2010 we start talking about *Contour crafting* and collaborations between NASA and the world of 3D printer. Contour crafting is the three-dimensional printing that uses cement as a printing material. NASA has made its appearance in the affair, stating that in the future houses will be built on Mars with this system, because it is extremely reliable - if we think about it, machines are hardly wrong and above all they are able to work continuously even in extreme conditions.

Another company worth mentioning is Formlabs, founded in September 2011 by Maxim Lobovsky, Natan Linder and David Cranor. The three students of the MIT Media Lab had the idea of projecting and developing a 3D printer based on three pillars: desktop-sized machine, easy to use and affordability of cost. In October 2012, Formlabs passed history becoming the highly funded crowdfunding projects of all time, raising almost 3 million dollars in Kickstarter campaign, money then used to produce its first machine, the FORM 1 3D Printer; this was the first of a series of photopolymer-based desktop printers after the expiration of stereolithogaphy patents.

Nevertheless, in November 2012 Formlabs was sued by 3D Systems for the use of that technology and then it settled patent litigation in exchange for 8% of net sales.

The turning point for the mass-production of 3D products was in 2017 when new software, which led to manufacturers across various industries to form 3D printing farms, was developed. (HISTORY OF 3D PRINTING–3D PRINTERS ARE OLDER THAN YOU THINK! s.d.)

4.2.1 3D Printing in healthcare

The first use of additive techniques in biomedicine was in 1999. The potential of 3D printing in healthcare made its first foray when, at the Wake Forest Institute for Regenerative Medicine, a synthetic scaffold generated from human cells was developed.

In the 2000s, more precisely from 2005 and 2008, the orthopaedic sector starts to reap the benefits of the research in this field. In fact, the 3D printing community focusing on printing prosthetics and human aid tools for public use, in 2008 3D printed the first functional prosthetic leg. A year later, Organovo produced the first 3D printed blood vessel. (HISTORY OF 3D PRINTING–3D PRINTERS ARE OLDER THAN YOU THINK! s.d.)

A further step has been successfully taken towards regenerative medicine in 2016, thanks to the printing of the first human bones.

In conclusion, in order to have the whole picture, we may think that Charles Hull could not imagine how big it would get. Nowadays, we cannot predict the future but if we use the past as a guide, we can expect advances in 3D printing for medicine, engineering, space travel, and more.

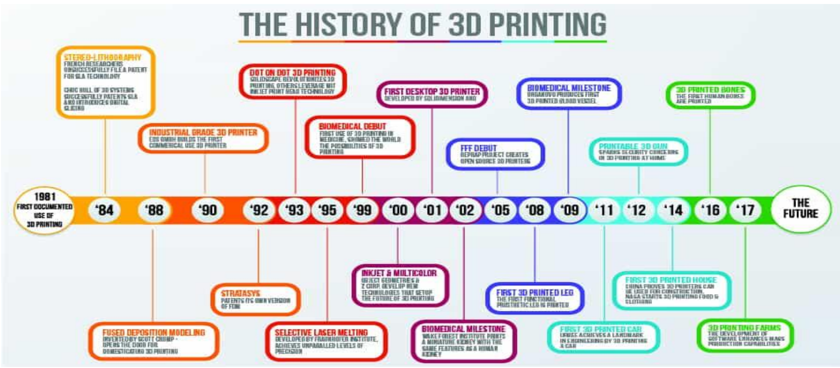

Figure 4-1 - History of 3D printing (HISTORY OF 3D PRINTING–3D PRINTERS ARE OLDER THAN YOU THINK! s.d.)

4.3 3D printing process

The process of creation of a 3D printed object, as has already been mentioned, can take place with several techniques. The most common technology is the FDM (Fused Deposition Modeling), given its low cost.

Now we focus merely on the general process. Starting from the design it brings to the final object and includes five many core steps: modelling of a 3D file, file creation and manipulation, printing, removal of prints and post processing. (Dalla modellazione 3D all'oggetto stampato: le 4 fasi che compongono il processo s.d.)

4.3.1 Modelling of a 3D file

The first stage in the production of a 3D printed object is the realization of a 3D model through a CAD (Computer Aided Design). After having identified the object to print, it is necessary to define the points which identifies the geometry of the object in a cartesian system, and drawing their exact position. This stage is used to produce a realistic model of the object that can be used in order to perform function tests and simulations, reducing time and cost workflow.

It is possible to identify three main kind of CAD software available nowadays, and the more appropriate one is determined by the typology of the printing object:

- Solid modelling
- Sculpting modelling
- Parametric modelling

4.3.1.1 Solid modelling

Solid modelling is a method used in engineering and architectural sphere making possible the realization of 3D model of any geometry. The CAD design takes place through the so called CGS, which creates complex objects starting from primitive geometric shapes such as cube, sphere and pyramid. The software today available for solid modelling are:

- Solidworks: it is in the market since 1995 and it is used for mechanical complex object;
- SketchUp: it is a @Last product and it is oriented to urbanistic and architectural design;
- Rhinoceros: it is used for free form modelling thanks to the use of NURBS (Non Uniform Rational B-Splines) which is able to realize any geometric entity even the most complex ones. Rhinoceros is the best practice in automotive and naval design and it is also used in the medical field;
- AutoCAD: it was realized in 1982 from Autodesk and it is today used in architectural and electrotechnics industries.

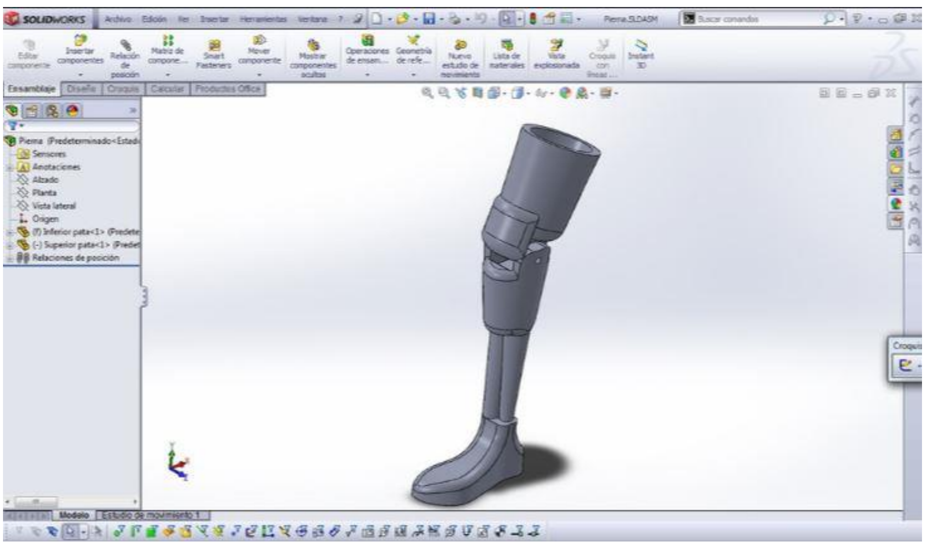

Figure 23 – Artificial limb model in Solidworks (David s.d.)

Anyway, software such as Rhinoceros and SketchUp have some additional tools which make them possible to also perform sculpting modelling.

4.3.1.2 Parametric modelling

Parametric modelling uses both additive and subtractive methods which by combing objects is able to realize a very precise model of the analysed object. Is performs its activities through scripts in which mathematical information about the object are contained. The leading software in the market are:

- <u>Grasshopper</u>: it is a plugin of Rhinoceros, easier due to the fact that it does not require scripting knowledge;
- <u>Openscad:</u> this CAD software is able to read some scripts and, starting from them, to realize the 3D model of the object. It requires familiarity with scripting languages;

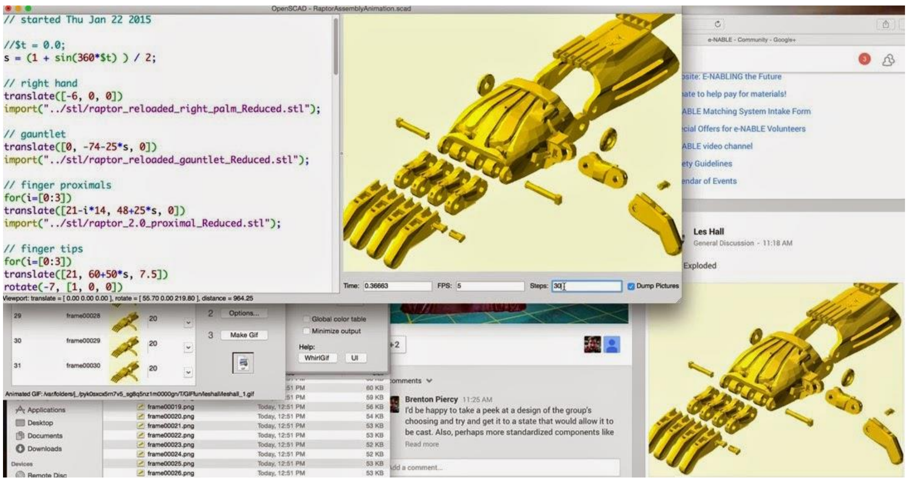

Figure 24 - Openscad hand mondel (Pearce s.d.)

4.3.1.3 Sculpting modelling

Sculpting modelling is the method used in all these cases in which the object has a lot of details and the surface is not regular for example faces, jewels and *natural* or *organic* objects. It takes it's name from the methodology used: starting from primitive geometric forms, the removing of material brings to the desired object. The CAD software able to perform this work are:

- ZBrush: it is a software for sculpting modelling, in the market since 1999. It is able to capture information about materials and colours and to create more realistic model;
- Scultpris: a more recent software release for the first time in 2009. It is used in sculpting modelling.

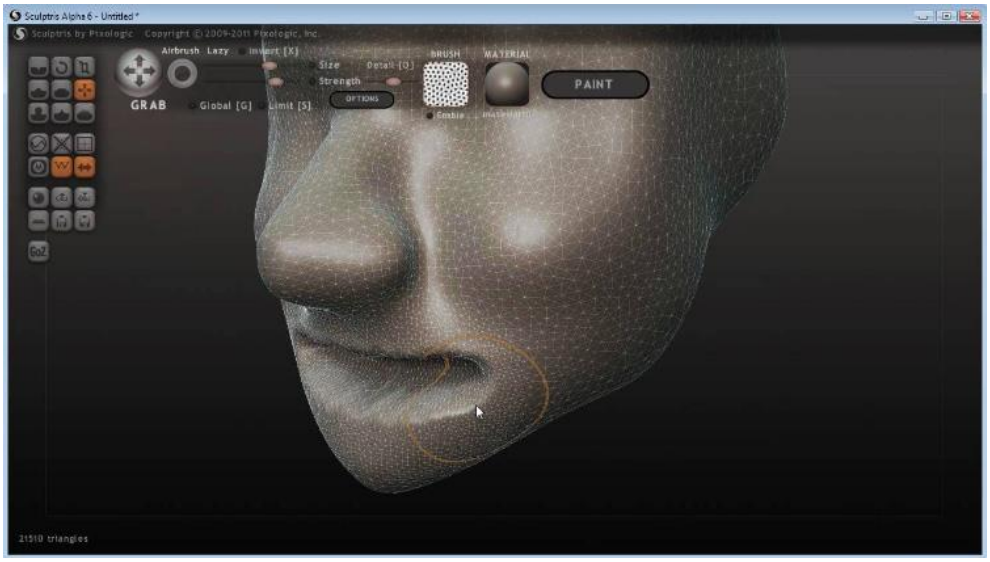

Figure 25 - Sculptris face model (Petty s.d.)

All of these methods and software are useful to create the model of an object *ex-novo* for example for architects for realizing the model of a construction, for engineers to design the shape of car.

However sometimes it is useful to start from an actual object and, by performing reverse engineering, generate the 3D model. Reverse engineering makes possible to know how a product is manufactured by disassembling it in all of its parts and then digitalizing in a 3D file. There are essentially two methods to perform reverse engineering:

- Physical measuring: it consists in measuring all the dimension of the object and then reporting it into a 3D software for modelling the object. This process can be done in two different ways, both of them requires physical contact. Coordinate Measuring Machine (CMM) is performed by a sensor which, touching each point of interest of the object, understands its characteristics and compares them with a 3D model. It is more focused on verifying parts dimensions rather than obtaining a 3D file, but it potentially could. It represents the more accurate method nowadays. Manual Measurement, instead, consists of measuring the object manually and then make a 3D file in some CAD

Figure 26 - CMM stand-alone machine

software. It is a low cost method but of course the more time-expensive.

