MEDICAL MANUFACTURING INNOVATIONS

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Abstract

The purpose of these studies was to improve the design and manufacturing process by selective laser melting, of new medical implants. After manufacturing process, the implants were measured, microscopically and mechanical analyzed. Implants manufactured by AM can be an attractive option for surface coatings to improve the osseointegration process. The main advantages of customized implants made by AM process are: the precise adaptation to the region of implantation, better cosmesis, reduced surgical times and better performance over their generic counterparts. These medical manufacturing changes the way that the surgeons are planning surgeries and engineers are designing custom implant. AM process has eliminated the constraints of shape, size, internal structure and mechanical properties making it possible for fabrication of implants that conform to the physical and mechanical requirements of implantation according to CT images. This article will review some custom implants fabricated in DME using biocompatible titanium.

Keywords: Additive manufacturing, implants, mesh, cervical plate, titanium, customized

1.   Introduction

Additive Manufacturing (AM) technology applications are very diverse and can be used in many fields, from industry to design or medicine. Applications of AM technologies in medicine are reported since 1994 [1, 2, 3, 4]. These applications have led to the development of customized implants that are physical prosthetic models made for each individual case in order to accurate reconstruction of bone structure. Custom implants are presurgicaly constructed based on medical data acquired by computer tomography or nuclear magnetic resonance using virtual 3D models and CAD/CAM techniques. Custom implants fabricated with AM have been used by different surgeons mainly for rebuilding post-traumatic or   post-tumor defects in the neocranium (cranioplasties) for reconstruction of viscrocranium defects but also for other defects and/or dislocations of the human skeletal system. Preoperative manufacture of customized implants offers many advantages compared to intra-operative modeling of alloplastic implants or autogenous bone grafts.

Fig.1 Manufacturing method of customised implants developed in DME and SLM equipment [14]
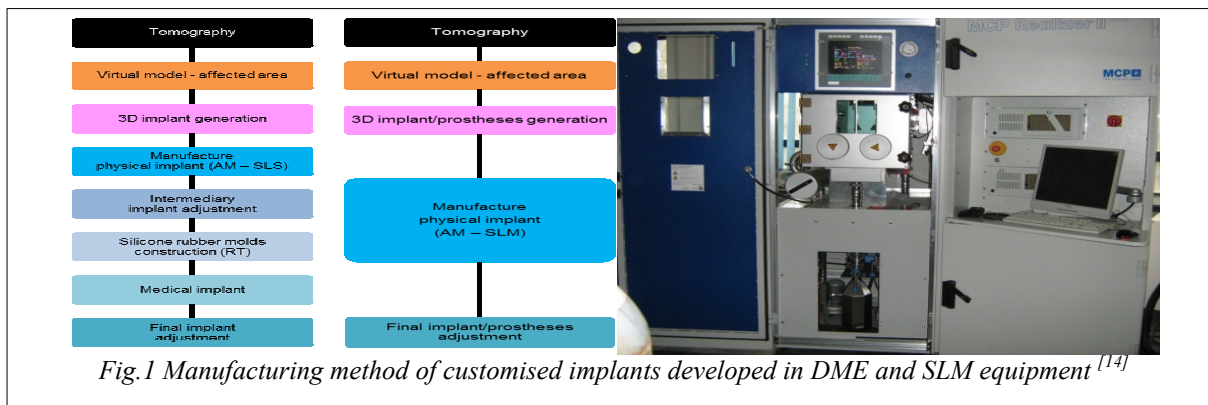
Researches in Department of Manufacturing Engineer (DME) were initiated since 1996 [5, 8]. It started by using silicone rubber to obtain casting molds. Some researchers [6] have used plaster molds for casting or injection molding of implants of biocompatible materials (usually poly-methyl PM and poly-methyl-methacrylate PMMA). Compared with plaster, the main advantage of silicone rubber is its elasticity [9] that allows preservation of model's fine details during the mold release. DME research in this area in collaboration with Department of Cranio-Maxillo-Facial Surgery (University of Medicine and Pharmacy Cluj-Napoca) has started since 1998. Using technical and technological facilities which existed at that time have been produced several physical models of polyamide implants by selective laser sintering (SLS) [7, 8]. Because the polyamide is not biocompatible the model was used as the master model for manufacturing silicone rubber molds to cast the implant of poly-methyl-methacrylate and poly-ethyl. Thus it was succeeded clinical to implement clinically personalized implants in viscero cranium defects reconstruction.

