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Additive Manufacturing Solutions for Improved Medical Implants

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1. Introduction

In recent years, European industry has been facing the challenge of losing competitiveness in mass production. Due to important factors such as lower labour costs, lower taxes or in-site access to raw materials, mass production has migrated to Third World countries. However, European industry is more advanced in technological aspects and is in need of a qualitative advantage in the development of new technologies. One of the efforts of European companies is directed towards the production of short series of customized products with added value. Major efforts have been done in order to customize products and give them an added value by developing new manufacturing technologies.

Additive Manufacturing (AM) is a powerful tool that offers the necessary competitiveness to European companies (Petrovic, 2011). AM technologies have been available on the market for many years. Initially, these technologies were considered only for prototyping - the first technologies that appeared on the market were capable of fabricating only polymer parts of low quality and low resistance. However, in the last decade, the sector of AM has experienced an important evolution with constant growth in sales of machine systems and rapid products (Wohlers, 2010). Numerous advantages of 'freeform fabrication' have driven new developments in processing principles and materials. New value-added materials have been released for layer-by-layer processing. On the other hand, new technologies have been developed to process demanding materials for different sectors. New energy sources have been introduced in order to process high melting point metal alloys such as Titanium, Cobalt Chromium, etc.

There are many terms commonly used for AM, such as solid *free form fabrication* (FFF), *rapid manufacturing* (RM), *additive layered manufacturing* (ALM) and *3D printing*. The latter may be the most descriptive for people not familiar with additive technologies. Unfortunately, this term may produce a wrong idea, since AM machinery is much more than any kind of printer. However, officially and according to ASTM F42 Committee, Additive Manufacturing is defined as "process of joining materials to make objects from 3D model data, usually layer upon layer, as opposed to subtractive manufacturing methodologies, such as traditional machining" (ASTM, 2010).

AM enables the use of **value-added design** in medical device manufacturing sector. Process of adding material in layers allows the fabrication of *designed, controlled and well-*

interconnected porosity which, combined with solid material, provides better bone ingrowth into implants. Also, AM implants are characterized by *rough surface quality* per se. Undesirable in other sectors, in medical implants rough surface is an advantage because it enhances bone-implant fixing. Furthermore, AM technologies perform fabrication of metal implants in a highly controlled atmosphere with restricted presence of oxygen, which results in especially *high purity*. Finally, layer-by-layer principle allows the fabrication of *customized net-shape implants* that fully fit patient's data. In addition, high power and processing velocity open the possibility of serial production of *standardized implants*.

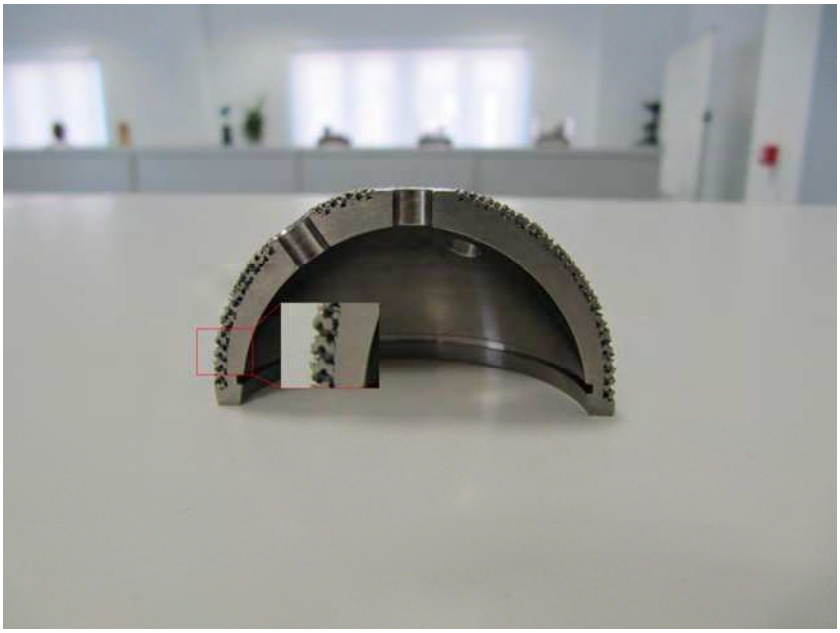


Fig. 1. Acetabular cup with designed porous surface (Courtesy of ARCAM AB).

The aim of this chapter is to illustrate the capabilities of AM on the example of a technology with one of the most powerful active principles: Electron Beam Melting (EBM).

2. Additive manufacturing process

Additive fabrication is performed directly from a 3D CAD file in which a geometrical model of part is stored. The part model can be designed in many different commercial 3D modelers but it is exported in STL file format. The STL file is imported into a specific software (such as Magics® by Materialise, Viscam® by Marcam, Netfabb® by FIT, etc.), where it is pre-

processed. The part is oriented for building and a support structure is made for the downfacing surfaces of the part. Afterwards, cross-sections of a given thickness, known as 'slices', are generated virtually from 3D CAD descriptions of the part and support structures. The slices are saved in a 'slice file' (ABF, SLI, SLC or any other format that may depend on patented technology). After pre-processing, the slice file is sent to the machine to be 'printed' slice-by-slice.

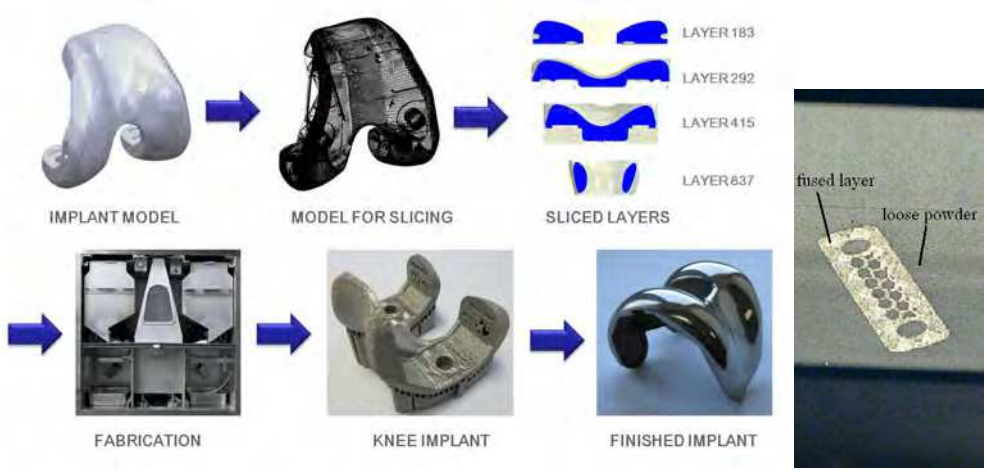


Fig. 2. Steps in AM process (left) and fused layer (right)

The fabrication process consists of two basic steps: *coating* and *selective melting*. The coating step is the process in which material is laid over the working surface in a very thin layer. The thickness of the layer depends on the chosen technology and it ranges between 0.03 mm to 0.20 mm. The selective melting step refers to the process of printing the part slice by the action of a source of energy. The active principle can be a *light source*, *laser beam*, *electron beam*, etc. It acts over the layer of material and produces fusion of slice's footprint to the layer below. The power of the energy source depends on the chosen technology: in the low end, we have Stereolithography that uses ~100 mW, and in the high end, we have Electron Beam Melting that uses up to 3000 W. Only the contour of part slice and its interior are fused (Figure 2, right); the rest of the material is left untouched and may be recycled (more or less, depending on the process and material). The actions of coating and slice printing follow each other until all the slices are correctly printed, generating the final three-dimensional part. Once fabrication has finished, the part is taken out to be cleaned of

material that is not fused and, if necessary, to be given further post-processing. The most common post-processing techniques are sanding, polishing, homogenization, thermal treatment, etc.

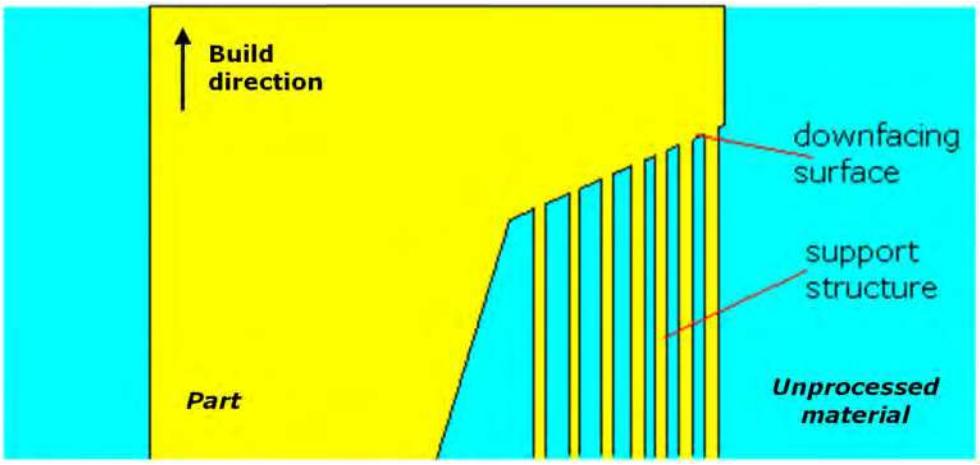


Fig. 3. Support structure for downfacing surfaces

It is important to highlight that, in general, material that is not processed (be it powder or liquid) is not capable of supporting fused material. Hence, if a part has overhanging zones, they may need to be supported by a *support structure* (Figure 3). Additionally, the support structure acts as a conductor of excess heat created in the process of selective melting. Finally, in some technologies, the support structure prevents warping of the part due to the thermal stress created during the process. Hence, the first step of pre-processing actually consists in generating an efficient support structure, which is then sliced and fabricated together with the part. The support structure is eliminated in the post-processing.

The most important advantages of Additive Manufacturing are:

1. *Time-to-market reduction for customized products*. Due to high speed of the process and being a direct fabrication method, the reconstruction of a model to fit in desired assembly is relatively fast;
2. *Product customization with complete flexibility in design & construction of a product.* Unlike conventional processes, AM can produce parts of almost any desired form and can almost be free from geometrical manufacturing constraints.
3. *Maximum material savings.* Material is added and not subtracted. For some applications, especially in the metal sector, case studies show that the waste of raw material is reduced by up to 40% when using additive technologies instead of subtractive (machining) technologies (Reeves, 2008). Also, 95% to 98% of the remaining material (powder or resin that is not processed) may be recycled;
4. *No tools, moulds or punches are needed.* The part is obtained directly from its 3-D CAD model with the absence of human errors in production.
5. *Full-density of final parts.* Unlike other powder based processes (powder metallurgy, MIM), additive technologies produce parts without almost no residual porosity.