- 3D scanning: this method allows to obtain a 3D model of the observed object without having any contact with it. Also in this case two different technologies are used and are: Laser Scanning which uses the laser technology as the name said and CT Scanning which uses X-Ray technology. The first one generates a beam laser which is able to obtain data from the object and create a 3D model of the object surface. The latter one, instead, realizes the 3D model starting from 2D images. The CT (Computer Tomography) scan rotates around the object: the detector creates images by capturing the photon beam emitted by the source. Both the surface and internal geometry are impressed and, in the end, all the slice are put together by an algorithm which generates the 3D model.

  It is also used in archaeology because it allows to obtain precious data without physical damaging the object of analysis.

Figure 27 - CT scan of a mummy (John s.d.)

4.3.2 File creation and manipulation

After having realized the 3D model by using software tools, it is possible to export the file to the printer, but it is necessary that this file is in a format that is readable from the printer. It is thus necessary, that the file is converted in one od the following format, depending on the technology:

- STL format: it stands for Standard Triangulation Language and it is in binary or ASCII format. The STL file compose by a solid which is the result of the aggregation of multiples triangles and each one of them is defined by the (x, y, z) coordinates of its vertex. It is simple and used especially in rapid prototyping;
- STEP format: Standard for Exchange of Product Model Data allows exchange, memorization and transfer between systems in a coherent way. It is structured as a series of different documents called STEP each of them posted separately;
- STEP NC Format: it is an extension of the previous one and it allows more materials and multiples geometries;
- VOXEL BASED format: the voxel is just a pixel added with the third dimension and it represents the smallest observable volume in space. Each voxel is characterized by colour and material, features that are represented in a scalar value. The conversion of a CAD file into a voxel is called *voxelization*;
- 3MF format: it stands for 3D Manufacturing Format and it is an XML file with all the information of the objects, not only colours and materials but also texture and mesh. It presents itself as a file which has no more the need to be converted, driving the process

since the beginning with no risk of losing information. (Gualdo s.d.)

The most common format is the STL one and, after having created the 3D model and having converted it in STL format, the file is ready to enter into the printing machine.

4.3.3 Slicing phase

The STL file needs to be subjected to the so called slicing process which consists in dividing the model into several slice and then the machine evaluates how to print each slice. The process is enabled by the so called CAM (Computer Aided Manufacturing), which converts the STL information into G-Code, a language that the printing machine is able to decode. Now, the printer is ready to work.

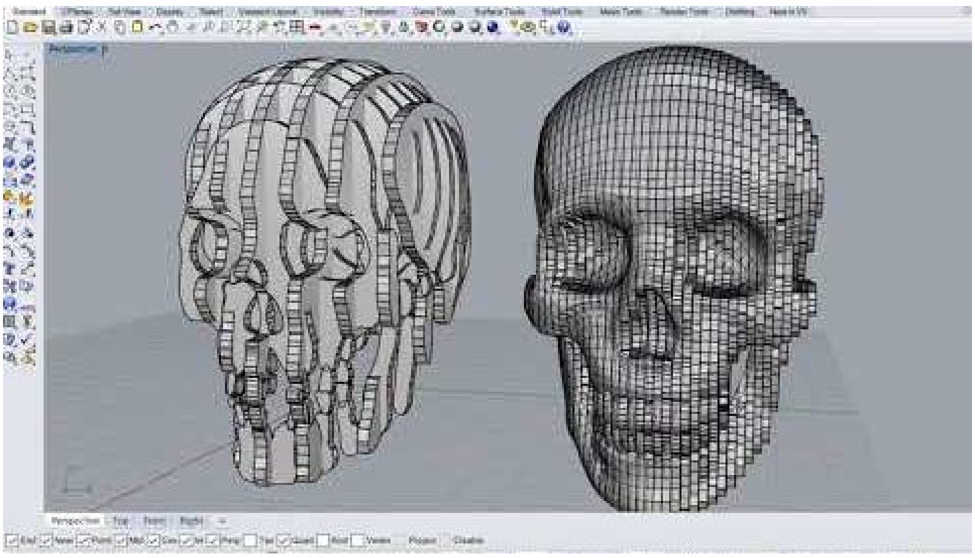

Figure 28 - Sclicing phase

4.3.4 Printing phase

The printing phase is almost automatically. Once that the printer is correctly settled it will first read the STL file and then will start to stretch out the material which, layer by layer, will create the object. The creation of the object takes place horizontally and each layer, physically converted from the slice, is about 0,11 mm; this means that proportionally to the dimension of the object the printing phase can take from hours to days. Hence, it is useful to have some client software which is able to check all the process in real time.

4.3.5 Removal of print and post processing

Both the removal of print and the post processing phase are different in relation to the additive manufacturing technique used in order to produce the product. Sometimes both of them are simple and do not require particular skills; other times, instead, there are some technologies which require an approach typical of a technical expert.

4.4 AM technologies

After having identified all the stages of the general AM process it's now time to go more in depth to the printing phase, analysing the different technologies available today.

In 2015 the ISO/ASTM 52900 Standard was created with the aim of create a well-defined classification and a common recognized terminology which unify the AM domain. It established 7 main categories of AM process which stand out for the underlying technologies.

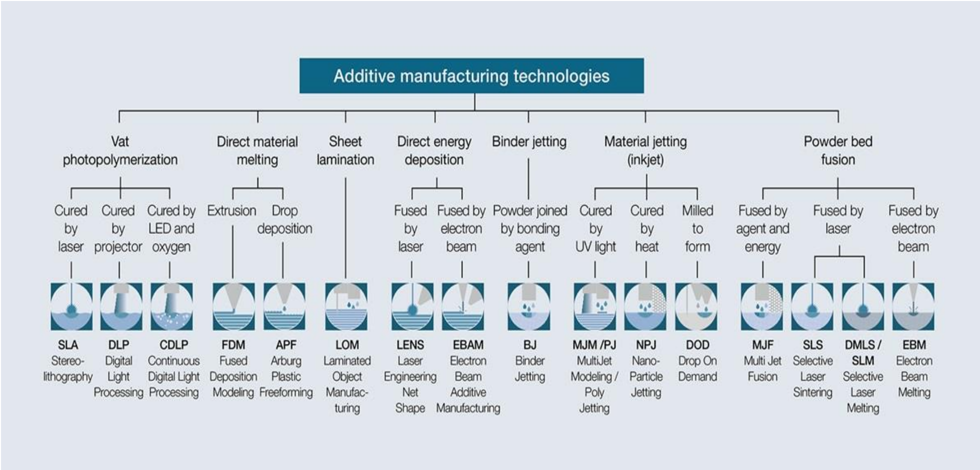

Figure 29 - Overview of the main AM technologies in industrial sector (Qaud s.d.)

The choose of using one technology in respect to another one is primarily related to the properties and functions of the object to produce, and secondly but not less important, to the material: polymeric or metallic one.

4.4.1 Powder bed fusion

The powder bed fusion is one of the two families of techniques which allows the AM of metallic materials, together with the direct technique. It uses a laser beam as a source of energy to concentrate in a small spot in order to obtain high energy density (so high solidification rates) which induces the fusion of the powder bed that then become solid. The powder bed fusion is able to deal with both metal materials and polymer, in particular the latter can be used with

SLS (Selective Laser Sintering) and SHS (Selective Heat Sintering). For metals, instead, we can find Direct Metal Laser Sintering (DMLS) and Electron Beam Melting (EBM). These techniques will be described more in depth in the following chapter.

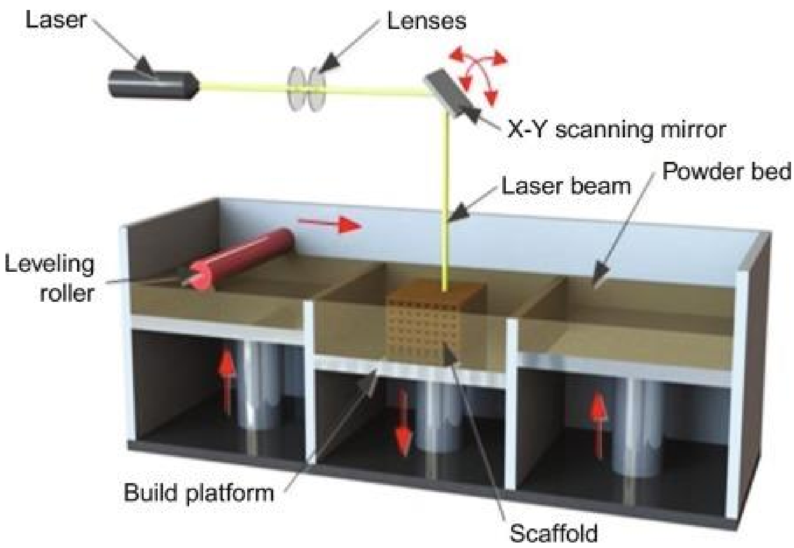

Figure 30 - Powder-bed fusion process (C.Vyas, et al. s.d.)

4.4.2 Direct energy deposition

Direct energy deposition technique allows the printing of metallic materials. It is similar to the powder bed fusion, but it differs in the positioning of the materials: in this case the material is not positioned in advance but it is released moment by moment by a nozzle, similar to the one which issues the source of energy. The source of energy can be a laser beam, an electron beam or a plasma arc which fuses the material.

This positive aspects of this technique are principally the fact that it can be used is different axes, eliminating the horizontal creation of the object, and the possibility to use concurrent materials. Nevertheless the most relevant drawback is represented by the cost that is expensive.

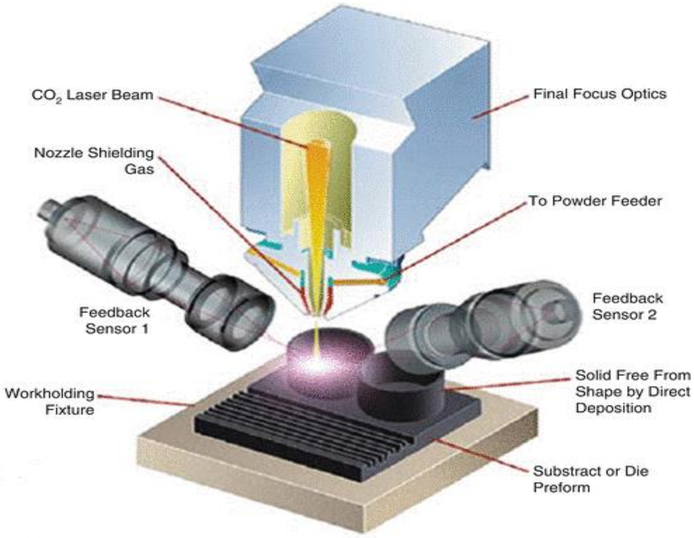

Figure 31 - Direct energy deposition process

4.4.3 Vat photo polymerization

It is the first additive technique that was invented and patented by the father of additive manufacturing Charles w. Hull in 1986.

Vat photo polymerization is an additive technology in which a liquid photopolymer resin is hardening by a UV light. Due to the fact that the material is liquid is it necessary to add some structural support. it is able to create product with dimensional accuracy also for object with an high level of detail, but on the other hand its products have no durability due to the fact that they are made by photopolymers.

4.4.4 Material jetting

Material jetting technique is similar to the one used by 2D printers: the material (only polymeric material) is issued by a nozzle which moves horizontally and it is deposited layer by layer on the surface of the printed object. The polymer is then hardened under UV light.

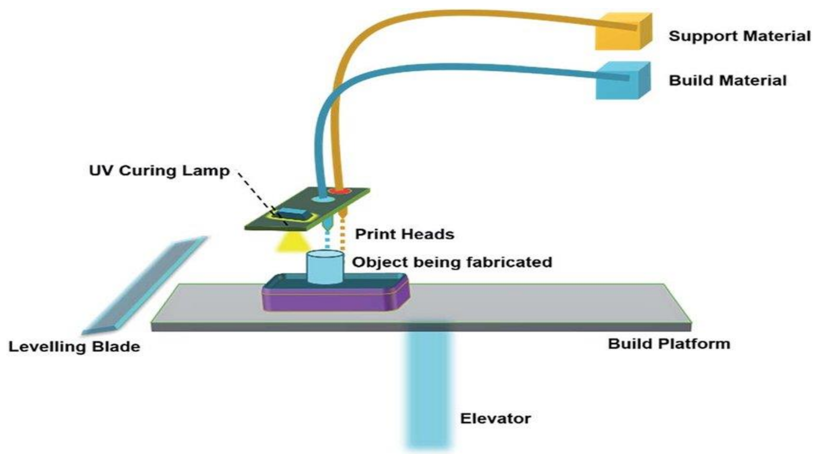

Figure 32 - Material jetting process

4.4.5 Binder Jetting

The binder jetting process is copyrighted under the name of 3DP technology. The process needs two different materials: the binder, which acts as a bonding agent and it is usually liquid and a polymer, which is the powder based material. The nozzle moves horizontally and for each layer of polymer there is one layer of binder one.