In figure 1 are presented two manufacturing methods of orthopedically customized implants that are elaborated up to now in DME [10, 11, 12, 13]. The current research project is offering a new approach based on the existing methods. They combine the experience of the team members that summed up along the years and the modern existing equipments of DME. Researches in this domain at DME were realized, in national premiere, in the BIOMAPIM project (www.biomapim.utcluj.ro) by the time of 2011-2013, by an inter and transdisciplinary collective, where even the undersigned had been a part of it as a member. This study will involve more researches that have an eye on elaborating a new composite material made by two components, one organic and other inorganic, resulting a biological composite named "biocomposite".
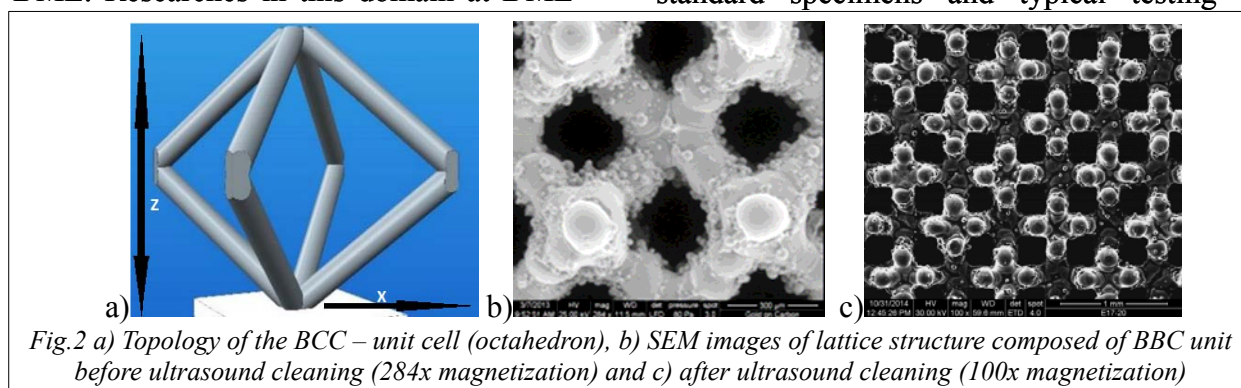
2. Materials and Methods

Pure titanium powder (TILOP 45) has 45 μm particle diameter, the melting point temperature around 1670°C and the following chemical constituents: 99.7% Ti, 0.08% Fe, 0.17%O, 0.03%C, 0.03% N, 0.01% H.

SLM ReaLizer 250 system (MTT Technologies, Germany) uses selective laser melting technology, an additive manufacturing process that provide 3D CAD data as a digital information source and energy in the form of a high-power laser beam (ytterbium fiber laser with 200W maximum power) to create three-dimensional metal parts by fusing fine metallic powders together.

Mechanical properties

Tensile and compressive properties were tested for the sheet specimens prepared using the SLM system at different speeds and laser power. Ultimate tensile strength (σ_{UTS}), ultimate compressive strength (σ_{UCS}) and Young modulus (E_Y) were determined by manufacture of standard specimens and typical testing

Fig.2 a) Topology of the BCC – unit cell (octahedron), b) SEM images of lattice structure composed of BBC unit before ultrasound cleaning (284x magnetization) and c) after ultrasound cleaning (100x magnetization)

procedures employed are given in earlier researches [15, 16, 17]. Using the same process parameters, the tensile strength of models can easily identified in special Tables. To verify and validate the results expressed for tensile strength and Young modulus tests were performed on standard specimens by Instron 3366 equipment and extensometer INSTRON 2620-602 according to ISO 6892:2009.

Porosity

The porosity was calculated as follows:

$$P = 10^2 \left(1 - \frac{\rho}{\rho_0}\right) \quad (1)$$

where ρ is the density of the sample, obtained by the ratio weight to volume calculated by the geometrical data of this specimen and ρ_0 the material standard bulk density. The total porosity of implants, calculated based on the relationship between the measured density of the samples and the material standard bulk density. The parts were weighed with an analytical balance (Partner AS 160.R2) with ± 0.2 mg precision. The implants must have at least 40% porosity to stimulate bone ingrowth. In a study by Esen and Bor [18] a minimum porosity of 55% was reported for direct connectivity of macropores with bone.