6. *Fabrication of free form enclosed structures.* Additive technologies are capable of fabricating free form channels as well as different forms of latticed structures.

However, from the point of view of their application in biomedical field, additive technologies are facing some challenges:

1. *Remove the 'stigma' of its original name 'Rapid Prototyping'.* Although AM has evolved to deliver ready-to-use products made from a wide variety of metals and polymers, it is still wrongly considered that AM is valid only for prototype fabrication.
2. *Validation of mechanical properties of existing materials and AM technologies.* Unlike conventionally produced parts, AM parts may not behave identically in all directions. Depending on particular additive technology, processed material has better behaviour when the load is applied along the direction of the layer as compared to the build-up direction.
3. *Development and characterization of new materials for AM.* Alloys like stainless steel, titanium alloys, cobalt chromium, etc. are already being processed. Nevertheless, there are many interesting materials that are under research or considered for further research (see Future development section).

Electron Beam Melting

EBM is one of free-form fabrication technologies capable of processing ferrous and non ferrous metallic powders to fully-dense material, using layer-by-layer principle. In the case of EBM, the energy is delivered through an electric circuit of 60kV that is created between a tungsten filament placed inside of the electron gun and the building plate (Figure 4).

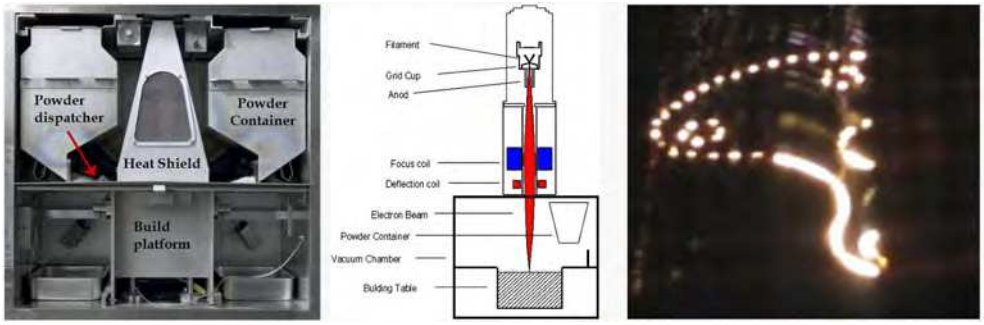


Fig. 4. Inside the EBM machine (left); scheme of an additive machine (middle); electron beam making the contour of tibia prosthesis.

The filament is heated by electric current and emits a beam of electrons which is conducted by a set of different coils until it impacts the powder surface. During the impact, electric energy is transformed to heat energy which fully melts the powder. The working chamber is kept under deep vacuum (order of magnitude 10^{-4} mbar). Hence, powder is released from containers and distributed over the build platform in fine 70-100 μm layers. The beam melts powder to a solid slice, following the cross-section of the part at that layer and merging it with previous slices (Figure 4). The build platform descends for the value of layer thickness and a new powder layer is dispatched. The process repeats until the part is completed.

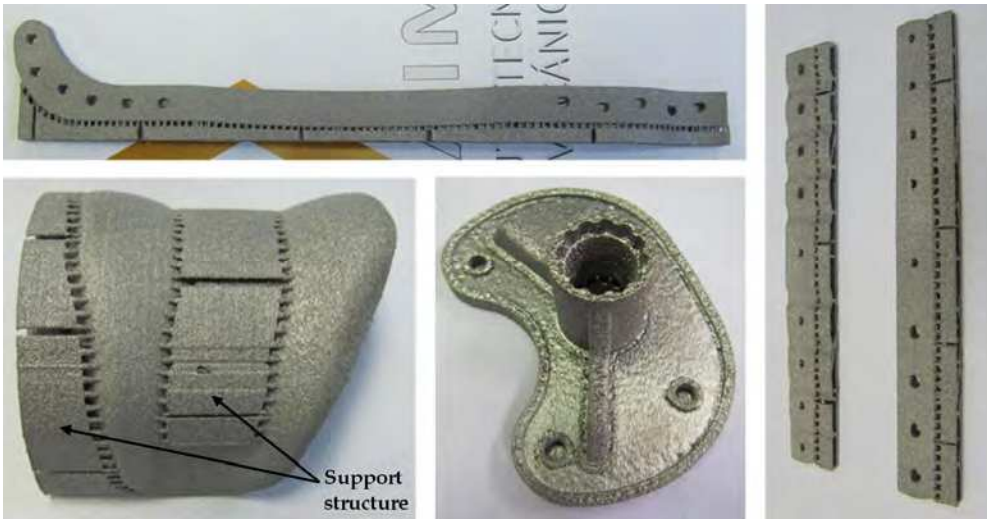


Fig. 5. Some of biomedical parts as produced on the machine (osteosynthesis plates Courtesy of CIMA).

In comparison with other AM processes, EBM has three major advantages very relevant for medical implants manufacturing:

- *Substantially higher nominal speed* which makes viable a serial production of medical implants (Figure 5).
- *Processing under vacuum* - the processed material has very high purity resulting in higher properties and better biocompatibility.
- *High processing temperature* (for Ti64 around 650°C) - less thermal stresses and less warpage in processed material.

3. Supply chain flow

Supply chain for medical implants fabricated by AM consists of six steps (Figure 6). Four of them belong to the fabrication process while the others are common to all medical device manufacturing processes (medical post-treatment and surgical intervention).

3.1 Implant reconstruction / design

As mentioned before, AM process can be understood as 3D printing of solid models. There are two different ways to obtain medical models:

- *Designing the model in some 3D modelling software.* Based on the statistic information about patients (age, weight, physical constitution, etc.), implants are designed together with tooling for the surgical operation (Synthes, 2007). This is a commonly used way to make standard implants in different sizes. When implanted, the osseous zone is adjusted so that the implant fits to properly repair the damaged zone. The model can be manufactured by a variety of processes (forging, CNC machining, etc.). However,

additive technologies introduce one important advantage: porous surface for better bone ingrowth (Figure 7). This *controlled* porous coating is designed in a specific software (in the case shown on Figure 7, it was Magics® by Materialise) and exported as a model coupled with the solid hip stem.

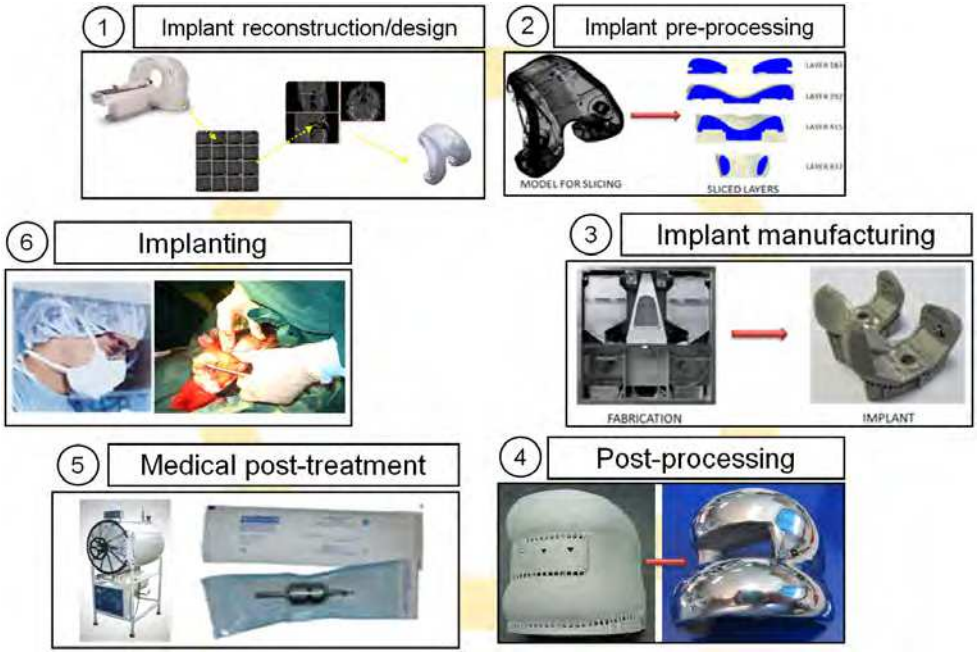


Fig. 6. Supply chain flow for medical implants.

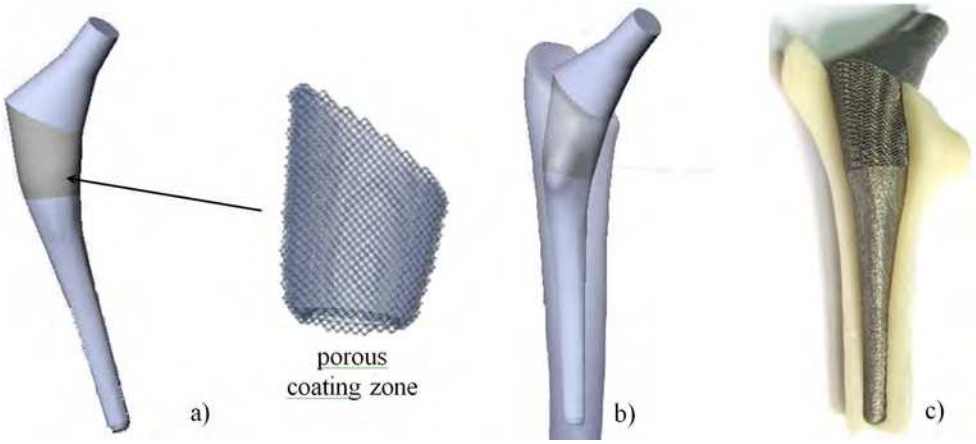


Fig. 7. Example of femoral hip stem: a) 3D model of hip stem with superficial porous zone, b) hip stem coupled with femur bone (model) and c) Ti64 hip stem coupled with polyacrilic bone replica.