This process requires an accurate post processing and does not guarantee high structural performance.

4.4.6 Sheet lamination

Sheet lamination process produces objects that are used for aesthetic purpose with no structural use. The object is obtained starting from sheet of metals combined together by ultrasonic welding; another possibility is to use paper as building material and in which welding is substituted by adhesive.

4.4.7 Material extrusion

Material extrusion is the most artisanal way to produce object with additive technique, in fact it is used in most domestic printer. The object is created layer by layer by the material issued by a nozzle which moves horizontally.

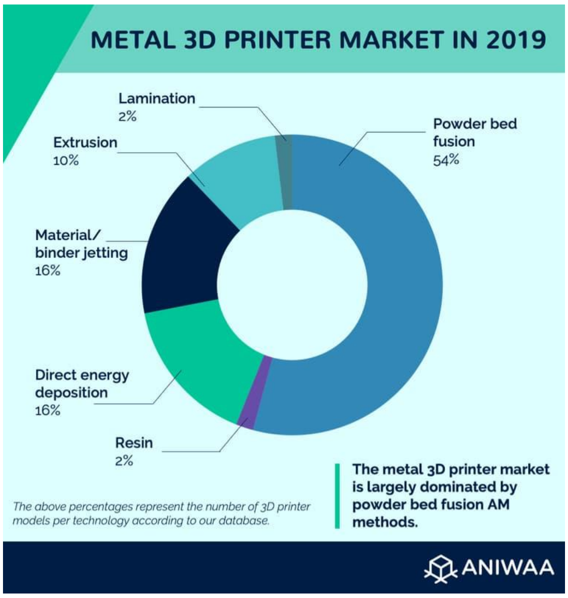

Figure 33 - Metal 3D technologies market (Cherdo s.d.)

Among all the techniques described, as the graph above shows, the market of additive manufacturing for metallic materials is dominated by the powder bed fusion with a 54% of the market.

4.5 AM diffusion

At the beginning of this chapter we described the history of Additive Manufacturing, saying that the origins of this technology dates back to the '80s but now we want to investigate how the diffusion phenomenon of AM occurred.

The first stage is the identification of the type of innovation that Additive Manufacturing represents and then its performances and diffusion; by choosing the perspective of analysis of 3D printers' producers the AM diffusion phenomenon is indagate through s-curves and hype effect.

4.5.1 AM Innovation type

First of all we have to indagate what kind of innovation AM is. 3D printing is considered to be a product innovation because, in the market there were no machines with the same aim of 3D printers. Moreover, it is also a process innovation due to the fact that it completely change the process of production: instead of subtracting materials in order to obtain the desired object shape, it represents a new paradigm, a new way of manufacturing products.

According to the taxonomy for technological innovation by Henderson and Clark we can classify the additive manufacturing technology as a radical innovation: both underlying technology and product architecture change. It is easy to think that 3D printers are just an incremental innovation of 2D printers, nevertheless it is wrong: 3D printing gives life to a brand new product, it is not just the attachment of ink.

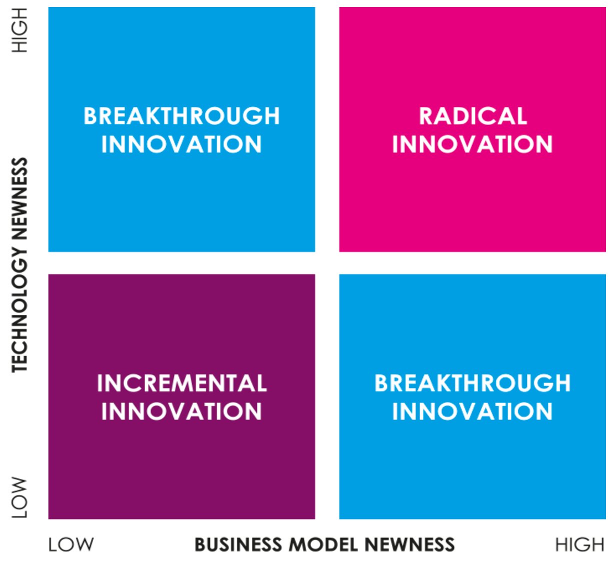

Figure 34 - The taxonomy by Henderson and Clark (Muckersie s.d.)

As consequence, the 3D printing technology represents a competence destroying innovation, given that existing firms which produce products in a traditional way are required to gain new and possible unrelated competencies and set aside their existing knowledge.

It is also possible to identify in additive manufacturing a disruptive innovation according to Christensen definition, because it has the power to disrupt, to totally change the market and its actor. A disruptive innovation changes the equilibrium of the market and is able to entirely turn the actors, for instance with market leaders which fall or exit the market and new entrants which achieve the leadership. In order for an innovation to be disruptive both supply side and demand side have an important role. Literature suggests three main reason for an innovation to be disruptive:

- inability of incumbent to join an emerging market, it is common that incumbents (manufacturers already in the market) are not able to switch to the new paradigm due to the sunk costs and the different competencies;
- also neglecting the emerging market is common among incumbents. This is explained by the Christensen effect according to which incumbents are focused on their business, they are aware of the performance of the new technology and keep look an eye on it, sometimes they also make R&D investment on it, nevertheless they tend to delay its introduction. This way of acting is myopic but its basis are "rational" and can be defined fear of cannibalization: a firm top management perceives in negative way the pursuit of a risky business models for a successful one.

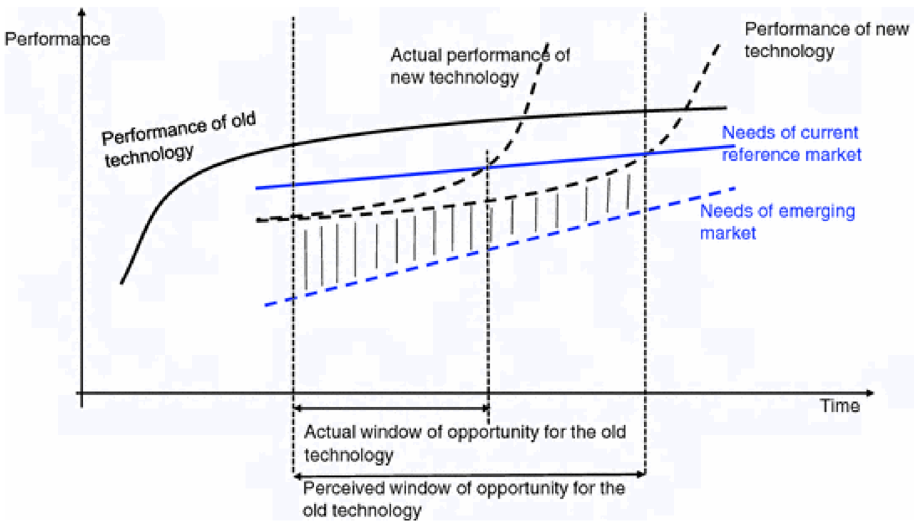

Figure 35 - The Christensen effect (Cantamessa M. 2015)

- incumbents and entrants have different goals, while the latter are concerned with survivor and with the minimization of the probability of failure, the former are focused on profitability, hence the maximization of NPV (Net Present Value). The different goals are reflected in the timing of entry of the two categories: while the entrants benefit from a sooner entry in the market, incumbents wait the moment in which the uncertainty of demand decreases. It is exactly the different timing of entry that creates the opportunity for the innovation to be disruptive.

For the incumbents, it is possible to delay the disruption of the new technology thank to the so-called sailing ship effect: the performances of the old technology could be increased creating a big gap between the performances of the old and the new technologies. The plateau of the old s-curve is not yet reached and the shift to the new one do not happen.

4.5.2 S-curves of 3D printers

When we want to depict how the performances of products in a certain industry change during time we have to follow a s-curve. Moving along the same s-curve an increase in the performance is due to evolutionary progress, while shifting to a new s-curve we face revolutionary progress. It is possible to see that every time in which we move from an s-curve to another the performances decrease, at the beginning. After that we have a rapid increase of them until the technology reaches the plateau and maintain constant its performances.

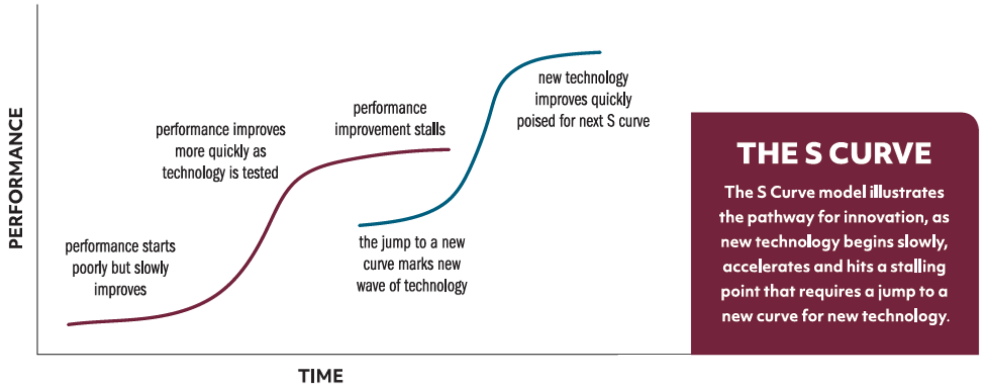

Figure 36 - S-curves model (Anderson s.d.)

An interesting point of observation is the one given by the cumulated adoption sales curve and the derivative of diffusion curve which represents the adoption sale curve.

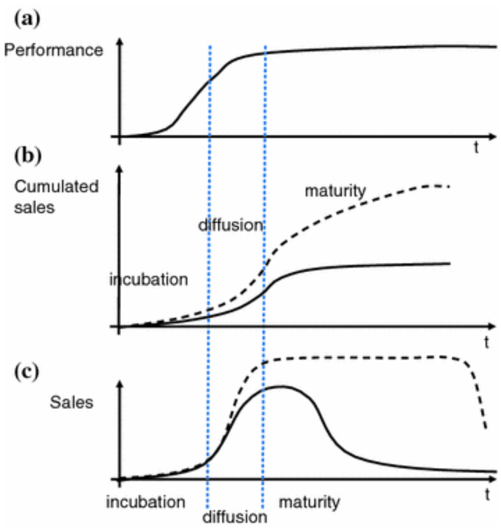

Figure 37 - Performance and diffusion s-curves (Cantamessa M. 2015)

By looking at these graphs it is possible to divide the diffusion of the technology in three different phases:

- incubation phase
- diffusion phase

- maturity phase

4.5.2.1 Incubation phase

Incubation is the first phase of technology diffusion: the performances are low but show an increasing trend, also cumulated sales and adoption sales are low this means that the adopters are a small number. This stage is quite critical, and AM has experienced this phase from ‘80s until 2000.

As Gartner consultancy has proposed, the incubation period is characterized by the so called Hype Effect which consist of a sequence of 5 phases, from its first appearing to its affirmation. The hype cycle of additive manufacturing is represented in the graph below by Gartner 2018 report. It is also reported the Hype effect graph of medical 3D printing from Gartner 2017 report.

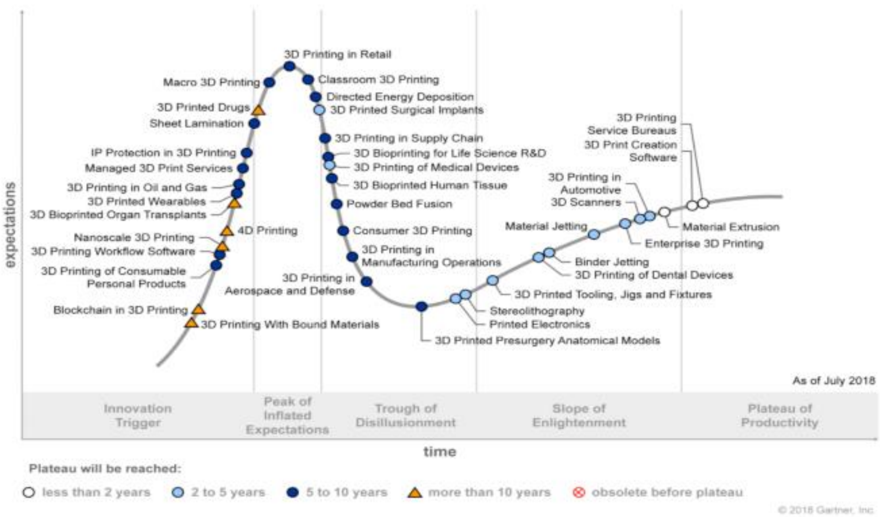

Figure 38 - AM hype effect (Gartner 2015)

In the first phase, *the technology trigger*, the new technology appears and market fall in love with it. The expectation about it continue to increase until reaches *the peak of inflated expectations* by having entered the industrial sector. At this point the technology enters a decline phase called *trough of disillusionment* in which the market loses interesting on it and dismisses it as a failure. It is at this time that the technology slowly matures and its realistic applications emerge in the so called *slope of enlightenment*, which is followed by *the plateau of productivity* in which the technology affirm itself.