Development of macroporous parts

Macro-porosity on parts was developing with lattice structures. This are made by elementary cell unit named body-centered cubic (BBC) and it is an octahedron. In figure 2 is presented the used elementary cell-type develop by RDesigner software and SEM images with lattice structures manufactured by SLM. These models utilizes simple unit cell or geometrical elements which can be linearly expanded into 3D lattice structures having adjustable strut or ligament dimensions and spacing to control the porosity or density, and it is controlled via x, y, z parameters which can be from 0.4 mm to 1.2 mm (elementary cells BBC) [19]. The

cord-supported for lattice structure has a diameter between 0.195 to 0.251 mm and in figure 2 shows a SEM images with this type of porous structure. These structures will be used to stimulate the growth of new bone tissue into pores. These degrees of porosity would lead to an interconnected porous structure which favors the cell ingrowth to the porous space, vascularization, and transport of metabolic products. In general, implants with pore sizes in the range of 50 to 500 μm are suitable for bone ingrowth [20, 21].

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 using MIMICS software. The model can then be manufactured through SLM technology.
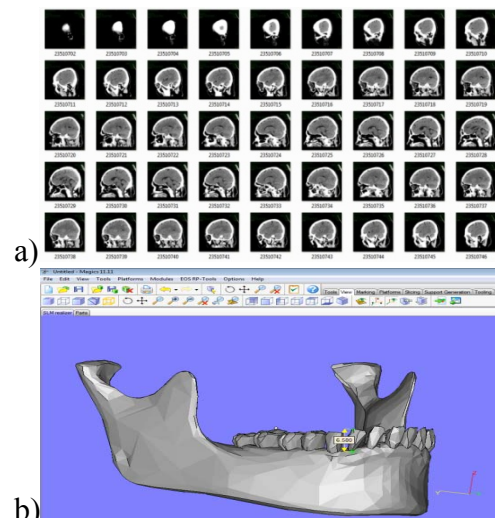
a)

b)

Fig. 3 a) CT images of patient head, b) 3D-CAD reconstruction of mandible

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 and surgical technique. In order to show above explained benefits of implant customization and fabrication with additive
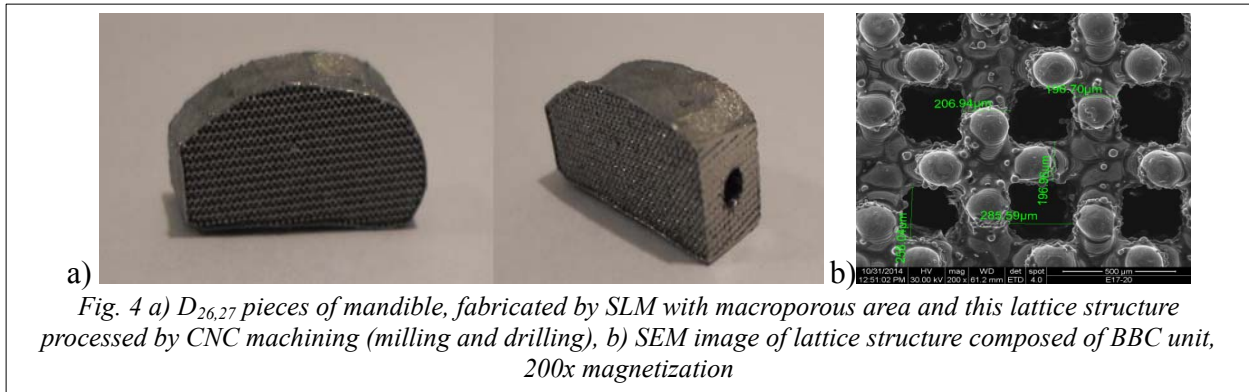
Fig. 4 a) $D_{26,27}$ pieces of mandible, fabricated by SLM with macroporous area and this lattice structure processed by CNC machining (milling and drilling), b) SEM image of lattice structure composed of BBC unit, 200x magnetization

technologies, several case studies have been made with customized implants (figure 3).