- *Reconstruction of model upon patients CT images.* For customized implants, the common path is to reconstruct the model via *scan-to-part*: a cloud of points is reconstructed upon CT images and subsequently converted into a 3D model. The model can then be manufactured in chosen technology (Figure 8). As in each process of reverse engineering, there is an error that is introduced during the reconstruction. In the scan-to-part process, the maximum introduced deviation was 1.4 mm - the majority of the model points have deviation comprehended between 0.45 and 0.65 mm (Figure 9, left). On the other hand, the fabrication process reproduces the model with the deviation inferior to 0.15mm in more than 80% of points (Figure 9, right) (AIMME, 2009).

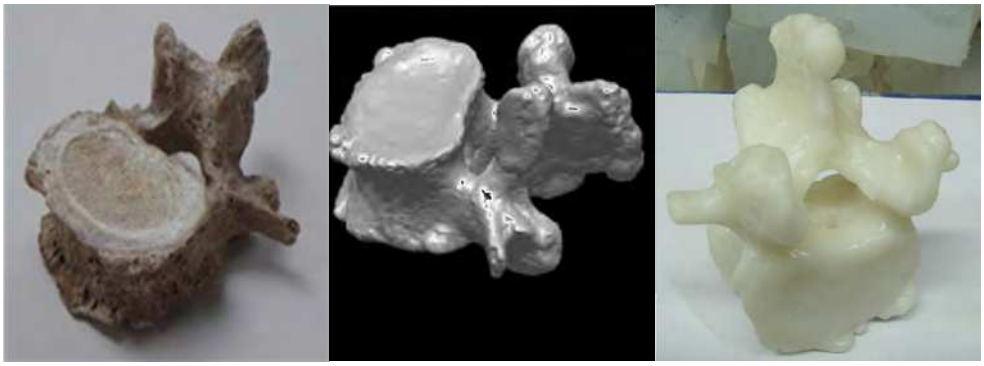
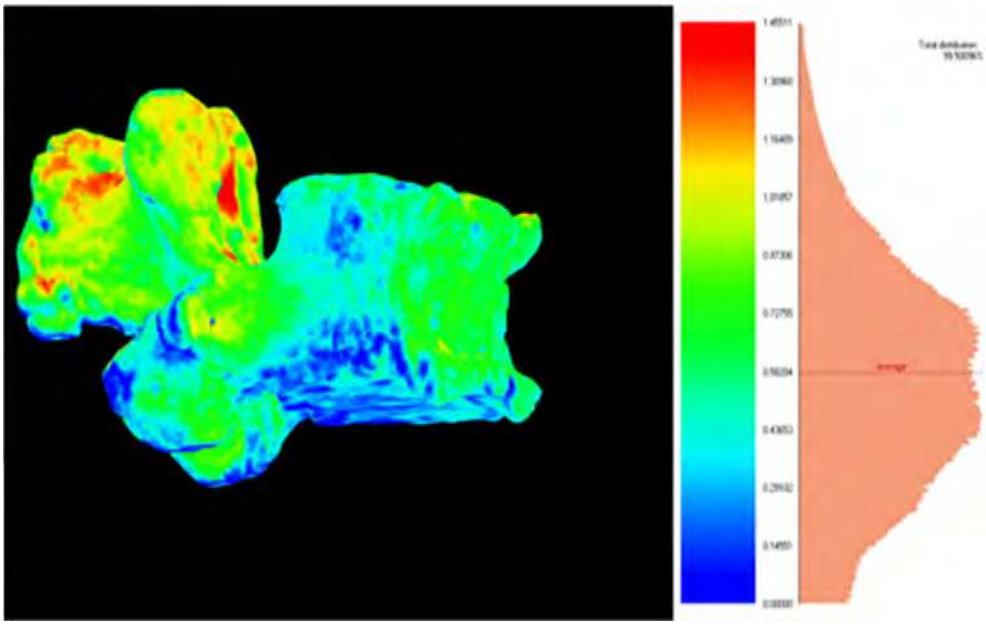


Fig. 8. Example of spinal vertebra: a) real bone, b) reconstructed model and c) polyacrilic bone replica made on Stereolithography.



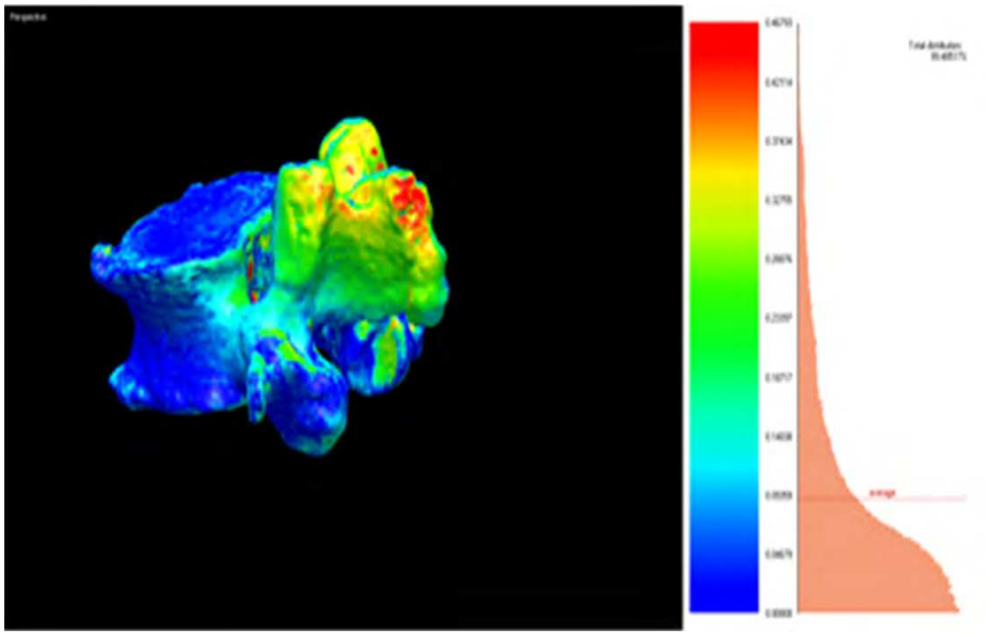


Fig. 9. Comparison by light digitalization: a) deviation of real vertebra vs reconstructed STL model, b) deviation of polyacrilic bone replica made on Stereolithography vs reconstructed STL model.

After completing the scan-to-part, in Additive Manufacturing the model is sliced virtually and then built layer by layer. This fact allows the fabrication of very complex shapes and forms. In biomedical applications, it allows the fabrication of near net-shape implants customized to the patient's data.

The same solutions of gradual porosity mentioned previously can be applied to customized implants.

3.2 Implant pre-processing

The planning of manufacturing process of implants in Additive Manufacturing consists of two steps:

- Implant model is *properly oriented on the build platform* for layer-by-layer fabrication in order to optimize surface quality, support structure, build time, build cost, etc. If necessary, the support structure is generated and optimized. As much implants as possible are packed for more efficient fabrication (Figure 10). For the time being this is done manually, but some tools for automatic assessment are being developed for knowledge assisted part orientation (Petrovic, 2010).
- *Implant and support structure are sliced for fabrication.* Slices are stored into a sliced file which is uploaded to the machine (Figure 11). The machine uses specific software to interpret the file and to send commands to print layers into a solid part. The same build, stored in the sliced file, can be build again without any pre-processing.

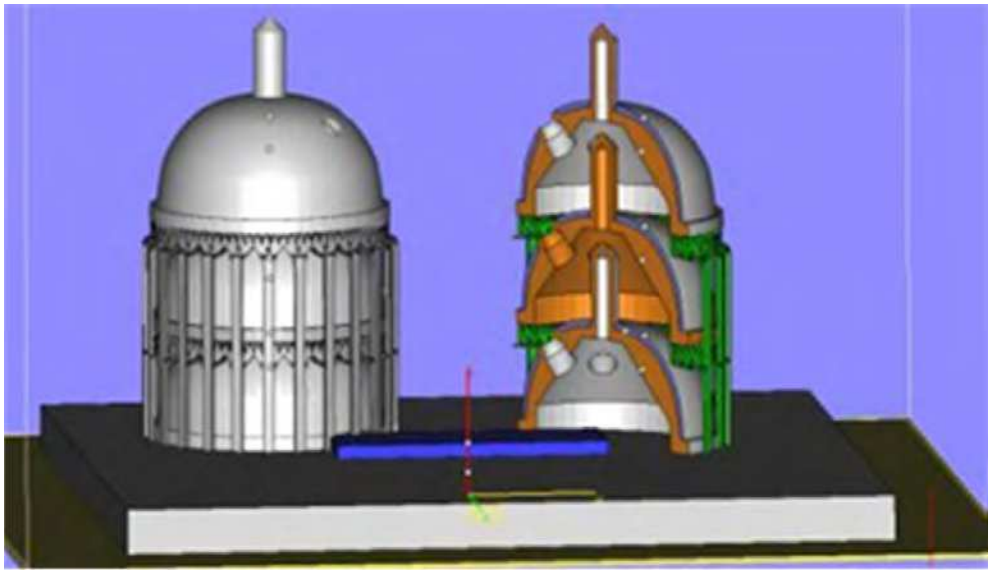


Fig. 10. Packing of implants for more efficient fabrication.

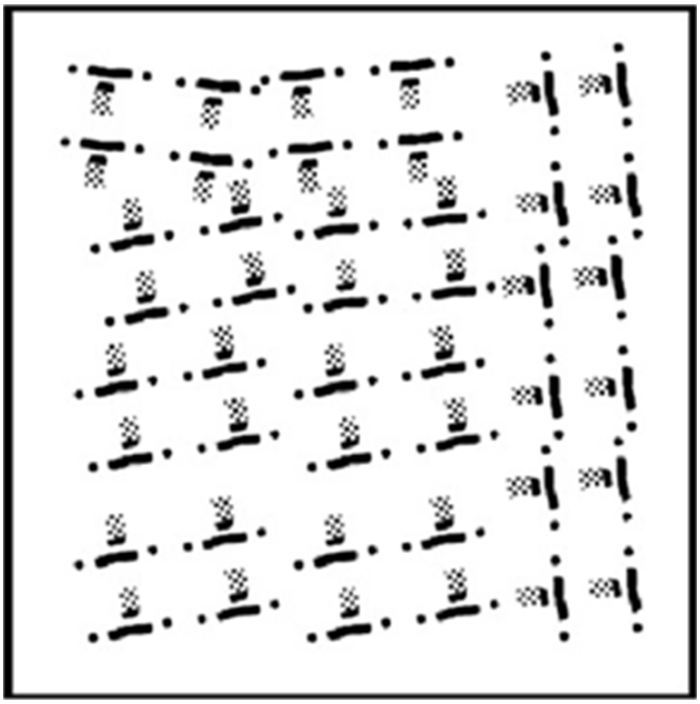


Fig. 11. One digital layer as represented in EBM Control software (black part is fused and white left unfused).