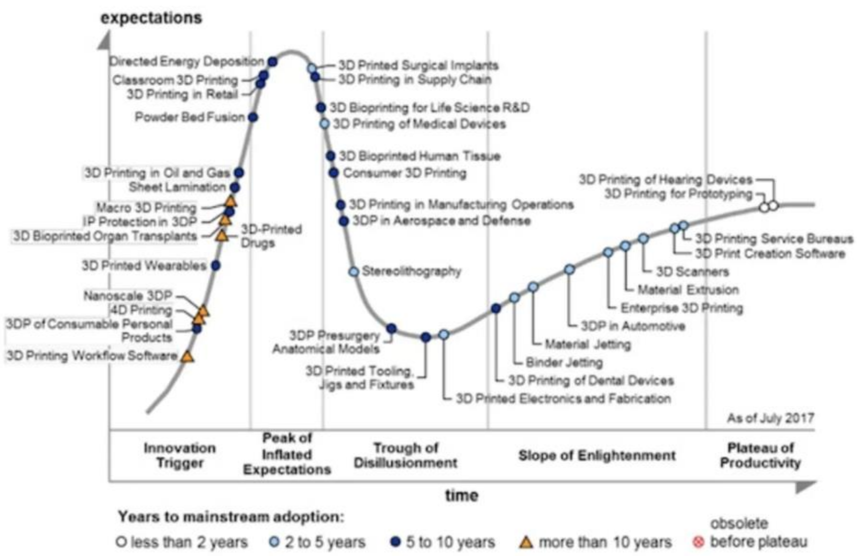

Figure 39 - Medical 3D printing hype effect (Gartner 2015)

4.5.2.2 Diffusion phase

AM is now in the diffusion phase: its performances are increased and also adoption sales do. The graph of metal AM system sales shows a rapid increase trend starting in 2013 and also the whole industry growth shows that gains continue to grow, evidencing a healthy industry.

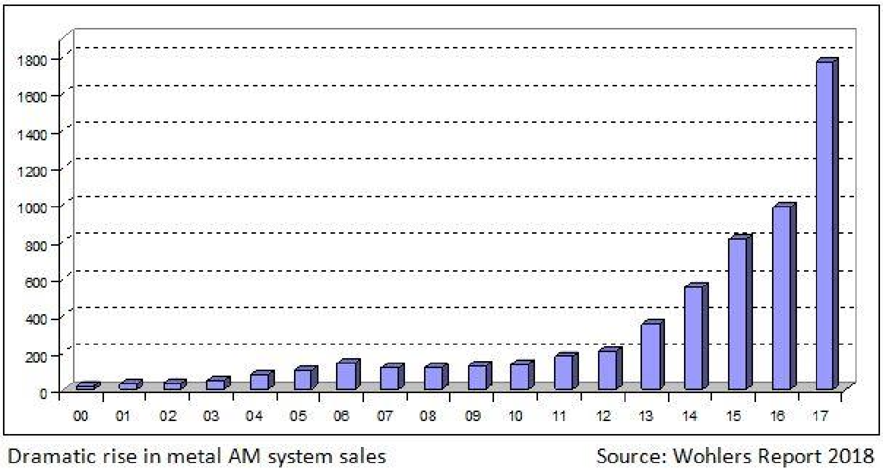

Figure 40 – Metal AM system unit sales

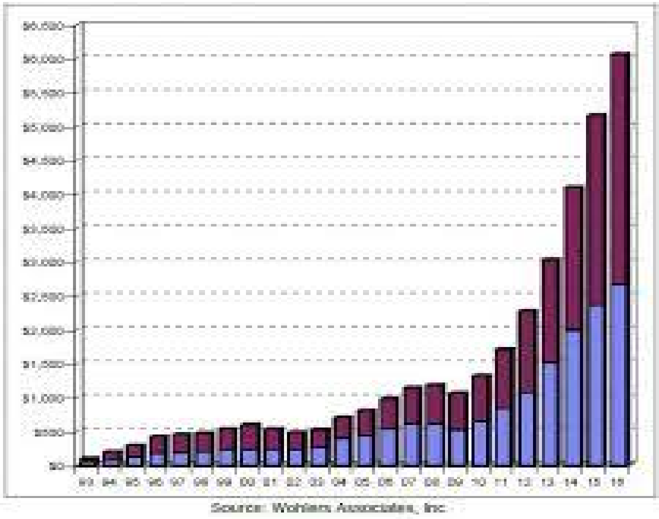

Figure 41 - AM industry growth

4.5.2.3 Maturity phase

The maturity phase will starts when the plateau of performances will be reached and so the technological limit of the 3D printers. In this stage, of course, since the technology has reached its limit it is important to focus firm's attention on marketing actions.

4.5.3 Additive manufacturing in medical technology

Additive manufacturing technology offers a great potential to medical technology manufacturers. The medical field, as reported by Wohler's report, is the one in which this technology can be widely applied with a 16% of market shares.

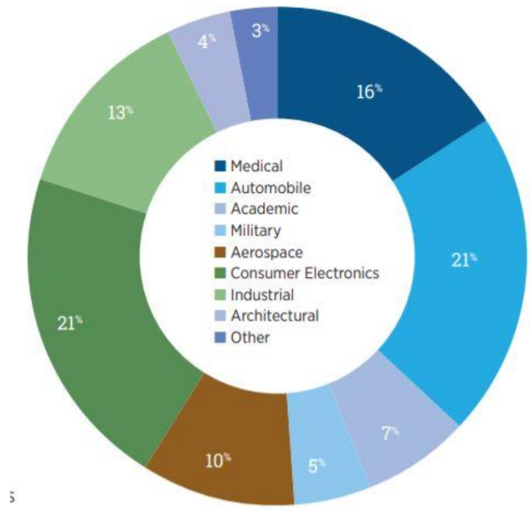

Figure 42 - Revenue split of additive manufacturing equipment customer (Fathers 2019)

Additive manufacturing is widely used for the production of medical implants, customized prosthesis and surgical equipment. Even if he market is growing fastly, it has to face stringent regulation due to the fact that medical devices are particularly mild products having to do with human body.

The main advantages that additive manufacturing technology bring to medical field are:

- First of all customization, that is really important in order to obtain more comfortable devices. Especially in reconstructive surgery or joint replacement it is extremely important. 3D printing changes the production moving from “mass production” to “mass individualisation”;

- Low volume and low cost production;
- Shorter supply chains which leads to reduced lead time. The production with 3D printers can decrease the lead time from 2 weeks to 48 hours. The production, in fact, is concentrated is a single site and it allows to eliminate the need for transportation and shipping. Moreover, the centralized structure can bring the producer closer to the customer, reducing supply chain minimising disruption;
- Complexity and variety of product. The more complex (the less solid) the product is the less costly it is. 3D printing also allows to realize a big variety of product with no substantial increase in cost of production. It is possible because, in order to do that it is necessary only to change the CAD file without any change in the production line;

Nowadays, however, the AM technology presents some drawbacks. The most impactful one is represented by the materials: they have to be biocompatible and the cost for them is really expensive. Moreover they are not recyclable, creating issues related to sustainability. Also the machine cost is high, especially for metal printing: the cost for one machine is about 300,000 – 1,500,000 euro.

Other drawbacks not related to cost are the one related to quality and reliability of the devices; as previously said the number of phases to perform to gain the finished products is high and often the quality control process is not acceptable. This also leads to the need for standards.

The speed of production is considered an advantage, but if the number of product increases approaching the mass production, 3D printer speed is not able to produce a such amount of products. This means that higher volume results in a slower production in respect to the traditional methods.

Chapter 5

5. Italian orthopaedic sector analysis

5.1 Introduction

After having acquired a general background on prostheses, the product, and on Additive Manufacturing, the technology, it's now time to analyse the Italian orthopaedic sector, the market in which the product and the technology are placed.

Due to the difficulty of finding data related to this specific sector, most of the data reported belong to the wider Italian medical devices industry, and when it is possible, they have been compared to Italian orthopaedic sector.

5.2 Italian Medical Devices Industry

The Italian medical devices industry is characterized by a large number of multinational firm that dominate the industry either at a national and international level. The sector includes two large segments: electromedical equipment (equipment for the imaging and ultrasound diagnostics, laboratory analysis equipment, pacemakers and defibrillators) and medical and dental instruments and supplies (prostheses, sutures, furniture for medical use, material medical-surgical, etc.); the sector of interest to us is the latter and it results in a more fragmentation with more specialized firms in respect to the former in which the concentration in extremely high with an increasing trend, due to the continuous M&A transactions involving multinational firm.

5.2.1 The sector in numbers

The entire medical devices industry in Italy consists of 3.957 firms, which employ more than 76.000 employees (CONFINDUSTRIA 2019). As already said, it is an heterogenous market in which small and highly innovative and specialized firms coexist whit big players.

The market of medical devices worth for 11.4 billion Euro, and it is strictly directed to the SSN (Servizio Sanitario Nazionale), the public health service, in the measure of 66%. It represents the 7.4% of the total public health expenditures, which is nevertheless below the average of the main European countries.

There is a total of 3.957 firms in the medical devices industry and more than half, the 53%, is constituted by manufacturing firms, only the 5% are services and the remaining part, the 42% is represented by distribution. The presence of such network makes possible the production and distribution of more than 1.5 million of medical devices per year.

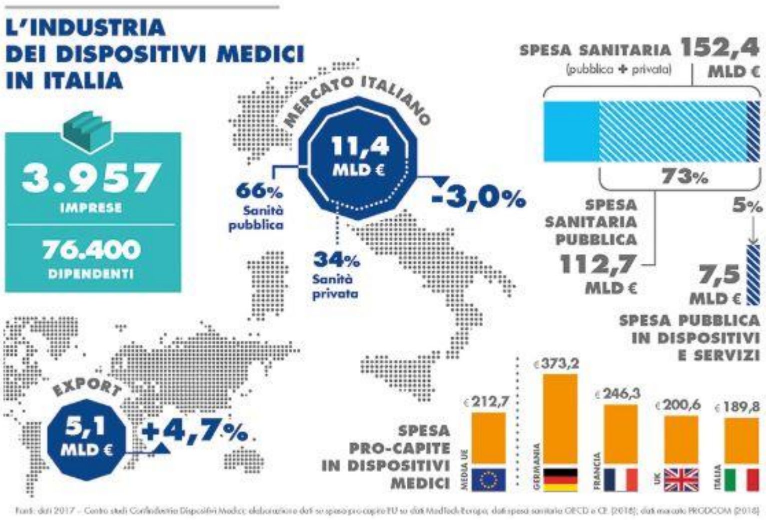

Figure 43 - Italian Medical devices Industry (CONFINDUSTRIA 2019)

Figure 44 - Medical devices firms (CONFINDUSTRIA 2019)

In the industry we can identify 8 main segment. The principal, in terms of numbers, is represented by the biomedical one, consisting in products such orthopaedic prostheses, pacemaker, stent, defibrillator which is the one of interest to us.

The production of orthopaedic prostheses, as already said, is included in the biomedical sector which accounts for the 44% of the total industry, with 1.743 firms active which creates a market of more than 5 billion of euro.

Figure 45 - Medical devices segments (CONFINDUSTRIA 2019)

In the last four years a significant number of start-up takes place in the industry; in the 2018, with a number of 334 the start-up represent the 8.4% of the total medical devices industry. Digital health is the more trod field, with a growth of 31 %, but it is interesting to say that the 1% of start-up deal with 3D printing.

The medical devices industry is concentrated in the north of the country, especially in two regions: Lombardy and Emilia Romagna, In Emilia Romagna is located the biggest biomedical hub of Italy and this means that the most innovative firms are located here. This is coherent, as we will see later, with the regional distribution of the firms covered in our analysis.

The central and southern areas of Italy are characterized by lower numbers both of firms and revenues. If we go deeper in the analysis we can see an high territoriality: the distribution of firms in the central area is not homogeneous at all, but almost the totality of the 760 firms (19 % of the entire national industry) is located in the province of Rome and Florence. The southern area is left behind with only the 15 % of the firms' industry active in these regions.