3. Case studies
Macroporous experimental implants

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 lattice structures allow void space for bone ingrowth, this bone ingrowth will enhance the fixation of the implant. Lattice areas also contribute to transferring loads between the implant and the bone, avoiding the previously mentioned effect of stress shielding [22]. It can be controlled the implant design and have freedom in the design of scaffolds or lattice structures (multiple geometrical solutions) for different pathologies. SLM technology manufactured these 3D geometries and after fabrication, implants will be coated with additional post-processes as plasma spray, microspheres sintering, biomimetic, etc. These lattice structures can be placed in different regions of the same implant and each lattice area could have different features (pore size, morphology, etc) if the application requires. It was possible to manufacture totally macroporous implant with only a contour having a 0.2 mm thickness (figure 4). Initially experiments were carried out on D_{26} and D_{27} parts, fabricated with 0.5mm BBC cell and the porosity obtained varies between 45-46%. These parts represent a piece of real human
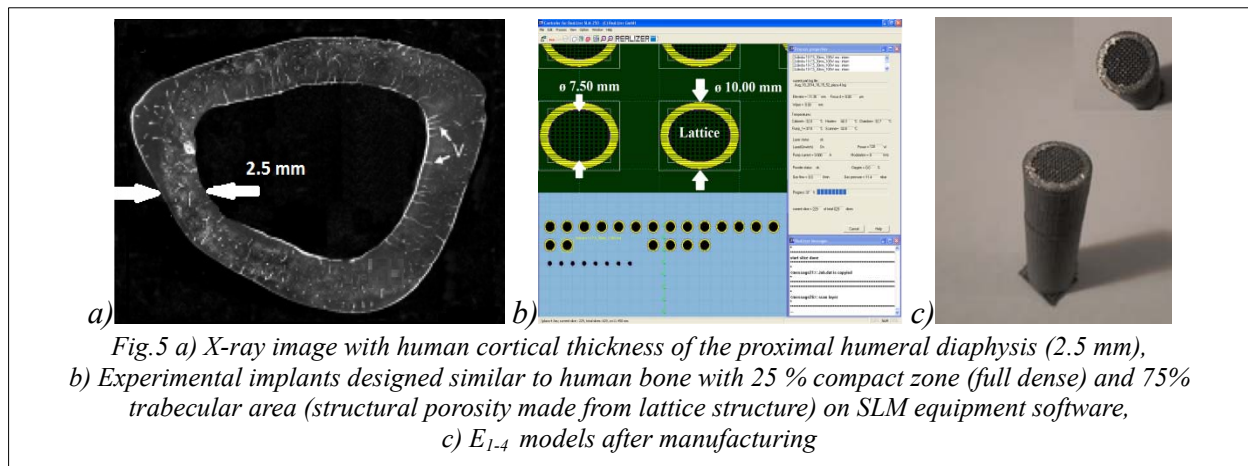
mandible showed in figure 3 and it can be even milling by CNC machining or drilling to insert dental screw. According to other studies mandible bone have Young modulus between 4-25 GPa and these experimental implants have the minim value (around 5 GPa) [23]. Ultimate compressive strength determinate on standard samples with the same structure and process parameters was between 80-90 MPa and mandible bone have 80-120 MPa.

Biomechanical properties of healthy bone depend on patient age and one of the most important characteristic of bone implants is the osteointegration. The osteointegration of the grafts is related to the degree of porosity and pore size. These grafts manufactured by SLM had pore size between 250-291μm and the cord-supported for lattice structure has a diameter around 0.2 mm (figure 4b). Based on the literature data and also on the size of osteoblasts cells (which vary up to 20-25 μm) was found that the optimum pore size have to be 50-550μm to stimulate the proliferation of osteoblasts cells [20, 21]. All the implants information was detailed in Table 1.

M. Tingart et al. develop a research about cortical thickness of the proximal humeral diaphysis where anteroposterior radiographs were taken of 19 human cadaver humeri [24]. The cortical thickness was measured at two levels of the proximal humeral diaphysis. The bone mineral density was determined for the humeral head, the surgical neck, the greater tuberosity and lesser tuberosity using dual-energy X-ray absorptiometry. The mean cortical thickness was 4.4 mm. The cortical