3.3 Implant fabrication

Once the pre-processing is done, implants are manufactured layer by layer on the machine. In the case of EBM, as mentioned before, the printing of the layers is done by the action of electron beam which performs a selective melting of material (fuses the black part on Figure 10 and leaves unfused the white part). The electron beam is very powerful and has a diameter of approximately 240 microns, which makes the contour of the layer – that is the surface of the implant when finished - a bit rough (Figure 12). This implies additional post-processing in the zones of the implant that need smooth surface. However, in order to get better surface quality, the technology has suffered some changes recently and a *Multibeam®* strategy has been introduced (Figure 12).

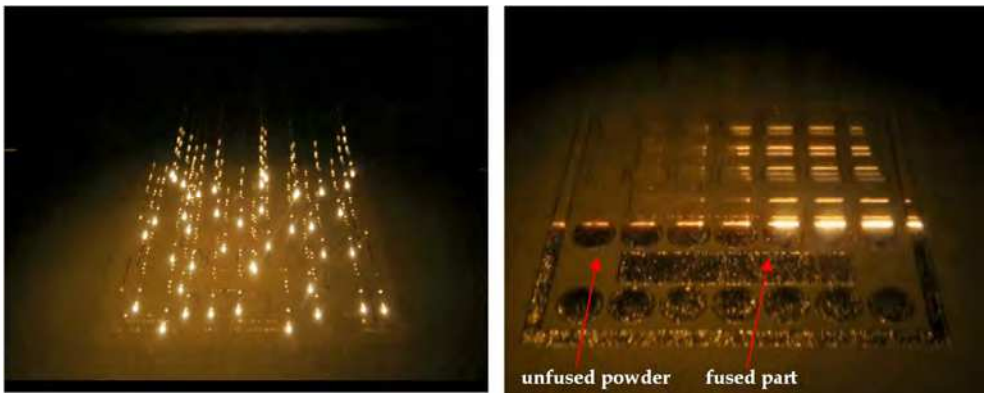


Fig. 12. Multibeam® strategy for better implant surface quality (left), fusing the layer (right)

3.4 Implant post-processing

After the fabrication has finished, the building platform with implants is taken out of the powder bed (Figure 13). Major part of the unfused powder is directly poured into a sifting system and filtered for reuse. However, in the case of EBM, the working temperature of the chamber reaches high value (650ºC for Ti64). Hence, the unfused powder is semi-sintered which is why, in order to clean the implants thoroughly, they are transferred to *Powder*

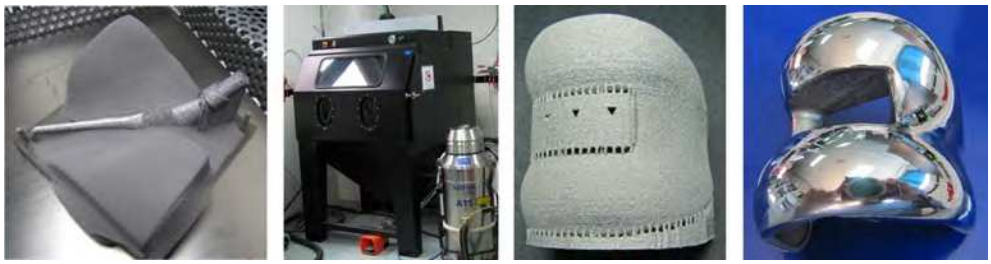


Fig. 13. Implant post-processing. From left to right: hip stem still involved by the powder bed; powder recovery system; knee implant as taken out from the machine and after support removal and hand polishing.

Recovery System (PRS). The rest of powder is wiped away by a jet of compressed air charged with particles of the same material that the implants are made of (so as to prevent implant contamination). After cleaning the implant, the support structure is removed by hand (it is designed to have small contact surface with implant and be easy to eliminate). Also, if necessary, additional machining and/or polishing of certain surface or zone is performed.

As can be seen from this analysis of the supply chain, main advantages of additive technologies are:

- *value-added design* (porous surface with controlled porosity),
- *use of additive rather than subtractive fabrication* which allows:
  - much bigger geometrical freedom;
  - recycling of major part of material (up to 98%);
- *automation* of the process, which permits to:
  - avoid human errors since the batch of models is stored in electronic way and prepared for "load & play";
  - make hundreds of implants in a week time with very optimized price, depending on size, since the same batch can be built again without additional preparation.

4. Processed material

The raw material in EBM is powder. Hence, it is reasonable to expect that the processed material contains residual porosity. However, the processed material on EBM is almost 100% dense because of complete local fusion of powder. Experimental results are offered to illustrate the capabilities of EBM in biomedical applications through two widely used materials: Ti6Al4V and CoCr ASTM F75 which are commercially available for processing on EBM. More materials are under development which will be mentioned in the 'Future Developments' section.

4.1 TiAl6V4 alloy

Ti6Al4V is a widely used biomaterial for many medical applications (Biomet, 2009), (Oshida, 2007), (Bronzino, 2006). Experimental results show that the properties of full-dense Ti64 processed on EBM fulfill the corresponding norm for medical implants (ISO, 2010), (ASTM, 2010) and are even superior to casted titanium alloys (Table 1).

Properties	Norm (ISO Standars, 2010)	Ti64 (EBM)	Ti64 (cast) (ASTM, 2010)
Yield strenght [Mpa]	760	849	825
Elongation [%]	10	15	10
Area reduction [%]	-	37	15-25
Young modulus [GPa]	-	125	-

Table 1. Comparative view of Ti64 properties: Electron Beam Melting (EBM) vs wrought Ti64.

However, the important advantage of Additive Manufacturing is the capability of producing designed porous material that can be combined with solid material in a single implant. Hence, it is interesting to take a look at the properties of porous material made on EBM. According to a several studies (Petrovic, 2011), (Parthasarthy, 2010), the properties of

porous Ti64 fabricated on EBM are comparable to commercially available materials (titanium foam, tantalum, etc.), even approaching to human bone properties as shown in Table 2. [1] [2] [3] [4]

Property	Porous Ti [EBM] [1]	Alternative foams
Porosity [wt %]	57.5	62.5 [2]
Compressive modulus [MPa]	2927	3000 [3]
Compressive strength [MPa]	195	65 [3]
Flexural strength [MPa]	101.98	105 [2]
Tensile strength [MPa]	~78 [4]	70 [2]
Fatigue properties	Fm = 3820 N R = 0.1 N ≥ 5.000.000 cycles	-

Table 2. Comparative view of porous Ti64 properties: Electron Beam Melting (EBM) vs commercially available materials

4.2 CoCr alloy

Cobalt Chromium is commonly used in fabrication of implants that are submitted to intensive wearing (knees, shoulders, elbows, etc.). Hence, it is very important for the material processed on AM to show good wearing resistance. For EBM CoCr that corresponds to ASTM F75 is commercially available. Experiments and tests have been made with this material (Petrovic, 2010) and confirm that the main mechanical properties comply with the corresponding norm (Table 3).

Property H/V	CoCr [EBM]	ASTM F75-07 (ASTM, 2010)
Tensile strength [MPa]	1171/1188	450
Yield strength [MPa]	776/769	655
Elongation [%]	5/7	8
Area reduction [%]	6/8	8
Thermal expansion coeficient [x10^{-6} 1/°C]	14-18/13-17	-
Wearing rate [x10^{-8} mg/cycle]	3.3/3.44	-

Table 3. Comparative view of CoCr F75 properties: Electron Beam Melting (EBM) vs corresponding norm.

5. Biological testing and validation

In addition to good mechanical behaviour, material produced by EBM has good biological response as well. Thomsen et al (Thomsen, 2009) have performed a study of surface characterization and early response of porous EBM material in rabbits. According to this

[1] Data for EBM porous Ti64 with pore size of 504 µm
[2] Data for Ti foam
[3] Data for tantalum foam
[4] Estimated value upon the results of samples with smaller and bigger pore size