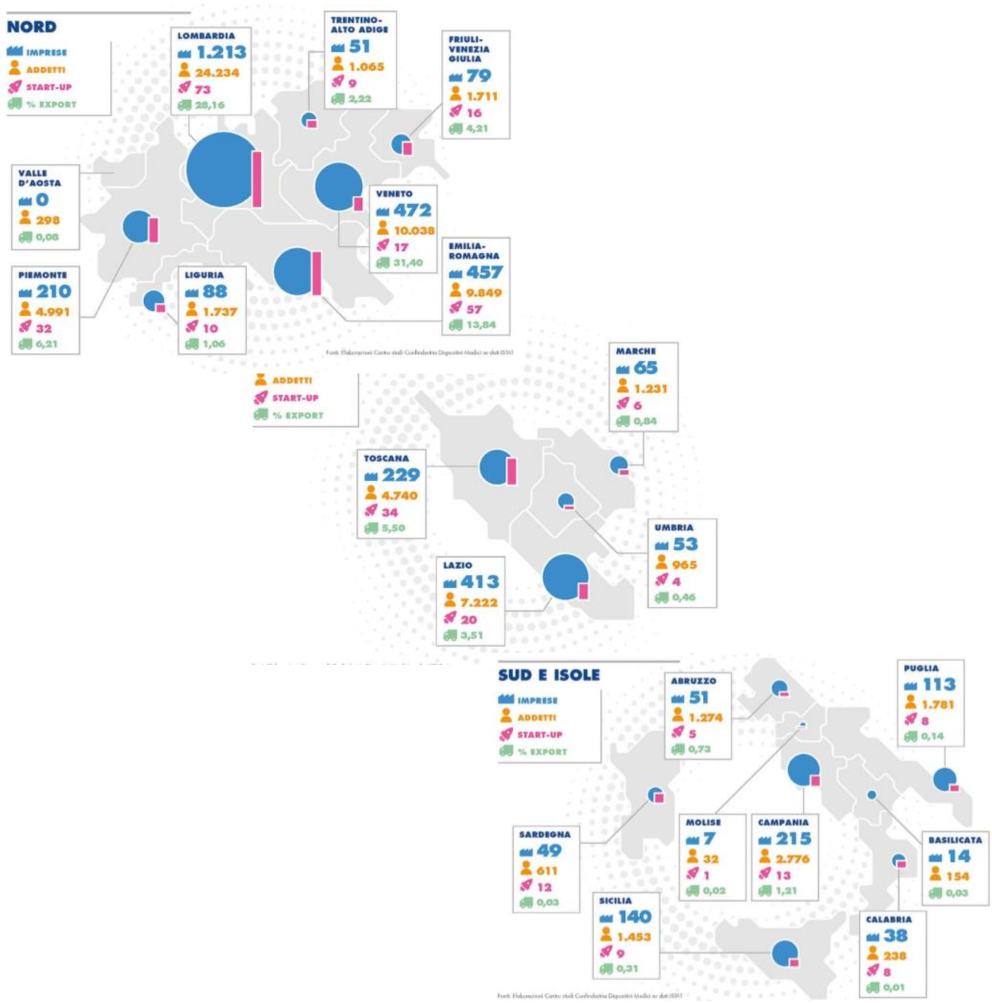

Figure 46 – Territorial distribution of companies, plants and people employed (CONFINDUSTRIA 2019)

In addition to territoriality, another characteristic of the industry is the highly degree of qualification of the employees. As reported by the CONFIDUSTRIA (CONFINDUSTRIA 2019), the 43% of employees have a degree and the 12% have been involved with research and innovation projects.

In the last years the Italian medical devices industry faced an increase between 4% and 5% in export, directed principally to USA, France and Germany, but also an increase in import between the 3% and 4%. This results in a considerable negative trade balance.

5.2.2 Medical devices demand structure

The demand of the Italian medical device industry accounts for the 66% in the public health service. By looking at the reports that the Ministry of health publishes each year, it is possible to understand the impact that the expenditures for orthopaedic prostheses has on the total public health expenditure.

In Italy the medical devices are classified, since the 22 September of 2005, with the use of the CND (*Classificazione Nazionale Dispotivi medici*) code. The CND identify a category of medical devices and it is made, at least, by one letter; going deeper into the classification some number follows the first letter. The category P identified the broader category of prosthetic devices. As reported in the *Ministero della Salute* report (Ministero della Salute 2017) the category P is the one which, with the 20%, accounts for most of the total public health expenditure. In particular, the expenditures for the category P09, the one of orthopaedic prostheses, is quantified in more than 425 million Euro and it is almost the half of the total, as reported in the figure below. (Ministero della Salute 2017)

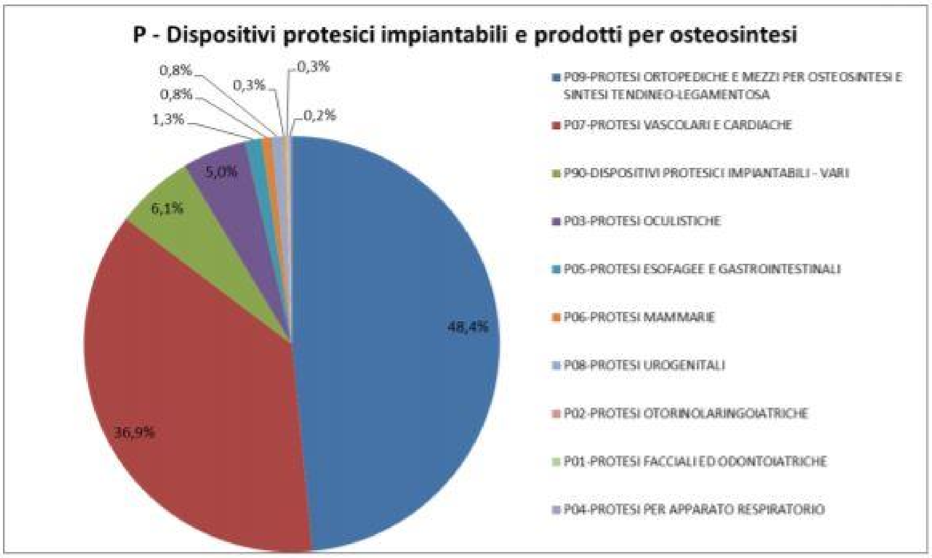

Figure 47 - Expenditure distribution for category P (Ministero della Salute 2017)

5.3 The Italian orthopaedic supply structure

In this subsection we analyse the more specific sector of orthopaedic medical devices.

By taking into account the previous section, we now compare the data exposed before with the one obtained by performing analysis on AIDA. (Aida 2019)

First of all it is necessary to identify which are the firms which constitute the Italian orthopaedic sector. In order to define this market segment 2 different sources have been used: the 2007 ATECO code and the KOMPASS database.

The ATECO code 325030 corresponding to the manufacture of *orthopaedic prosthesis, other prosthesis and aids (including repairs)* and the ATECO code 325011 corresponding to the manufacture of *medical-surgical and veterinary materials* have been considered . ATECO stands for ATtività ECOnomiche (in English Economic Activities) and is an automatic coding tool adopted by the Italian statistical institute ISTAT for national statistical surveys with economic nature. Other company have been identified by KOMPASS database, which allows to find the company which manufactures a specific product od interests.

The revenues for the sector represents the 26% of the biomedical sector and the 11% of the total medical devices industry, (obtained by crossing data from CONFINDUSTRIA and AIDA).

The competitive scenario of the sector is characterised by:

- Low Threat of new entrants due to the high barriers to entry. They are represented by high investment needed in R&D, technology and innovation, IP rights and difficult to manage long payment terms of public administration;
- high competition;
- medium bargaining power of supplier;
- high bargaining power of customers given the long payment terms;
- low threat of substitutes due to the absence of extra-sector products. The substitution process is internal to the sector due to the technology innovation.

5.3.1 Concentration ratios and territorial distribution

The market degree of concentration is an indicator of the supply structure of an industry. It is representative of the power that the leading firms have on the entire industry.

The degree of concentration of the medical device industry and, in particular of the orthopaedic sector, is constantly increasing also due to the policies of M&A implemented in recent years by the multinationals present in the sector.

Two different concentration indexes have been computed here: the HHI (Herfindahl–Hirschman Index) and the CR_4.

The Herfindahl–Hirschman Index is a statistical measure of market concentration and it is used to determine market competitiveness. It is computed as:

$$HHI = (MS_1 * 100)^2 + (MS_2 * 100)^2 + (MS_3 * 100)^2 + ... + (MS_n * 100)^2$$

Which means that it is the sum of the market shares (MS_i) squared, were the market shares of each company are computed as the sales of the company divided by the sales of the total market, where n is the number of firms:

$$MS_i = \frac{Sales_i}{\sum_{i=1}^{n} Sales_i}$$

The HHI index has value in the range of 0-10.000, where 0 is the perfect competition and 10.000 is the monopoly. A market with an HHI index lower than 1.500 is considered competitive, a market with an HHI between 1.500 and 2.500 is a moderately concentrated, and a market with an HHI of 2.500 or greater is a highly concentrated marketplace.

The HHI for the sector has been identified with a value of 1.697 which means that the sector is moderately concentrated. It is in line with the study sector reported before.

The concentration ratio Cr_i shows the percentage of market shares that the of the first i firms detain on the market, this means that the lower the value the higher the competition. The CR_4 of the sector have been identified in 57.33 %, confirming a non-higher degree of competition in the market.

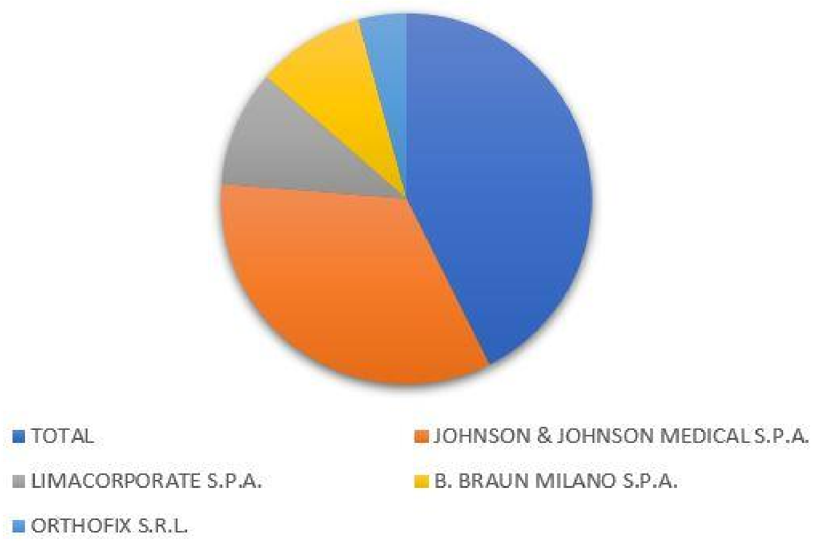

Figure 48 - Concentration ratio

The geographical distribution of the firms in the orthopaedic sector follows the one of the broader medical devices industry.

As shown in the figure below, the higher number of firms are concentrated in Emilia-Romagna and Lombardy, coherently with the CONFINDUSTRIA analysis on the wider medical devices industry. More generally, it is in the north of Italy that the majority of company are located.

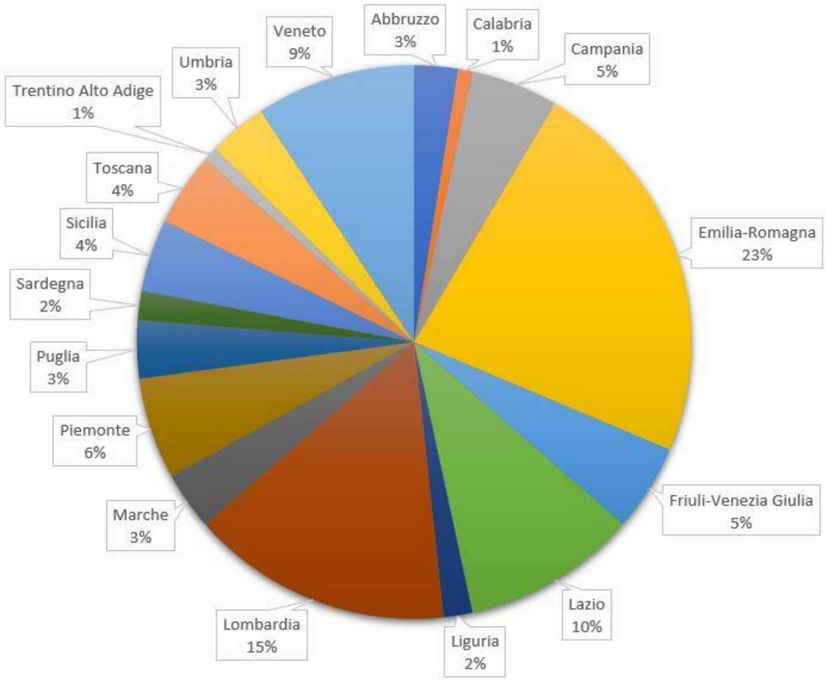

Figure 49 - Geographical company's distribution

Chapter 6

6. AM impact on the Italian orthopaedic manufacturing sector

6.1 Introduction

This chapter represents the core of the thesis, by presenting the results of the analysis conducted about the economic impact of the adoption of additive manufacturing in the Italian orthopaedic sector.