Properties		Implant Model					Cortical Bone [24]
		D_{26}	D_{27}	E_{1-4}	E_{9-12}	E_{21-24}	
Process Parameters	Scan Speed [mm/s]	375	300	1000	1000	833	
	Power [W]	88	88	100	100	120	
Dimensional Error, D_e [%]		+ 0.54	+ 0.57	+0. 67	+0.45	+0.41	
Porosity, P [%]		46.51	45.65	37.29	52.54	44.03	0.4-1
Young Modulus, E_Y [GPa]		5.01	5.01	7.53	8.38	13.69	4-25
Compressive yield streght, $\sigma_{0.2}$ [MPa]		-	-	157.87	172.65	256.34	
Ultimate compressive strength, σ_{UCS} [MPa]		89	81	294.32	335.48	512.59	145-190 79-120
Roughness on Z-axis	R_a [μm]	10.64	11.78	11.08	10.22	12.05	
	R_z [μm]	61.27	68.34	59.38	59.79	68.11	
	R [μm]	14.59	15.02	13.56	12.81	14.92	

Table 1. Implants characteristics

Fig.5 a) X-ray image with human cortical thickness of the proximal humeral diaphysis (2.5 mm), b) Experimental implants designed similar to human bone with 25 % compact zone (full dense) and 75% trabecular area (structural porosity made from lattice structure) on SLM equipment software, c) E_{1-4} models after manufacturing

thickness of the proximal diaphysis is a reliable predictor of the bone quality of the proximal humerus [24]. In order to develop a similar bone implant like real human bone was developed experimental implants namely E_{1-4}, E_{21-24} and E_{9-12}. These experimental implants have the form of cylinder with different macro-porosity designed in RDesigner and various values for BBC cell like: x=y=z=0.5 mm (E_{1-4}), x=y=z=0.6 mm (E_{21-24}) and x=y=z=0.7 mm (E_{9-12}), being in accordance with the human bone (cortical and trabecular tissue). The full dense area represents the cortical bone (2.5 mm thickness) and lattice structures have similar construction like trabercular bone   (7.5 mm thickness) presented in figure 5.

As summarized in Table 1, the elastic moduli of SLM-processed samples were   5-13 GPa for porous parts which have the porosity levels of 37% to 52%. As evident, Young's moduli of all samples are much lower than those of 316L stainless steel   (210 GPa) and chromium cobalt alloys   (240 GPa) which have been used as surgical implants for the past years. More importantly, porous samples with this porosity show an elastic modulus similar to human bone (4–25 GPa). This low range of Young's modulus can prevent stress shielding effect and consequently revision surgery. These promising results of low elastic modulus samples resulting from SLM with porous samples could be applicable for biomedical implants.

In these initial experiments, after SLM process the surface roughness of parts has values for R_a between 10 to 12 μm and it need to be improved. Further studies are needed to determine all the physico-mechanical characteristics and compare to human bone.
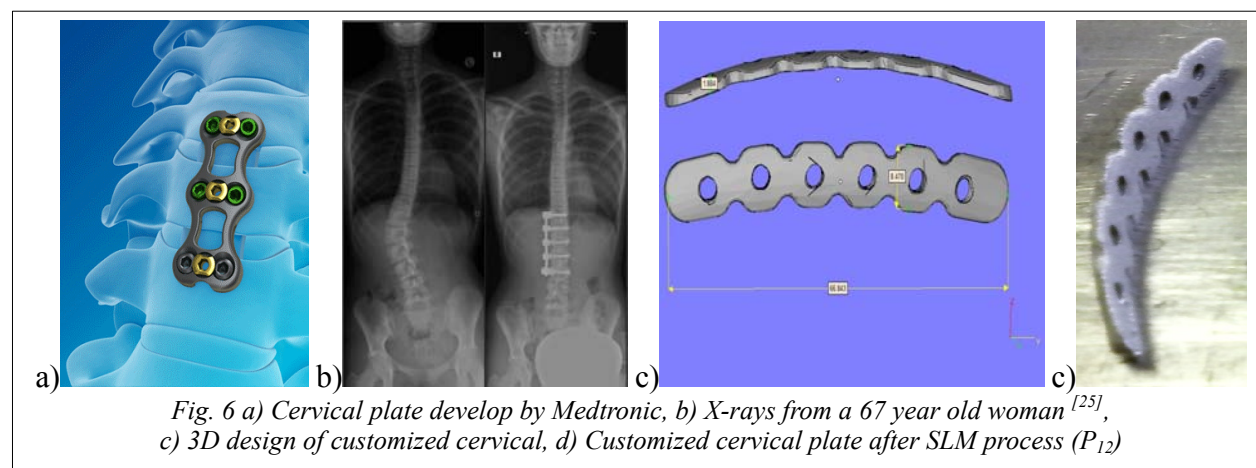
Cervical plate