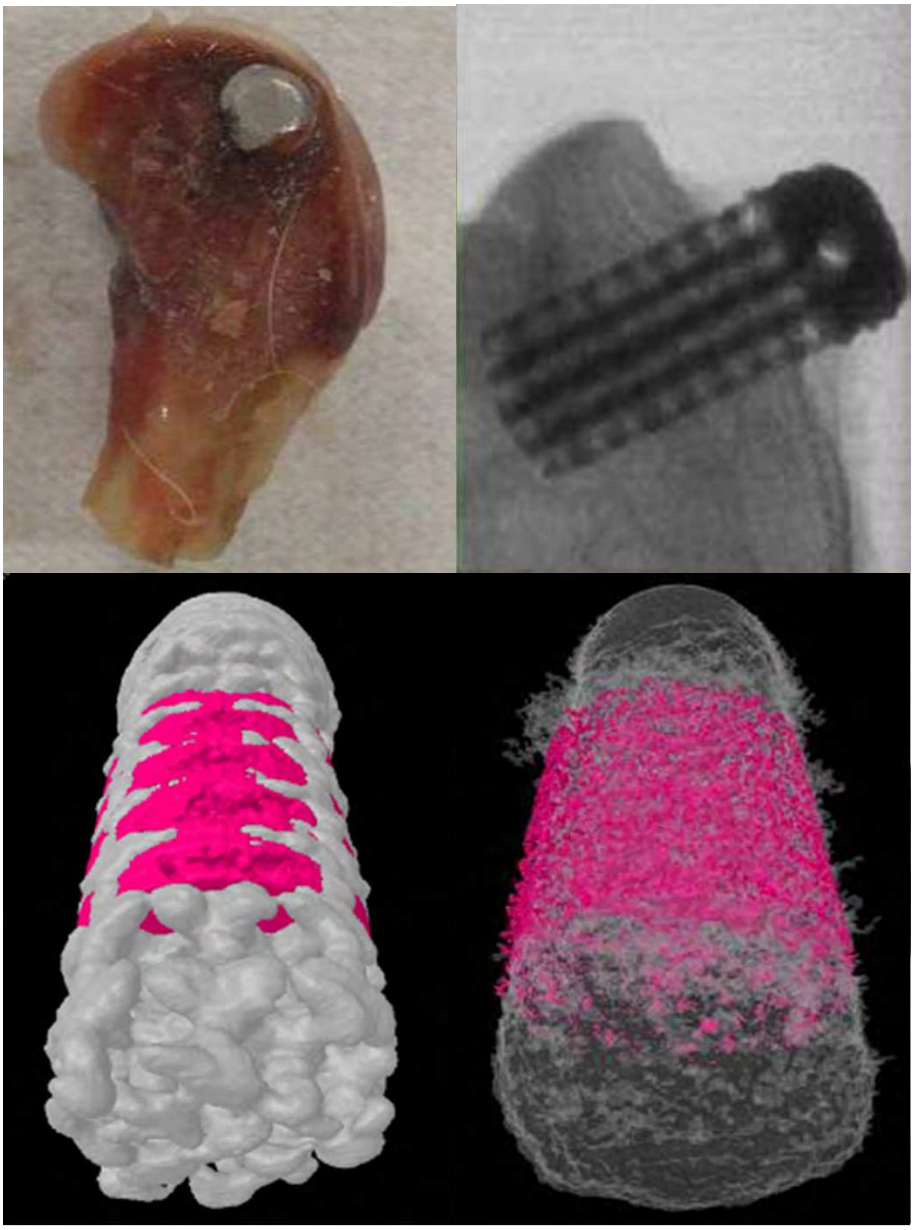


Fig. 14. Results of bone ingrowth testing of porous Ti64 in New Zealand rabbits (Courtesy of Instituto de Biomecánica de Valencia): a) excised sample for pull-out test; b) CT image of EBM sample; micro CT reconstruction of EBM (c) and conventional (d) Ti64 sample.

study the as-produced EBM Ti6Al4V implants had increased surface roughness but similar surface chemical composition compared with machined, wrought Ti6Al4V implants. Also, the general tissue response was similar with a high degree of bone-to-implant contact for all implant types. The results show that the surface properties of EBM Ti6Al4V display biological short-term behavior in bone equal to that of conventional wrought titanium alloy.

Furthermore, the bone ingrowth of EBM scaffolds in rabbits has been evaluated as well (Petrovic, 2011). For evaluation of bone ingrowth, EBM samples were compared to the samples provided by two medical device manufacturers, BIO-VAC and Eckermann. Five samples of each type were implanted in the femur of rabbits (Figure 14b). The control period was 8 weeks. The results show that after 8 weeks between 64 and 86% of void space was filled by the bone tissue. In addition, no adverse effect (infection, inflammation, rejection, etc.) was noticed in animals submitted to this study.

6. Applications

As explained in Supply Chain section, AM technologies manufacture directly from digital information of the part (digital files with 3D geometry) and do not need any kind of auxiliary tooling during the manufacturing process. Normally, the use of tooling (moulds, machining tools, etc) makes crucial influence on the product geometry, since desirable product features cannot be produced.

These manufacturing constraints are not present in AM processes. Using AM processes, designers are not limited or conditioned by conventional manufacturing constraints and can focus only on the optimum design of the product according to its application. AM technologies permit greater freedom in product design, enabling the manufacturing of much more complex geometries and in many cases, geometries that are impossible to manufacture with another fabrication method.

As a matter of fact, EBM has few manufacturing constraints, in terms of producing complex geometries and scaffolds structures and also offers the highest production speed (AIMME, 2009). Its high productivity makes economically viable the fabrication of high added value implants. Although it must be said that due to high processing temperature in EBM process, unfused powder is sintered around the part or scaffold. In certain geometrical features the cleaning process may be difficult, especially in large scaffolds with very small pore size.

The main advantages of using EBM as a Manufacturing technology for implants consist in:

- Full customization. Implant geometry can be customized to the anatomy of the patient and to its specific injury or pathology and fabricated by EBM, with its inherent benefits.
- Controlled and designed porosity. The inclusion of porous regions on the surface of the implant improves the bone osteo-integration in the patient body.

For the time being, three titanium (Ti64, Ti64 ELI and Ti grade 2) and one cobalt chromium (CoCr ASTM F75) alloys are being commercialized by the EBM technology provider and widely used for medical implants. There is a big number of case studies of customized implants that have been implanted in human body. There are also standard implants with added value certified for sale in EU and worldwide. In this section, the authors demonstrate the advantages of AM through different types of application, such as:

- Customized implants.
- Scaffolds with controlled designed porosity.
- Production of small-medium series of value-added biomedical products.
- Production of standard value-added biomedical products.
- Research in the biomedical field.

6.1 Customized implant

Currently, CT imaging has improved, in terms of resolution and 3D details, obtaining very accurate information from the patient. With this information, implants can be designed taking into account patient's anatomy, type of injury, surgical technique, etc. As previously mentioned, the design process starts from scanned information of the patient (Computed Axial Tomography (CAT), Magnetic resonance imaging (MRI) or Radiography). The implant design and development process are also supported by the previous experience of the design team (scientists, engineers, surgeons, etc). The new customized implant design is commonly validated by Finite Elements Analysis (FEA or FEM). In the case of a structural analysis, the solution shows a 3D map distribution with the stress level (strain, displacement, etc) along the geometry (Figure 15).

Principal benefits of customized implants are:

- Implant design adapted to the patient's anatomy and pathology.
- Diminishing of the stress shielding effect.
- Avoiding of manual adjustment of standard implant during surgery.

6.1.1 Design adapted to the patient

Customization of implant geometry is especially important in long duration prostheses (between 10-15 years), i.e. hip and knee prostheses, since the implant geometry adapts perfectly to the anatomy and injury of the patient (Figure 15). In other words, the size and weight of the prosthesis should be the strictly necessary for every patient, increasing the level of comfort. These benefits can be better understood comparing with standard prostheses and usual surgical procedure. When a standard prosthesis is implanted, the surgeon must decide which implant size could fit in the patient. It may be necessary to choose the bigger size. In this case, the surgeon has to create sufficient space for putting in and fixing the prosthesis. It implies to cut and remove more bone tissue and the patient has to carry with a bigger prosthesis. The removal of bone could be critical in the case of younger individuals (< 60 years) (Ratner, 2004), where it might be necessary to perform a revision surgery. Revision prostheses are bigger, causing further increase of fitting place and therefore the removal of more bone tissue. In contrast, the use of customized implants implies that the surgeon has just to create the minimum necessary space in order to fit the implant and leaves intact much more bone tissue for future revisions.

6.1.2 Diminishing of stress shielding effect

It is worth mentioning that customized implants could diminish the negative effect of stress shielding. Stress shielding refers to the reduction in bone density (osteopenia) as a result of removal of normal stress from the bone by an implant (for instance, the femoral

component of a hip prosthesis). According to Wolff's law (Wolff, 1986), bone in a healthy person or animal will remodel in response to the loads it is placed under. Therefore, if the bone load decreases, bone will become less dense and weaker because there is no stimulus for continued remodelling that is required to maintain bone mass. During the design process of the customized implant stress shielding can be taken into account and minimized by means of different designs and MEF structural analyses in order to achieve two aims:

- The implant should transfer bearing loads to the bone in order to avoid bone resorption.
- Decrease the stiffness (Young modulus) of the implant in order to make it similar to bone stiffness.

In case of standard implants, the size chosen by the surgeon doesn't adapt perfectly to the biomechanics of the patient and there will be a higher probability of bone resorption since this standard implant doesn't transfer loads properly to the nearby bone tissue.

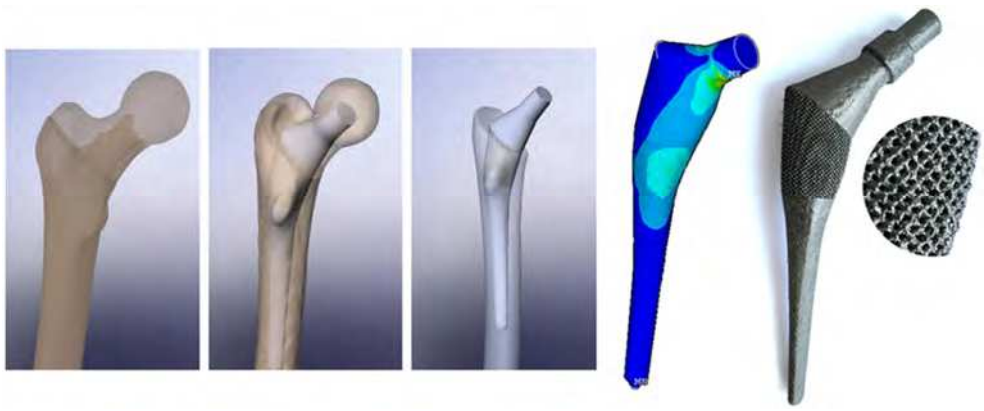


Fig. 15. Customized hip prosthesis developed in Project FABIO (Delgado, 2010).
This design was manufactured by means of EBM including a porous region for improving osseointegration and implant fixation in the body.
(Courtesy of AIMME, IBV, ASCAMM, TECNALIA).

In conclusion, the use of standard implants not only implies to remove more bone tissue than with tailor-made implants, moreover there is a also higher probability of bone resorption. Therefore, the future revision surgery might be more complex since the patient has lost more bone tissue in the damaged area.

6.1.3 Avoiding manual adjustment of standard implants

Another very important benefit of using customized implants is that surgical operations are shorter. During the operation, surgeon must adjust standard implants manually to the patient's anatomy and pathology in order to be able to place and fix them. This cannot be done until the surgeon has intervened the damaged zone (Figure 16).



Fig. 16. Tooling for standard plate deformation and adaptation. (Courtesy of AO Foundation Engineering).