First of all we describe the sample characteristics, also with graph obtained with STATA, a software for statistics and Data Science used to carried out all the analysis reported below.

Then we comment the answers received by the participants to the survey, and finally we expose the results of the statistical analysis conducted by crossing economics data taken from AIDA with the survey answers given by the participant.

6.2 The sample

The sample of the analysis has been identified through 2007 ATECO code and the KOMPASS database.

It is constituted by the first 100 firms of the 2007 ATECO code 32503, and other 19 firms classified as orthopaedic prostheses manufacturer by KOMPASS database (11 of them are classified with the 2007 ATECO code 325011).

The time span taking into consideration goes from 1999 to 2018 for most of the firms in the sample. By carrying out the data analysis using the statistical software STATA, some adjustments have been conducted in order to clean some inconsistent and dirty data of the balance sheets. The adjustments regards: the interpolation of data each time in which there is lack of value (when it is possible), the use of price and salary indexes (downloaded from ISTAT) in order to take into account deflation and the standardization of the duration of year in the case in which was clear that the balance sheet information was related to a smaller period than one year (for example first year of activity).

The sales revenues of the sector shows a decreasing trend from 2009 to 2013 which reverses and becomes increasing until 2017. The decreasing trend is due to the disposal of company business lines of some of the major player in the market. The explanation of such an impact is lies in the degree of concentration of the market.

Another variable taking into consideration is the average number of employees per year, which shows an big fall in 2010, for the same reason explained before and after a period of plateau an increasing trend. The average number of employees per year is about 40, showing that some big players operate in the market. The same trend is also reflected in the Total Cost of Personnel.

Another variable of interest is the Added Value for which the trend is shown in the graph below.

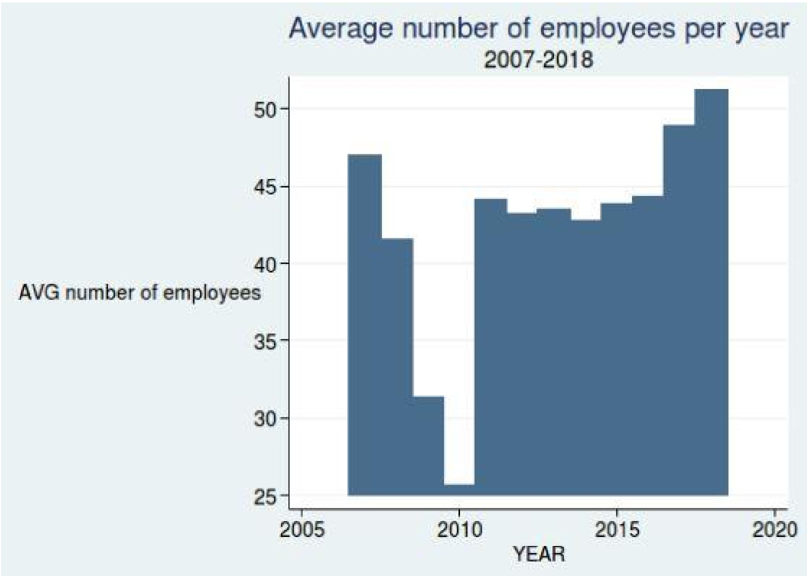

Figure 50 - Average number of employees per year

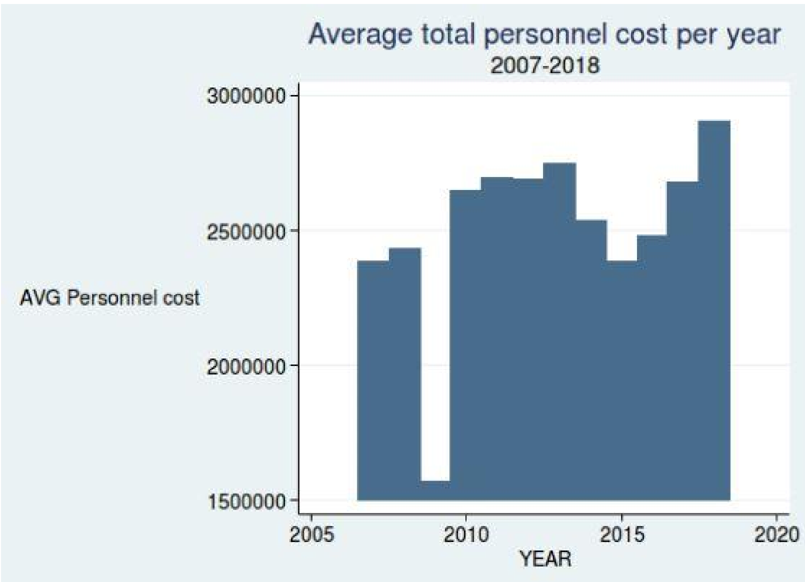

Figure 51 - Average cost of personnel per year

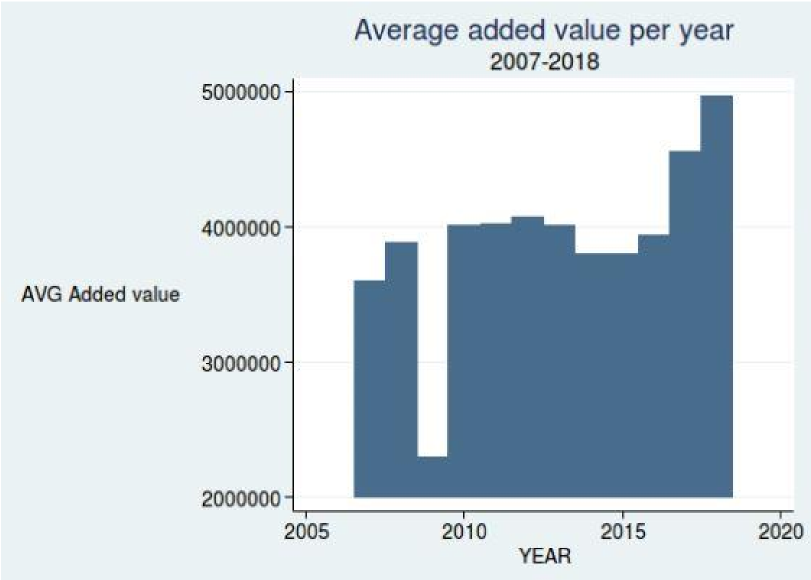

Figure 52 - Average Added Value per year

6.3 The survey

After having identified the sample we will now describe the survey questions and relative answers. Each firm of the sample has been telephonically contacted, successively a marked letter signed by the academic supervisor coupled with the survey has been sent to invite the participation in the investigation.

The rate of response is about 54.6%, having collect answers from 65 over 119 firms which have been identified as manufacturer of orthopaedic prosthesis.

First of all we ask if the firms belongs to a group of company or not. The answer report that the 67% of the sample does not belong to a group while the remaining 33% does, and it is interesting to say that the best ranked firms, in terms of sales revenues, belong to a group of company. For the ones who answered yes, we furthered asked if the ownership of the company is foreign or not: the 35.29% belongs to a foreign group, instead the remaining 64.70% are Italian companies.

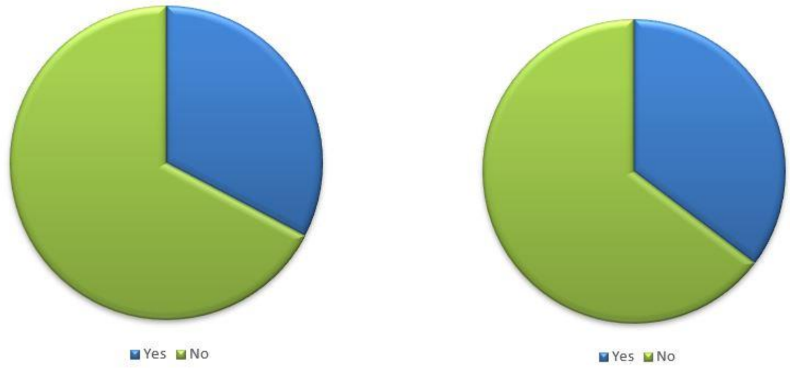

Figure 53 - Questions 1 and 6 "Does the company belong to a group of company?", "Is the company part of a group whose property is not Italian?"

The following question asked if the company is a family business or not, indagating the legal institution. The answers shows that only the 36.53% of the respondents settled a family business against the remaining 63.46% which are in partnership.

Figure 54 - Question 2:"Is the company a family business?"

The third question wants to indagate where the production is located. As we aspect, the 60% of the production is located in Northern Italy, against the 16% of both Central and Southern Italy. A marginal part of the production is abroad, in European Union and Asia.

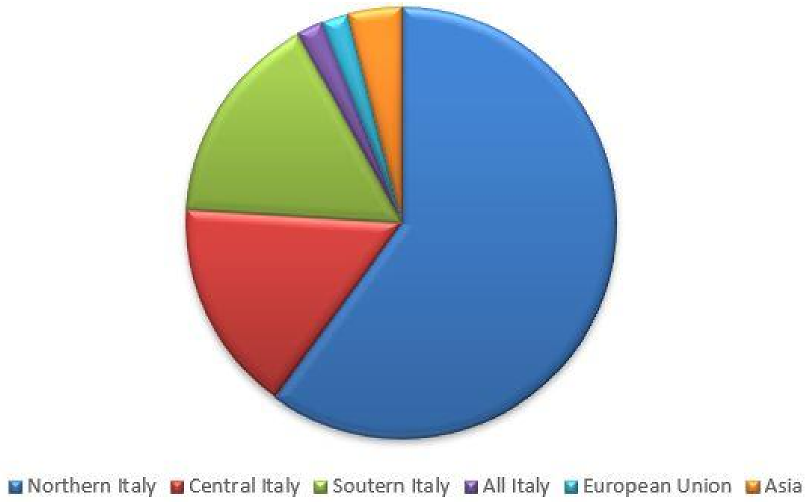

Figure 55 - Question 3: "Where is the production mainly allocated?"

Successively we indagate the production strategy of the company, asking whether they produce in a single site or in more than one, adaption a decentralized strategy. The majority of respondents (69.38 %) adopt a centralized strategy; the high customization required by the products results in the fact that the production site is near to the final customer in order to achieve the best wear-ability possible, moreover outsourcing the production has some critical threads such the increase of logistic costs, the loss of quality control and maybe the most important the transfer of know-how.

The next questions asked where the firms' suppliers are located. As for thee localization of the firms, also the location of the suppliers is mainly in Northern Italy, with a percentage of the 59%, followed by Central Italy with 11.36% and Southern Italy with 4.54%. The 18% of suppliers are located abroad but in the European Union. Only 3 respondents prefer suppliers from Asia (2,27%), Italy and USA (2,27%), and Italy and European Union (2,27%). Totally the 75% of manufacturers prefer Italian suppliers.

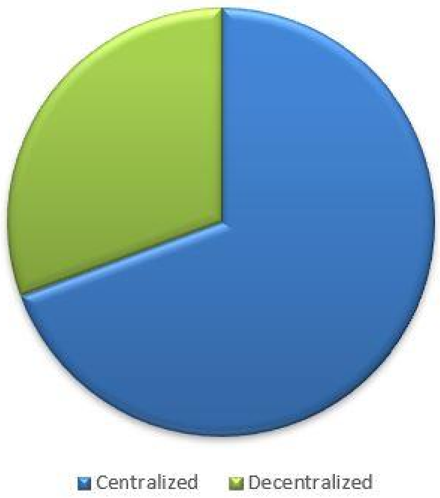

Figure 56 - Question 4: "Which is the production strategy currently adopted?"

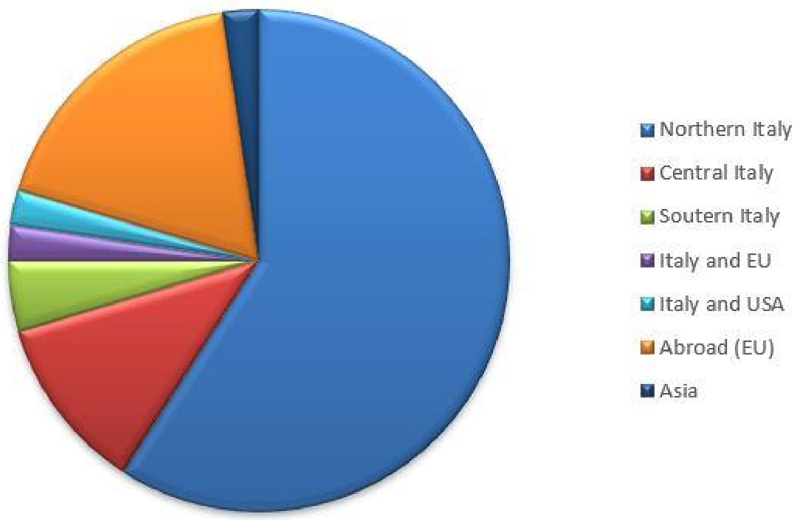

Figure 57 - Question 5: "Where is most of the company's suppliers located?"