The anterior cervical plate system presented in figure 6 is a ratcheting plate featuring segments that translate under compression, but maintain their position under tension. Test results demonstrated that the unidirectional plate had less motion in flexion-extension and maintained a more consistent graft load when compared to bidirectional design. This system is intended for use in temporary stabilization of the anterior cervical spine during the development of spinal fusions in patients with: degenerative disc disease, trauma, tumors, deformity, pseudoarthrosis, and failed previous fusions [26]. Spinal implants made from titanium are used in cases where bioabsorbable anterior cervical plates would not be sufficiently robust. It is important to stabilize the spine with a stronger spinal implant for a better fixation. Dr. Dachs obtained a successful, safe and reliable procedure for the correction of thoracolumbar and lumbar scoliosis using instrumented anterior spinal fusion [25]. It provides effective deformity correction and good maintenance of the correction. Fusion can be limited to the major structural curve, with reliable spontaneous correction of the thoracic curve (figure 6 a, b).

There are currently a multitude of dynamic plates available, with new designs being frequently introduced. Dynamic anterior plates have been popularized to controlled settling, thereby promoting load sharing across the construct. A current study compares similar patients and demonstrates no clear advantage of the use of a dynamic plate over the cheaper, simpler static plate after multilevel anterior cervical discectomy and fusion for degenerative pathologies [27].

Considering this study, figure 6 presents also the 3D design of a customized spinal prosthesis and the final product obtained through additive manufacturing process (SLM). It was fabricated 3 customized cervical plate with 6 threaded holes and the plate have a thickness of 1.8 mm, a width of 8.4 mm and a length of 66.8 mm. For fabrication was used process parameters mention in Table 2 and the mechanical properties obtained was similar to external fixators because it was used the same process parameters. The surface roughness presents in Table 2 was obtained with-out any post-processing treatment. This customized cervical plate fabricated by AM process was used in a clinical study develop by surgeons from "Victor Papilian" Faculty of Medicine, "Lucian Blaga" University of Sibiu.

a)   b)   c)   c)

Fig. 6 a) Cervical plate develop by Medtronic, b) X-rays from a 67 year old woman [25],
c) 3D design of customized cervical, d) Customized cervical plate after SLM process (P_{12})

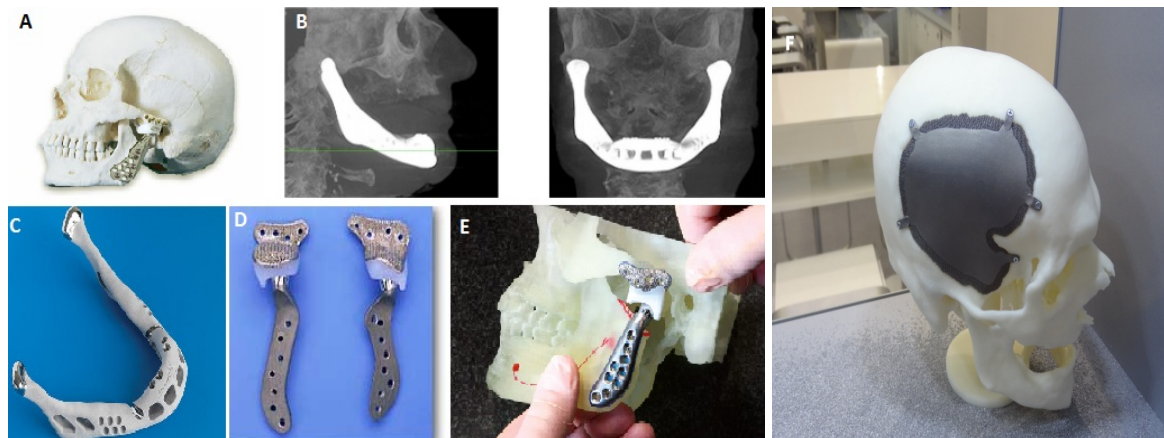promote cervical spine fusion by allowing   **Midface reconstruction**

Fig.7 a) Total joint replacement by TMJ Concepts, b) X-ray images showing the AM-produced lower jaw reconstruction implanted into the patient (left: side view; right: front view), c) The 3-D printed custom-made implant was coated with hydroxyapatite, University of Hasselt, d) and e) Temporomandibular joint produce through CNC machining, f) Titanium porous cranial implant fitting to the cranium mode, Concept Laser

TMJ concepts manufacture patient-fitted prostheses for reconstruction of the temporomandibular joint, customizing the joint allows for maximum fixation. The condylar head is made of cobalt-chromium-molybdenum, and the body is composed of titanium alloy. Pure titanium mesh is used for the fabrication of the mandibular fossa, and its articular surface is made of ultra-high-olecular-weight polyethylene (figure 7).