In the case of customized implants is not necessary for surgeon to perform these modifications because the implant has been designed and manufactured totally adapted to the patient from direct scanned information (CAT, RMI, etc). It has been proved that the shorter the surgical operation the faster the patient's recovery and this improves patient's life quality. Further advantages of shorter surgical operation are:

- *Lower exposition to external bacteriological agents* (even in sterile atmosphere) leads to lower infection probability (one of major risks during traumatologic and orthopaedic operations).
- *Lower dosis of anesthesia is necessary.* This factor may be critical in certain cases.
- *Less recovery time in the hospital.* Therefore the costs of the surgical operation are reduced and more patients can be treated.

In addition, the adaptation of the conventional implant shape during the surgical operation produces 2 important drawbacks:

- When deformed, the implant has been damaged since the material has suffered plastic deformation. This deformation produces local strengthening while reducing ductility, which leads to the change of implant behaviour. This is especially critical in long term prostheses that bear cyclic loads, since this plastic deformation may reduce its fatigue strength and total implant durability, the implant has suffered a very harmful deformation equivalent to lots of cycles in normal conditions of use.
- The second inconvenience is that corrosion may appear due to the fact that plastic deformation may break the passive layer of the contact area (Pitting Corrosion). Localized corrosion can occur as a result of imperfections in the oxide layer. This can result in a large degree of localized damage because the small areas of active corrosion become the anode and the entire remaining surface becomes the cathode (Ratner, 2004).

After above mentioned, the benefits of using customized implants seem to be clear. Anyhow, the customization design process of an implant can drive to very complex geometries difficult or even impossible to manufacture by conventional manufacturing techniques such as machining, casting, forging, etc. Conventional manufacturing processes can be normally discarded for the following reasons:

- Casting, forging and HPDC are not economically viable due to the investment in the mould only for a unique part.
- In case that machining of customized geometry is possible, the more complex the geometries to produce, the more machining operations and setups are needed and the less economically competitive, comparing with AM.

6.1.4 Case studies of customized plates

In order to show above explained benefits of implant customization and fabrication with additive technologies, several case studies have been made with customized implants for animals. In these case studies, implants have been manufactured using EBM technology and implanted in dogs in a close collaboration of Metal-Processing Technology Institute AIMME, CIMA Research Group (University of Vigo) and FAUNA Veterinary Clinic (Rodiño, 2010), (CIMA, 2011). Customized implants for ten different patients have been developed, three of which are going to be presented in this section. Specific osteosynthesis plates were designed by researchers from CIMA together with the veterinary surgeon using the procedure mentioned in the Supply Chain section - upon medical images of each patient the model was reconstructed and manufactured on the EBM technology to be implanted. AIMME has offered technical advice related with the manufacturing technology (EBM) during the design process, has manufactured implants by means of EBM and also has performed finishing operations in order to get the optimum surface roughness in every case.

Case of BABY

The first patient Baby, is a 3-year old Yorkshire Terrier. He was admitted in December 2009 presenting a radius-cubital diaphysal oblicuous fracture with severe loss of radiographic density due to osteoporosis and disuse of the leg in question. If the X-ray images of healthy and injured leg are compared (Figure 17), it is evident that a 20-25% of radius-cubital length

had been lost. This was a challenging experimental case with few chances of successful outcome. Bearing in mind that there wasn't any commercially available plate, of this size and capable of being adapted to the damaged zone, the surgeon and CIMA researchers decided to design a customized titanium plate.

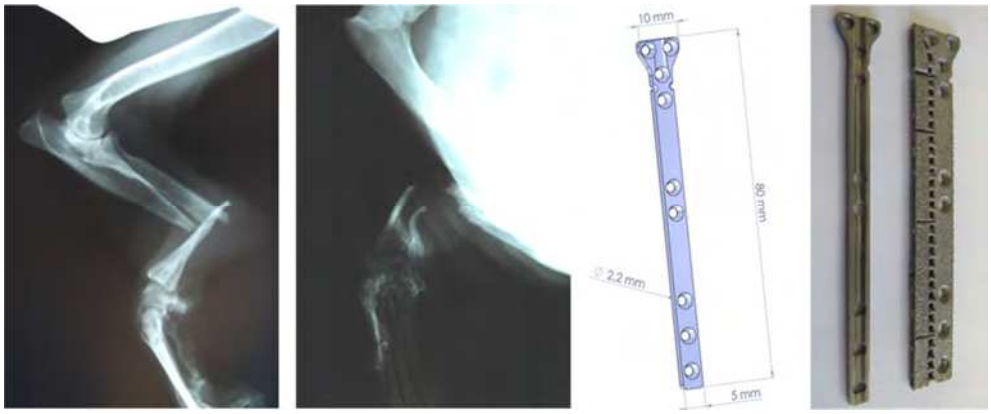


Fig. 17. From left to right: X-ray of the fracture suffered by Baby; customized CAD design of the plate and the plate as built on EBM and finished. (Courtesy of CIMA, University of Vigo and Veterinary Clinic FAUNA www.clinicafauna.es).

Figure 18 shows the outcome of the surgical intervention which took place in February 2010. The surgeon decided to apply an arthrodesis with the aim of preserving the leg and recover its functionality. Fifteen days after the intervention, Baby was submitted to a control of mobility and use of the leg, an almost normal mobility was observed. In addition, Baby's owner reported that, the dog recovered its normal impulses to jump and run, even after much time without being able to walk.



Fig. 18. From left to right: X-rays of Baby after the plate has been implanted and Baby leaning on its injured leg (Courtesy of CIMA and FAUNA).

Case of ARGOS

Argos is an 8-month Bordeaux Mastiff of 50kg. He was diagnosed a bilateral hip dysplasia with grade I patella luxation in the right knee. Initially, the surgeon performed a triple pelvis osteotomy using a standard commercial plate. Only 3 days after the surgical intervention, during the first control, a loosening of fixation screws was detected. The proposed measure was to increase the size of the screws from M3.5 to M4.5 (Figure 19).



Fig. 19. X-rays after implanting the commercial plate: loose screws after the first intervention (left) and new bigger screws after the second intervention (right) (Courtesy of CIMA and FAUNA).



Fig. 20. From left to right: new customized design; plate after being built and finished and X-rays after the intervention (Courtesy of CIMA and FAUNA).

In order to prevent risks of screw loosening, the surgeon sought for a more feasible solution for the left hip side. Due to previous experience with customized plates, the surgeon treated left hip dysplasia with a customized plate made on EBM (Figure 20). As expected, the first revision revealed that the screws on the right hip (commercial plate) started to migrate again while the screws on the left hip (customized plate) stood as tight as after the intervention. It

was also observed that a primary consolidation (the best possible) took place thanks to the proper load distribution.

Case of FITO

Fito is a 4-year old German Sheppard of around 40kg. Fito was hit by a car and suffered femur fracture. X-rays showed a multiple diaphysal fracture with big bone splinters. The bone fracture was repaired with a standard titanium plate and 12 screws of M3.5. During the intervention, the surgeon noticed that the plate had to be modified by hand to fit the damaged zone. Surgeon was modelling the plate with a pair of surgical pliers, and verifying visually that the plate was fitting properly. However, as mentioned before, this approach has two principal drawbacks: the surgical intervention is prolonged and the material of the plate suffers plastic deformation, which reduces significantly its fatigue behaviour and even causing precocious plate fracture.



Fig. 21. From left to right: lateral and frontal view of the fracture; X-rays immediately after the intervention and X-rays after the plate fracture was detected
(Courtesy of CIMA and FAUNA).

The later drawback appeared after only 3 days, Fito started to limp severely, presenting an angular deformation in the femoral zone. The plate suffered a fracture and completely lost its functionality (as shown on the last image of Figure 21).

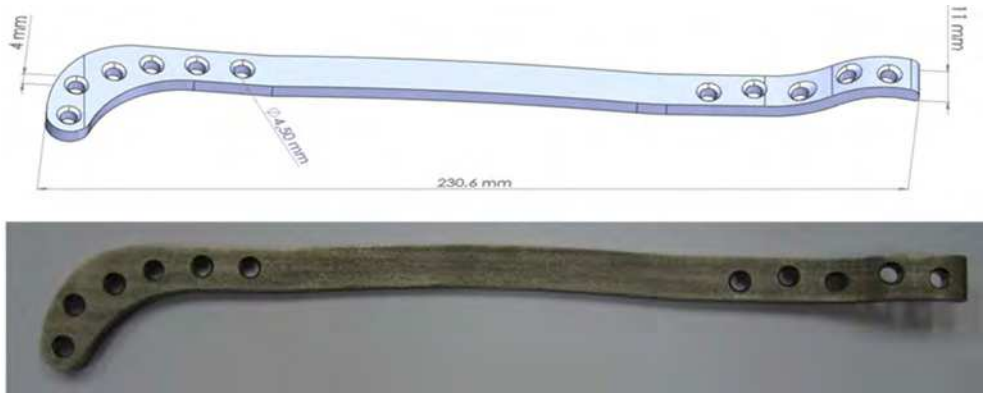


Fig. 22. Customized CAD design (above) fracture fixation plate build on EBM (below).

In order to avoid this problem a specific customized plate was designed and made in Ti64 ELI (Grade 23) ASTM F136 (ASTM, 2010) on EBM (Figure 22).



Fig. 23. Left: images showing size and weight of the customized plate. Right: post-surgery X-rays image of the plate (Courtesy of CIMA and FAUNA).

All case studies exposed above have shown that the use of customized implants makes the recovery of patients faster with fewer problems related to posterior revision surgeries, such as screw loosening, plate damage and fracture. In addition, it is important to highlight that, in some of these cases, plates were successfully removed after the bone was recovered, detecting that the bone had completely recovered its functionality.

Regarding Additive Manufacturing, these case studies show that EBM technology is a powerful tool for the manufacturing of customized implants due to:

- its production speed (less than 10 hours in the fabrication by EBM for each customized plate);
- excellent mechanical properties obtained in Ti6Al4V ELI;
- rough surface finish – unlike other surfaces that were polished, the plate surface in contact with the bone was left rough upon surgeon's request to allow better bone fixation.

Accordingly, the EBM process has been validated as one of the main options in case of customized implants: not expecting to replace existing production processes but to be an excellent alternative with certain advantages.