The question number seven asks if the company has already adopted additive manufacturing technologies or not. As we can see in the figure 57, the 55.66% of respondents have not adopted AM, while the 44.23% have already do. The next questions (from 8 to 15) have been addressed just to the firms that have already adopted 3D printing technologies, so to whom said yes, in order to investigate how they use it.

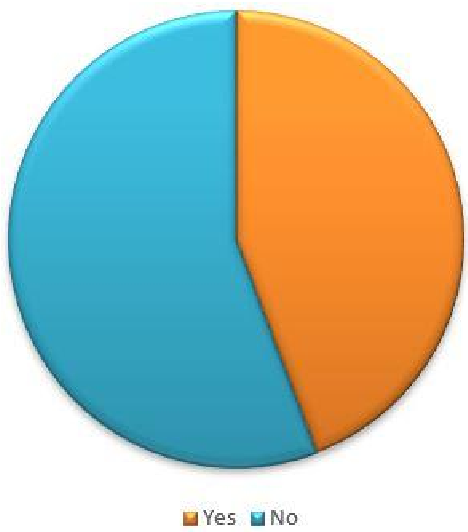

Figure 58 - Question 7: "Has the company made investments in additive technologies?"

The eight question asked which is the kind of feed material used to produce with AM. The 69.56% uses additive manufacturing technologies with polymers and only the 17.34% with metal; a small percentage of respondents uses both of them (4.34%) and with the same percentage we have also the companies which use latex derivatives and carbon and titanium. The reason of this results as to be addressed to the difficulty to manage additive manufacturing technologies with metals, especially in products like orthopaedic prostheses in which the respect of the dimensional tolerance is crucial.

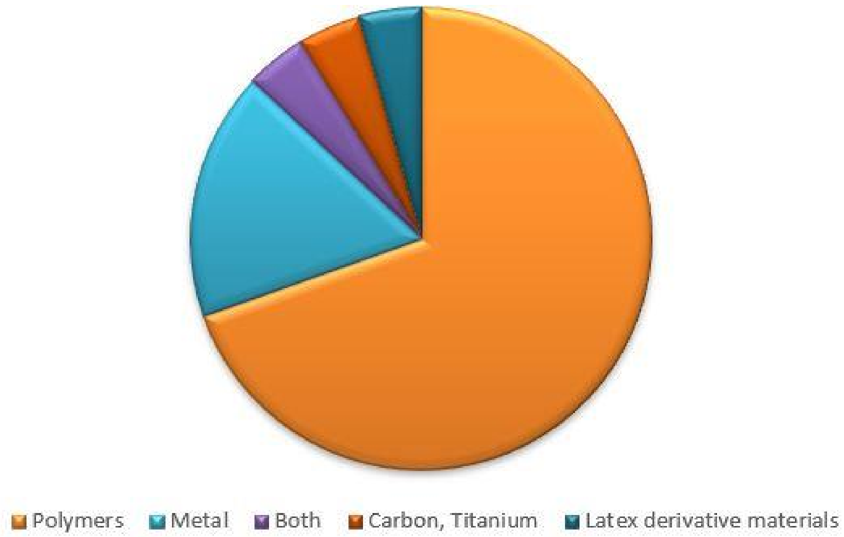

Figure 59 - Question 8: "Which materials do you use additive technologies for?"

The ninth question is an open one, in which the respondents was asked to list the specific technology adopted. It emerges the 47.36% does not report the specific technology said only 3D printer. The remaining 26.31% adopt the FDM (Fused Deposition Modelling), both SLM (Selective Laser Melting) and EBM (Electron Beam Melting) are used in the measure of 10.52% and the remaining 5.26% adopt DMLS (Direct Metal Laser Sintering).

Question number 10 asks in what year the company made the first investment in AM technologies. It is really important because it is necessary to know when the company begins to use AM technologies in order to understand its impact in the company's performance. We will indagate if there is some differences in the companies' performances before and after the adoption of additive manufacturing technologies. The result is shown in the figure below.

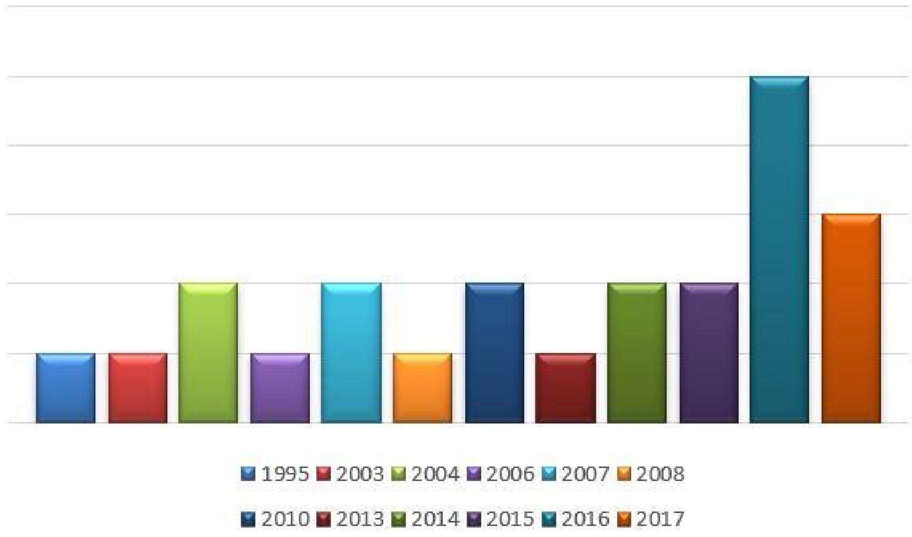

Figure 60 - Question 10: "When did you make the first investment in additive technologies?"

The following questions try to investigate the amount of money invested in AM technologies and what are the objective that the companies want to gather. As the figure 60 shows, most of company had invested a small amount, in the range of 0 – 15,000 €.

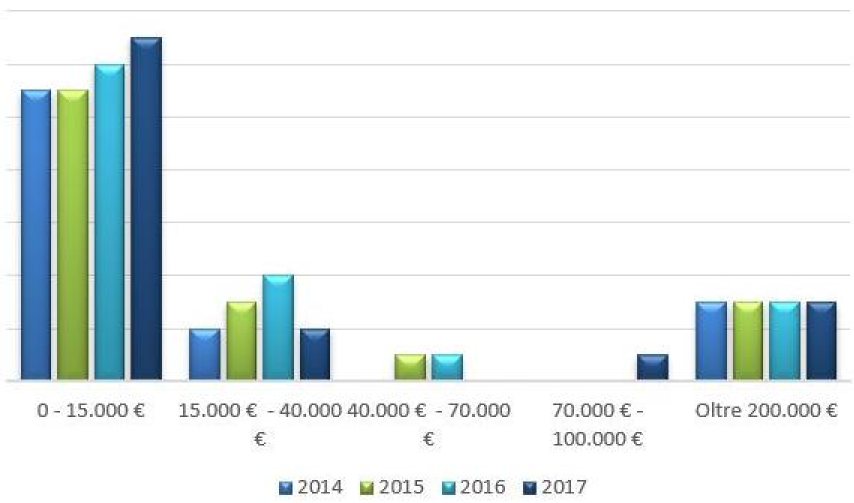

Figure 61 - Question 11: "Which is the amount of investment in additive technologies in each year from 2014 to 2017?"

Only 3 big companies invested more than 200,000€ each years. It seems that all companies invested in an amount proportional to their fixed assets at the time of investments.

Question number 12 has the aim to indagate which are the objective that the companies has proposed to achieve by using additive manufacturing technologies. They were asked to rank the following objectives from 1 to 5, where 1 is the most important:

- Reduction of production cost;
- Increase in product variety;
- Greater match with customer needs;
- Reduction of time series production.

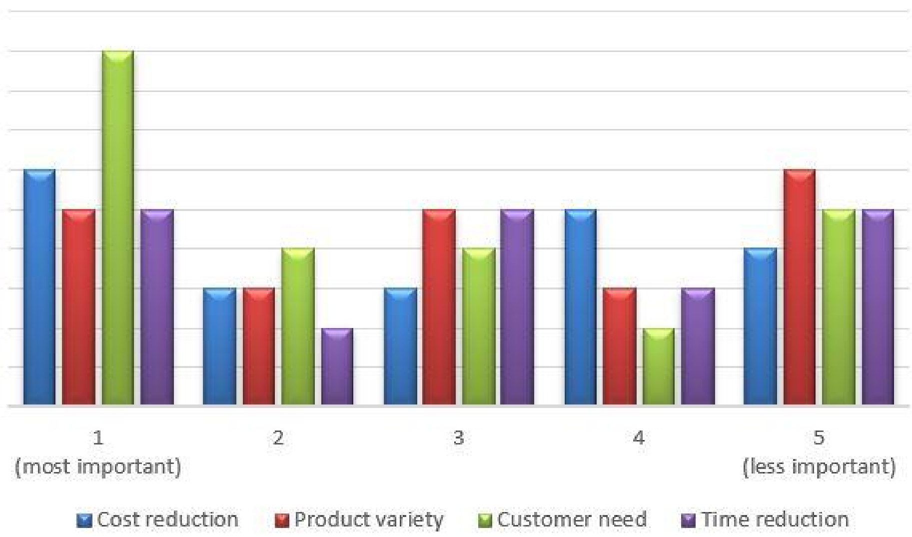

Figure 62 - Question 12: "Which have been the main objectives that the company has proposed to achieve with the investments in additive technologies carried out in 2014-2017?"

The graph shows that the satisfaction of customer needs is the most important objective of the companies, followed by the reduction in production costs. The less relevant, instead, is represent by the reduction of time production.

The 55.66% of respondents who have not adopted AM were asked why they decided to continue the production with traditional method instead of approaching the new paradigm of AM technologies. From the reading of the answers to this open questions, in emerges that the most of them did not adopt AM due to impossibility to respect dimensional tolerance (AM quality issues) or due to financial issues or even for issues related to mass production.

After that we ask to non adopters, if they had already planned investments in AM technologies and why did they make this choice or not. In the figure below it is exposed the result of this question: more than 70% had no planned any investments, the remaining 28.57% has planned investment (almost 21% in medium term and only the 7% in short term).

Figure 63 -Question 17: "Have you already planned future investments in additive technologies?"

The last question of the survey is addressed to all the respondents and it propose to understand if, according to the respondents, AM technologies could help in solving some supply critical issues. As the figure below shows, most of respondents believe that AM could partially solve the issues related to supply chain (52.94%); only the 15.68% believe that AM could solve this issues and the 31.37%, instead, are more critical and do not tryst the AM technologies at all. This result explains why the most of non adopters do not have planned any investment.

Figure 64 - Question 18: "Do you think that a production supported by additive technology could solve or at least mitigate the critical issues of its Supply Chain?"

6.4 STATA analysis and conclusion

6.4.1 Introduction

In this last paragraph we will analyse the results coming from crossing the data downloaded from AIDA, regarding the balance sheets of the companies of the selected sample, and the data obtained from the submission of the survey.

6.4.2 STATA analysis

The first interesting finding comes from the analysis on the dimension of the firms which answer the survey. They have been carried out in order to understand if the size of the firms affects the adoption of additive manufacturing technologies and also the rate of participation to the submitted survey.

It emerges that bigger companies (splitting the sample in two subgroup in which the first 50 companies, ordered by sales revenues, are considered to be big) are the ones which answer more, even if the difference is the 6% (52.94% - 47.06%). The remaining 13 observation are the ones for which we obtained information only by phone.