The world's first additive manufactured full mandible was implanted in a patient by Dr. Jules Poukens and his team in Belgium is seen in figure 7 b) and c). In recent years the model of the cranium with the defect is fabricated using additive manufacturing technologies. Figure 7f) shows a large titanium mesh cranioplasty implant with porous contact area.

Using bioresorbable materials, implants can be manufactured which dissolve in the human body and are replaced by natural bone structure. For large implants an interconnecting porous structure should be integrated in the implant for a good vascularisation. Additive manufacturing technology can directly develop these internal structures. The structure can be designed by consequent following the guidelines of the medical expert. Figure 9 presented a cranial implant made of composite powder (β-TCP / PDLLA) abricated by SLS process [28]. The mechanical properties of fabricated test geometries are in the medium to high range of human cancellous bone and the implants are therefore suitable for application in non load-bear-ing bone defects. In vitro experiments show good
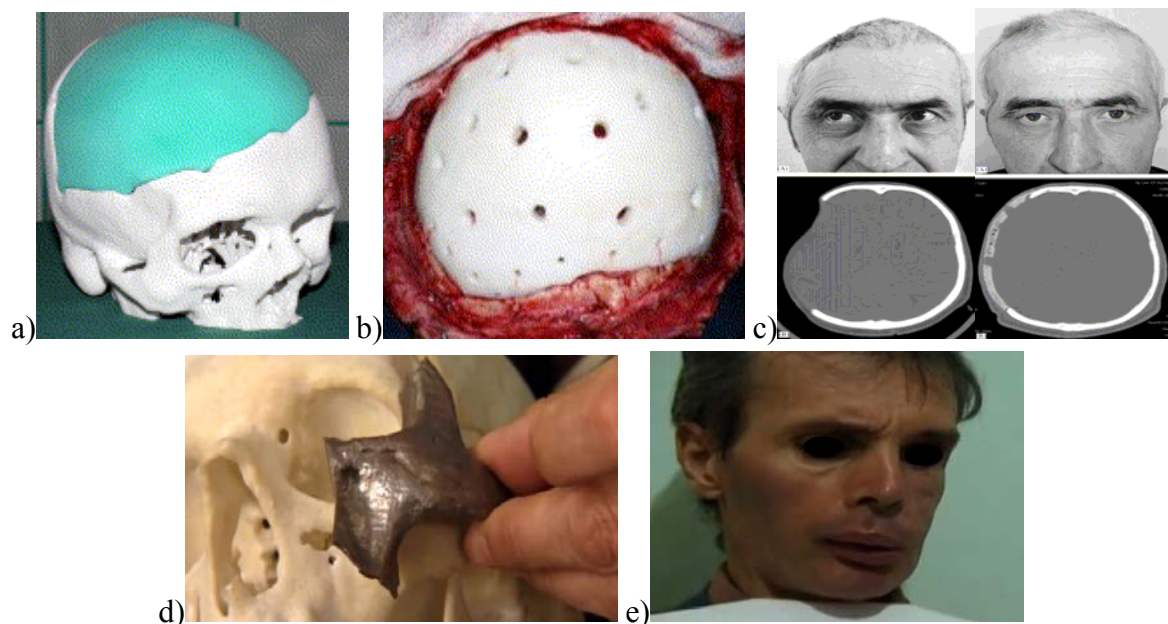

Fig.8 3D reconstruction of patient specific implants made in DME, a) Master model of implant, b) Intraoperative fixation of polymethylmethacrylate implant , c) Patient before and after reconstruction surgery, d) Reconstruction of patient specific titanium implant, e)Patient after 4-month post-operative

proliferation and no cytotoxicity of human osteoblasts on SLM test geometries.