6.2 Scaffolds with controlled designed porosity

As exposed previously, EBM technology enables one-step manufacturing of prostheses that combine solid and porous zones (scaffolds). By means of 3D CAD software, these scaffolds can be designed with the desired pore size, morphology, well-interconnected porosity and gradual transition from solid (body implant) to porous (scaffold), as shown on Figure 24. Designers can control the implant design and have freedom in the design of scaffolds (multiple geometrical solutions) for different pathologies. Only AM technologies are able to manufacture this kind of 3D geometries. For the time being, implants are coated with additional post-processes as plasma spray, microspheres sintering, etc. In contrast with EBM

technology, these coatings are not able to produce regular or controlled scaffolds and provide less freedom in design (Ratner, 2004).

In bimetallic implants, there is a substantial risk of galvanic corrosion generated when materials with different electronegativity are placed in the same solution (Ratner, 2004), (Pedeferri, 2007). Conventionally made implants are usually coated with different methods and materials (plasma-sprayed titanium, Ti wire mesh, porous coatings made of CoCr or Ti, etc) for creating rough surfaces for encouraging bone ingrowth and proper fixation. With these conventional methods different metals might be combined and risk of galvanic corrosion may appear. In EBM, there isn't such a risk, due to the fact that part and scaffold are manufactured in the same material in one-step process (Figures 1 and 24).

Porous regions in contact with the bone tissue promote osseointegration (direct structural and functional connection between living bone and the surface of a load-bearing artificial implant), creating better fixation between the prosthesis and the bone. Due to the fact that scaffolds provide void space for bone ingrowth (Figure 14), this bone ingrowth will enhance the fixation of the implant. Scaffolds also contribute to transferring loads between the implant and the bone, avoiding the previously mentioned effect of stress shielding.



Fig. 24. Porous cranial implant (Courtesy of Arcam), customized acetabular cup (Courtesy of Arcam) and hip stem (FABIO Project) (Delgado, 2010).

EBM technology enables manufacturing of implants with different kind of scaffolds. These scaffolds can be placed in different regions of the same implant and each scaffold could have different features (pore size, morphology, etc) if the application requires. In addition, it is possible to manufacture totally porous implant (Figure 24).

Summarizing, EBM enables the manufacturing of implants with scaffolds, designed by means of CAD 3D tools (controlled porosity), which enhances the development of a new typology of high added value implants that are designed and manufactured according to the needs of the patient and not the other way around. This is possible because the EBM process doesn't have constraints imposed by traditional manufacturing processes. So as to illustrate above mentioned discussion, in the next paragraphs several kind of applications and high added value implants are going to be presented.

6.3 Production of standard value-added biomedical products

EBM technology is being used by biomedical industry for production of large series of standard implants (different sizes) but with the added value of a 3D scaffold designed by computer. These are successful cases of Italian manufacturers Ala Ortho and Lima, with

different products in the market. They manufacture acetabular cups with different 3D scaffolds which offer better response in the human body. These products have obtained the CE Mark and are being implanted in humans (Figure 25).



Fig. 25. Acetabular cup implants made on EBM by Italian companies: Cotile Fixa Ti-Por® by Adler Ortho® (left & middle) and DELTA-TT® Cup by Limacorporate (right) are already available on the market.

6.4 Production of small/medium series of value-added biomedical products

EBM technology can also be used for the production of small/medium series of implants with a competitive price, since it offers an interesting alternative to other manufacturing processes where previous investment in tooling is necessary. A variety of industrial sectors use tooling for manufacturing of large series (millions of units) where the cost of the tooling is included in the final price of each produced part. The larger the production, the smaller the cost fraction included in each part. This is not economically viable in the case of small-medium series, since the cost fraction derived from tooling increases as the number of parts decreases. The case of a customized implant is the low end of small series production (Figure 26).

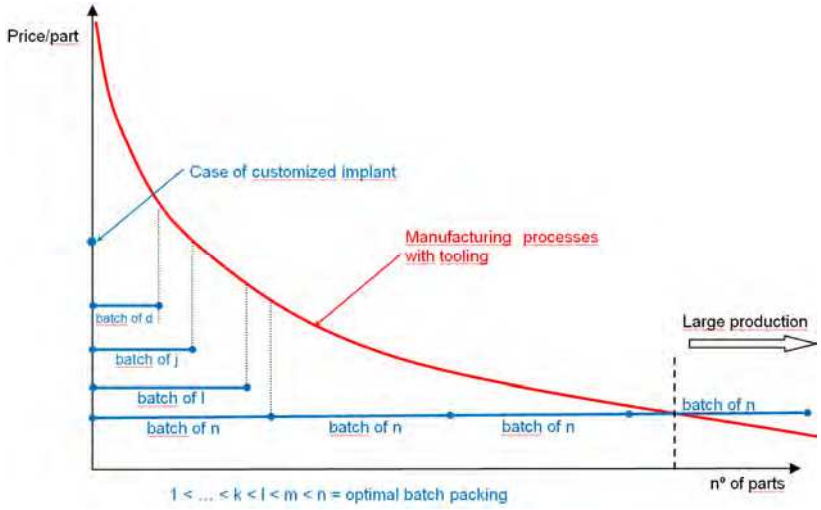


Fig. 26. Comparison of the cost per part using manufacturing processes with tooling and AM technologies.

In the case of manufacturing implants with EBM technology, there is no need of tooling, since EBM uses the digital file of the implant (3D CAD) for its direct fabrication as described in section 2. As a consequence, EBM makes profitable the production of small/medium series production because the cost of the batch remains always the same (for a determined geometry and batch size) without depending on the size of the whole production (Figure 26). All these economical aspects have several positive implications for EBM:

- For manufacturing of greater variety of implant sizes on EBM, unlike traditional manufacturing processes, it is not necessary to have a huge stock of moulds and tooling, since 3D models of different sizes are stored electronically and manufactured on demand.
- Semi-customization of standard products is also viable on EBM. Small modifications can be introduced in the standard implant model in order to treat specific pathologies with special requirements. The Spanish company LAFITT designed and manufactured a Total Hip Prosthesis with special indications (ASTM, 2010). Ten prototypes were manufactured by EBM in Ti6Al4V ELI in 36 hours. These prototypes are being evaluated by several tests. If results from tests are positive LAFITT may consider EBM technology as a production method for medium-small series, case of prostheses with special indications (Figure 27).
- The gradual evolution of the implant design and the addition of improvements between a fabrication and the next one are possible, due to the feedback and experience from already implanted cases, new findings, competitors, etc. At this point implants manufacturers that use conventional manufacturing techniques have two options:
  - Make costly tooling corrections in order to improve some features and keep product competitive and up-to-date or
  - Keep producing parts with the original implant design until the mould is paid off by a determined number of sold units. Then, the design of the implant can be updated by corrections on the mould. The fact that for standard implants there are several sizes implies one mould for each size. More demanded sizes can be updated earlier than the others because of moulds investment depreciation.
- As mentioned before, AM favours manufacturing batches in which every part is different in size, shape, special features, etc. This is possible because lots of parts can be packed inside EBM process chamber which has a capacity of 200x200x350 mm. One example is the case developed by the Spanish company SURGIVAL. This company has designed osteosynthesis plates for the treatment of different fractures in the human body (Radius distal, Proximal and Proximal Humerus plates). In total, 21 plates (different models and sizes) were manufactured in 7.5 hours by EBM in Ti6Al4V ELI fulfilling the standard ASTM F136 (grade 23). These plates are shown on Figures 28 and 29.

6.5 Rapid prototyping for the research in the biomedical field

EBM is being widely used for Research & Development in the biomedical field due to its production speed and design freedom which permits shortening the development periods. For this reason it is used for manufacturing prototypes in order to validate new products and concepts. As an example, the Spanish company SURGIVAL has developed a hollow tibial prosthesis for knee arthroplasty. The prosthesis has sensors for detecting osseous

loosening by means of telemetry. For this application this tibial prosthesis was manufactured in 6 hours by EBM in Ti6Al4V, consisting of two parts: the main body and a cover for the introduction of sensors inside (Figure 30).

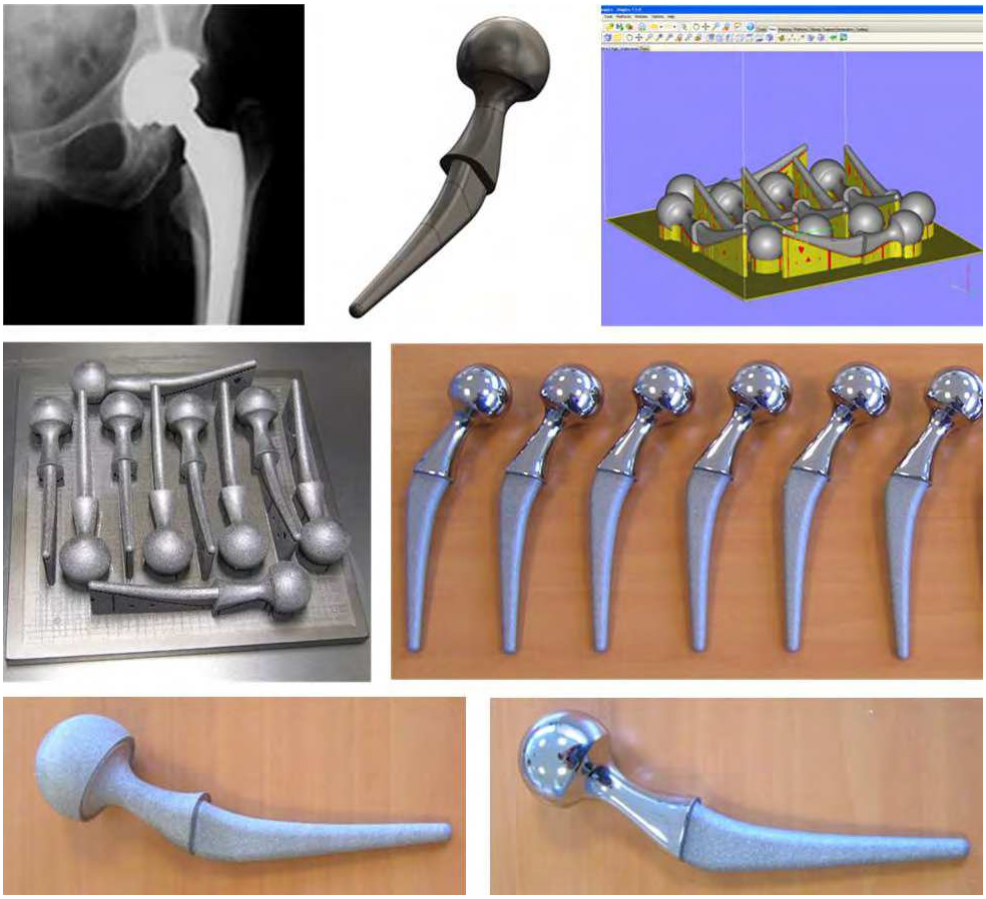


Fig. 27. LAFITT case. Upper row: radiography of a Hip prosthesis implanted; 3D image of the design of a Total Hip prosthesis for special indications; Virtual preparation of batch for building in Magics®; Middle row: 10 prototypes manufactured by EBM and complete batch of 10 prostheses finished ready for testing; Downer row: Comparison between Hip prosthesis before and after polishing.