1 if yes, 0 if not	grande No	Sì	Total
0	10 76.92 29.41	3 23.08 10.00	13 100.00 20.31
1	24 47.06 70.59	27 52.94 90.00	51 100.00 79.69
Total	34 53.12 100.00	30 46.88 100.00	64 100.00 100.00

Pearson chi2(1) = 3.7102 Pr = 0.054

Figure 65 - Firm size and response

The second analysis carried out has the aim to understand the association between the size of the firms and the adoption of AM. The results in the figure below, shows that even in this case the size of the firm is relevant. The bigger companies represent the majority of the adopters with the 65.42% (15 over 8) and the minority of non adopters with the 42.86% (12 over 16).

additive	grande No	grande Sì	Total
No	16 57.14 66.67	12 42.86 44.44	28 100.00 54.90
Sì	8 34.78 33.33	15 65.22 55.56	23 100.00 45.10
Total	24 47.06 100.00	27 52.94 100.00	51 100.00 100.00

Pearson chi2(1) = 2.5342 Pr = 0.111

Figure 66 – Firms size and AM adoption

The most significant analysis has been carried out by building a regression linear model, on some variable of interest. The linear regression is "a linear approach to modelling the relationship between a scalar response (or dependent variable) and one or more explanatory variables (or independent variables)". (Wikipedia 2019)

The analysis has been carried out with a panel of data, which means that the observations are obtained by sampling the firms in different time periods. The panel allows a greater number of observations and consequently a better estimation and especially the possibility to study the dynamic behaviour.

It has also been performed a robust regression analysis with the aim of weighting the observations differently based on how well behaved these observations are.

Moreover we have also execute a linear regression with the addition of dummy variables; the dummy are referred to years with the objective of capture any possible time-related effects.

The variables selected for the analysis are:

- Labour productivity, defined as sales revenues over number of employees;
- Added value per employee;
- EBITDA: Earnings Before Interest Taxes Depreciation Amortization.
- Market shares;

As regard the labour productivity the four analysis have been carried out and before them we also performed a parametric t-test and a non-parametric test. All the results are coherent and shows that the labour productivity of the adopters increase every year (but the confidence interval is not so good to allow us to reject the null hypothesis), from the seventh year after the adoption of additive manufacturing technologies the labour productivity of the adopters is significantly greater than the one of non-adopters and we can strongly reject the null hypothesis. Also the robust regression and both regression with the addition of the dummy variable confirm these results, as showed in the figures below. These results can be explained by saying that the use of additive manufacturing technologies requires a greater degree of competence which grows over the years of use, until it leads to results. (STATA 2019)

Variable	post	post_1	post_2	post_3	post_4	post_5	post_6	post_7	post_8
post	1613.37								
	19006.13								
	0.93								
post1		-25584.93							
		19972.51							
		0.20							
post2			16064.08						
			21133.98						
			0.45						
post3				19950.03					
				21874.80					
				0.36					
post4					25137.50				
					21872.28				
					0.25				
post5						27565.35			
						21752.22			
						0.21			
post6							32027.50		
							22123.39		
							0.15		
post7								38511.33	
								23071.30	
								0.10	
post8									46297.94
									24860.88
									0.06
_cons	199446.26	210462.99	194568.88	193969.98	193311.63	193524.56	193464.53	193328.16	193413.92
	11328.83	10686.22	10245.02	9834.29	9268.49	8814.13	8456.36	8166.93	7932.05
	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00
N	314	314	314	314	314	314	314	314	314

Figure 67 - Labour productivity linear regression with fixed effects

Variable	post	post_1	post_2	post_3	post_4	post_5	post_6	post_7
post	-12817.75							
	25998.45							
	0.62							
post1		-53972.44						
		26325.17						
		0.04						
post2			9936.30					
			27546.74					
			0.72					
post3				21513.91				
				28255.29				
				0.45				
post4					24243.87			
					27879.03			
					0.39			
post5						26004.71		
						27557.73		
						0.35		
post6							30418.25	
							27861.40	
							0.28	
post7								45643.29
								28724.07
								0.11
N	314	314	314	314	314	314	314	314

Figure 68 - Labour productivity linear regression with year dummy

Variable	post	post_1	post_2	post_3	post_4	post_5	post_6	post_7	post_8
post	1613.37 14894.77 0.91								
post1		-25584.93 40328.39 0.53							
post2			16064.08 21947.67 0.47						
post3				19950.03 26384.19 0.46					
post4					25137.50 28516.70 0.39				
post5						27565.35 28230.18 0.34			
post6							32027.50 28071.24 0.27		
post7								38511.33 28509.36 0.19	
post8									46297.94 31183.46 0.15
_cons	199446.26 6925.60 0.00	210462.99 16182.73 0.00	194568.88 7688.67 0.00	193969.98 8234.56 0.00	193311.63 7810.31 0.00	193524.56 6832.78 0.00	193464.53 5900.33 0.00	193328.16 5084.47 0.00	193413.92 4568.28 0.00
N	314	314	314	314	314	314	314	314	314

Figure 69 - Labour productivity robust regression

Variable	post	post_1	post_2	post_3	post_4	post_5	post_6	post_7
post	-12817.75 22464.12 0.57							
post1		-53972.44 51093.43 0.30						
post2			9936.30 17791.40 0.58					
post3				21513.91 25555.46 0.41				
post4					24243.87 27371.67 0.39			
post5						26004.71 27192.05 0.35		
post6							30418.25 27550.15 0.28	
post7								45643.29 29583.74 0.14
N	314	314	314	314	314	314	314	314

Figure 70 - Labour productivity robust regression with year dummy

For what concerns the added values per employee we can see from the figure below that the added value of adopters is higher than the one of non-adopters, since the first years, however we are not able to confirm that it is a result of the adoption of additive technologies. This trend is showed in all the 4 analysis, we report only the robust regression for simplicity.

The third variable of interest is the EBITDA which represents the earnings before interest, taxes, depreciation and amortization and it also captures the potentially positive impacts on operating costs.

Variable	post	post_1	post_2	post_3	post_4	post_5	post_6	post_7
post	12133.62 5611.16 0.04							
post1		7567.61 8765.77 0.40						
post2			12719.11 6607.63 0.07					
post3				13529.91 6517.74 0.05				
post4					13838.81 6648.25 0.05			
post5						12569.83 6311.92 0.06		
post6							12164.75 5955.17 0.05	
post7								13852.35 5886.95 0.03
N	314	314	314	314	314	314	314	314

Figure 71 - Added value per employee robust regression

The robust regression with the year dummy, reported below, shows that the EBITDA for adopters is smaller than the one for non-adopters in the first years after the adoption; the increasing trend allows, at the fifth year, a greater value of the variable for the adopters rather than the other ones. However the degree of confidence is not enough small to allow us to reject the null hypothesis.

Variable	post	post_1	post_2	post_3	post_4	post_5	post_6	post_7
post	1.10e+06 1.35e+06 0.42							
post1		1.43e+06 1.69e+06 0.41						
post2			1.67e+06 1.82e+06 0.37					
post3				1.95e+06 1.96e+06 0.33				
post4					1.89e+06 1.68e+06 0.27			
post5						1.68e+06 1.45e+06 0.26		
post6							1.45e+06 1.29e+06 0.27	
post7								1.73e+06 1.49e+06 0.26
N	298	298	298	298	298	298	298	298

Figure 72 - EBITDA robust regression with year dummy

The last variable of interest is the market shares. The analysis shows interesting results: in the first years after the adoption the market shares are lower for adopters; the increasing trend inverts situation at the third year. The growth becomes significant four year after the adoption .

Variable	post	post_1	post_2	post_3	post_4	post_5	post_6
post	0.07 0.10 0.50						
post1		0.02 0.12 0.90					
post2			-0.01 0.14 0.96				
post3				0.19 0.14 0.19			
post4					0.37 0.13 0.01		
post5						0.37 0.12 0.00	
post6							0.39 0.11 0.00
_cons	0.85 0.07 0.00	0.88 0.07 0.00	0.89 0.07 0.00	0.81 0.07 0.00	0.75 0.06 0.00	0.76 0.05 0.00	0.78 0.04 0.00
N	202	202	202	202	202	202	202

Figure 73 - Market shares linear regression

6.4.3 Conclusions

After the analysis performed we can say that the investments in AM technologies lead to an increase in labour productivity and market shares. The effects of the investments, nevertheless, are not immediate and require some years of adjustments in order to appreciate the benefits of this technologies. (STATA 2019)

Appendix A

Questionnaire

Questionario sulle tecnologie additive

1. Indirizzo email *

____

2. L'impresa fa parte di un gruppo di imprese? (per gruppo si intende un insieme di più imprese controllate - direttamente o indirettamente - dalle medesime persone fisiche o dalla medesima impresa)
Contrassegna solo un ovale.
   - Sì — *Dopo l'ultima domanda in questa sezione, passa alla domanda 6.*
   - No — *Dopo l'ultima domanda in questa sezione, passa alla domanda 7.*

3. È un'impresa a conduzione familiare?
Contrassegna solo un ovale.
   - Sì
   - No

4. Dove è allocata principalmente la sua produzione?
Contrassegna solo un ovale.
   - Nord Italia
   - Centro Italia
   - Sud Italia
   - Estero (Unione Europea)
   - Altro: ____________________

5. Qual è la strategia produttiva attualmente adottata?
Contrassegna solo un ovale.
   - Su sito unico
   - Su più siti produttivi

6. Dov'è localizzata la maggior parte dei fornitori dell'impresa?
Contrassegna solo un ovale.
   - Nord Italia
   - Centro Italia
   - Sud Italia
   - Estero (Unione Europea)
   - Altro: ____________________

Gruppo imprese

7. **L'impresa fa parte di un gruppo la cui proprietà non è italiana?**
Contrassegna solo un ovale.

- Sì
- No

Adozione tecnologie additive

8. **L' impresa ha effettuato investimenti in tecnologie additive?**
Contrassegna solo un ovale.

- Sì *Passa alla domanda 8.*
- No *Passa alla domanda 16.*

Adozione tecnologie additive: Sì

9. **Utilizzate tecnologie additive per la lavorazione di:**
Contrassegna solo un ovale.

- Polimeri
- Metalli
- Altro: ____________________

10. **Quali tecnologie additive avete adottato? (lista di diverse tecnologie)**

____

____

____

____

____

11. **Quando è stato effettuato il primo investimento in tecnologie additive? (specificare anno)**

____

12. **Quale è l'ammontare di investimento in tecnologie additive in ciascun anno dal 2014 al 2017?**
Contrassegna solo un ovale per riga.

	0 - 15.000 €	15.000 € - 40.000 €	40.000 € - 70.000 €	70.000 € - 100.000 €	100.000 € - 200.000 €	Oltre 200.000 €
2014						
2015						
2016						
2017						

13. **Quali sono stati i principali obiettivi che l'azienda si è proposta di raggiungere con gli investimenti in tecnologie additive effettuati nel periodo 2014 - 2017?**
Indicare in ordine decrescente, 1 il più importante
Contrassegna solo un ovale per riga.

	1	2	3	4	5
Riduzione dei costi di produzione	◯	◯	◯	◯	◯
Aumento della varietà della gamma dei prodotti	◯	◯	◯	◯	◯
Maggiore corrispondenza con i bisogni dei clienti	◯	◯	◯	◯	◯
Riduzione dei tempi di passaggio dalla progettazione alla produzione in serie	◯	◯	◯	◯	◯

14. **Utilizza le tecnologie additive per:**
Seleziona tutte le voci applicabili.

- [ ] Rapid prototyping (Ricerca & Sviluppo)
- [ ] Produzione
- [ ] Altro: ____________________

15. **Ritiene che una produzione supportata da tecnologie additive potrebbe risolvere o, per lo meno attenuare, le criticità della sua Supply Chain?**
Contrassegna solo un ovale.

◯ Sì *Passa alla domanda 15.*
◯ No *Interrompi la compilazione del modulo.*
◯ In parte *Passa alla domanda 15.*

Criticità Supply Chain

16. **Quali sono o potrebbero essere gli impatti delle soluzioni tecnologiche additive sulla vostra Supply Chain?**
Seleziona tutte le voci applicabili.

- [ ] Aumento dell'efficienza (es. riduzione del tempo ciclo dell'ordine, riduzione dei livelli di scorta, etc.)
- [ ] Aumento della flessibilità
- [ ] Riduzione del numero di fornitori
- [ ] Possibilità di diversificazione delle materie prime/tecnologie utilizzate
- [ ] Altro: ____________________

Interrompi la compilazione del modulo.

Adozione di tecnologie additive: No

17. **Quali sono i motivi per non aver ancora investito in tecnologie additive?**

____

18. **Avete già pianificato investimenti futuri in tecnologie additive?**
Contrassegna solo un ovale.

- ◯ Sì, a breve (entro un anno)
- ◯ Sì, a medio termine (entro i prossimi 5 anni)
- ◯ No, non abbiamo pianificato nessun investimento

19. **Ritiene che una produzione supportata da tecnologia additive potrebbe risolvere o, per lo meno attenuare, le criticità della vostra supply chain?**
Contrassegna solo un ovale.

- ◯ Sì *Passa alla domanda 15.*
- ◯ No *Interrompi la compilazione del modulo.*
- ◯ In parte *Passa alla domanda 15.*

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