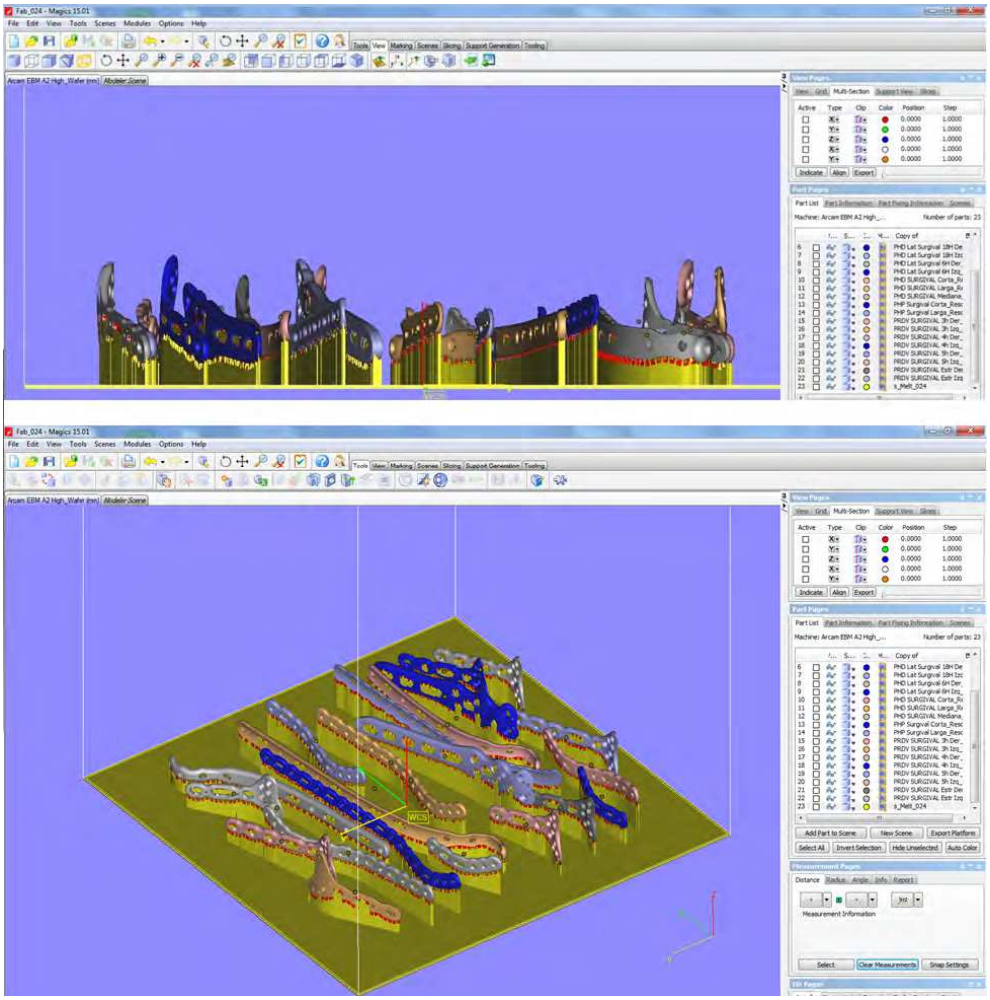


Fig. 28. Virtual preparation of batch for EBM building: case of 21 customized radius distal, proximal and proximal humerus plates manufactured in a single build (Courtesy of SURGIVAL).



Fig. 29. SURGIVAL case. 21 customized radius distal, proximal and proximal humerus plates manufactured in a single EBM build (Courtesy of SURGIVAL).

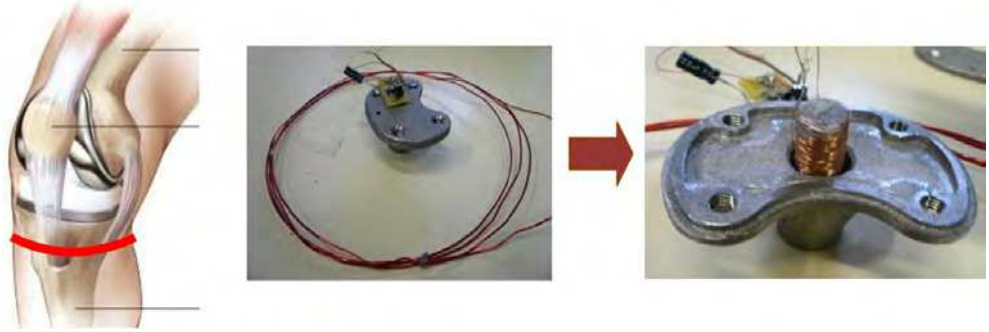


Fig. 30. Sensorized Tibial prosthesis manufactured by EBM in Ti64 for detection of osseous loosening. INTELIMPLANT CDTI's Project (Courtesy of SURGIVAL).

7. Future developments

As shown in the Applications section, EBM technology has proved to be a very powerful tool for manufacturing of high added value products. At the same time, EBM is a relatively recent manufacturing technology (first machine sold in 2002) and has much more room for improvement. For both reasons, there are different R&D attempts being performed along the world in order to obtain new findings applicable to new biomedical implants and for supporting the biomedical industry. These attempts are being performed in different R&D areas, such as:

- Materials
- EBM Technology
- Software

The following advances are not relevant only for biomedical sector but do offer competitiveness to additive manufacturing of medical implants.

7.1 Materials

In the biomedical field, lots of efforts are being made in order to develop new materials and/or improve material properties (metals and polymers) for biomedical applications. Also, the evolution of manufacturing processes, Coatings and Surface Implant Modification are remarkable areas of work.

Nowadays, metals are the best option for long time load-bearing prostheses. For this reason, the development of new metallic biomaterials for long-term prostheses and adequate the manufacturing processes in order to achieve best possible properties is a matter of great interest.

In particular, Titanium alloys are very interesting for research due to its excellent properties such as high corrosion resistance, low modulus, high fatigue strength, low density (lower than most common metallic materials), good mechanical properties, etc. There are two relevant areas under development:

- *Biocompatibility improvement:* Some attempts are being done for improving traditional Ti6Al4V alloys, i.e. Ti6Al7Nb and Ti5Al2.5 alloys improve material biocompatibility and mechanical properties, substituting Vanadium by Nb or Fe respectively (less toxic). These alloys have similar mechanical properties to traditional Ti6Al4V but providing with higher biocompatibility and slightly lower modulus. (Ratner, 2004), (ASTM, 2010), (ASTM, 2010).
- *Lower Modulus*. Beta-type Ti alloys with a low elastic modulus has proved to be effective for inhibiting bone absorption and enhancing bone remodelling. The addition of some alloying elements like Mo, Zr, Ta, etc permits to stabilize the BCC (beta) phase at room temperature. Moreover, it is well known that the Young modulus of β-type Ti alloys are considerably smaller than those of the α- and (α + β)-type Ti alloys. (Ratner, 2004), (ASTM, 2010), (Niinomi, 2008).

Although for the time being these alloys are not commercially available for EBM technology there are many efforts to adjust the processing parameters (AIMME, 2011).

7.2 EBM technology

As a proof of the improvement potential of this technology, recently a new manufacturing beam strategy named MultiBeam® has been developed and released. This strategy allows EBM to produce finer details and obtain better surface finish, splitting the high energy electron beam in multiple finer beams (less power/beam) so the energy input in every location on each layer can be accurately controlled. MB strategy opens the possibility of manufacturing implants with better surface finish and finer scaffolds (Figure 12). Some attempts with finer beams and powders are being performed in order to achieve higher resolution with the EBM process.

7.3 Software developments

Great efforts in different areas are being made in software developments since AM technologies work with digital files of parts.

- New 3D CAD (Computer Aided Design) tools will permit more freedom in design, since most commonly used commercial 3D CAD tools are conceived for conventional manufacturing processes and don't allow to design easily new concepts with complex geometries, i.e. scaffolds, fractals or bionic features. There are several commercial software tools available, i.e. 3-Matic® which allows common Computer Aided Design (CAD) operations on 3D anatomical data (STL format), Magics®, Netfabb® or AutoFab® which permit automated design of scaffolds structures. Further improvements are being developed in these commercial tools.
- KBE tools. Expert systems for process planning automation which will permit the automated orientation and location of a batch of different parts in the building virtual platform in order to obtain desired features or properties on each part, surface finish, mechanical properties, etc. (Petrovic, 2010).
- Specific CAE tools, for scan to part reconstruction (Mimics®), automatic guidance in implant design in STL format (3-Matic®), assisted an automated topological optimization of lattice structures (Within®), etc. Further improvements are being developed in these commercial tools.

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Comprehensive and systematic scientific researches in cell biology and molecular biology have promoted the evolution of traditional medicine. Scientists are now able to interpret a few perplexed medical difficulties with the emphasis on molecular levels. This book focuses on frontier progress in modern biomedical science dealing with regenerative medicine, gene medicine, nanobiomedicine, and medical devices. Each chapter is intently chosen and written by professional experts in the field of biomedical science. Biomedicine is a valuable guide for the readers to become aware of current advancement in rapidly moving field of biomedicine.

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