In the right side of figure 9 it can be seen the same 3D CAD model of zygomatic bone previously presented manufactured also by selective laser sintering. The white powder PA 2200 has high strength and stiffness, good chemical resistance, excellent long-term constant behavior, high selectivity and detail resolution, biocompatible according to EN ISO 10993-1 and thermal conductivity 0.144 $Wm^{-1}K^{-1}$. This powder is recommended to medical applications (e.g. prostheses) because it has a low thermal conductive value.

Figure 9 shows another method that was used to produce customized implants with the following steps: 3D CAD reconstruction, fabricated the master model of implant by SLS process and PA 2200 powder material, create a silicone rubber mold with the master model and then in this mold was fabricated the implant from a polymethylmethacrylate material (PMMA). PMMA was used as the reconstruction material and these personalized implants were developed for 10 patients (9 men and 1 woman) who previously received a craniectomy. The symmetry gained after cranioplasty was quantified by volumetric analysis using 3D reconstructed postoperative computed tomographic imaging. No infectious episodes or signs of plate rejection were encountered and the custom-made implants

Table 2. Implants characteristics

Properties		Implant Model			
		B_1	P_{12}	F_7	F_8
Process Parameters	Scan Speed [mm/s]	400	400	833	833
	Power [W]	120	120	120	120
Dimensional Error, D_e [%]		+0.2	+0.2	+0.6	+0.7
Porosity, P [%]		0.5	0.4	33.4	57.8
Young Modulus, E_Y [GPa]		96.7	96.7	45.4	18.2
Yield tensile strength, $\sigma_{0.2}$ [MPa]		410	410	Was not possible to analyze because of their shape	
Ultimate tensile strength, σ_{UTS} [MPa]		441	441		
Roughness	R_a [µm]	2.1	10.2		
	R_z [µm]	10.7	59.7		
	R_q [µm]	3.5	12.8		

for cranioplasty showed a significant improvement in morphology. The implants could be very useful for repairing large and complex-shaped cranial defects and bone reconstruction of other sites [29, 30].

Figure 8 d) and e) shows the zygomatic implant manufactured by SLM in our department before and after post-processing. A similar implant was donated to a man (45 years old) in distress, who suffering a car accident and the left side of midface was completely destroyed (zygomatic bone). The advantage of this titanium implants compared to implants made from plastic (polymethyl methacrylate PMMA) is that titanium is more stable and is integrated into the bone structure. The surgical act and implant method for manufacturing was an
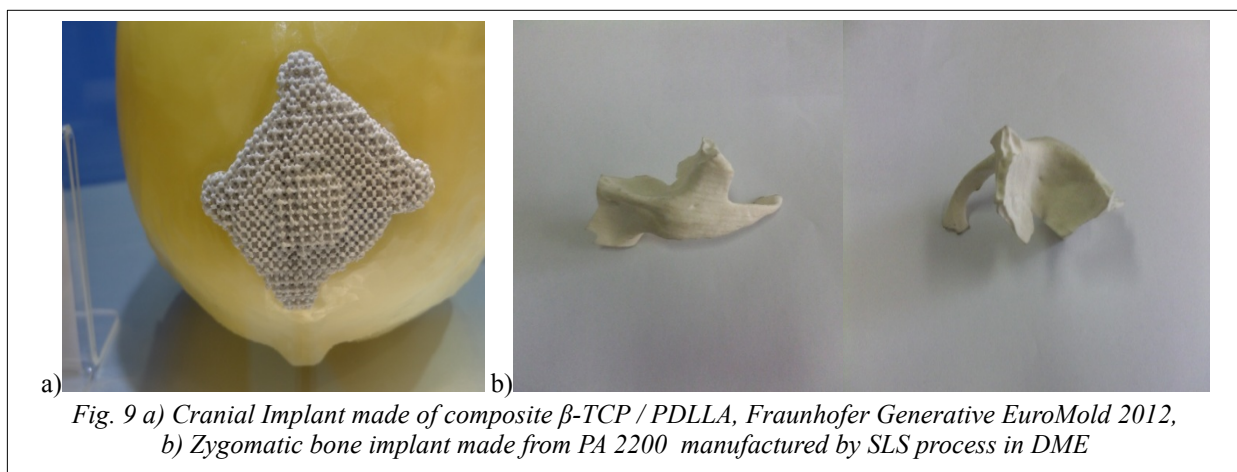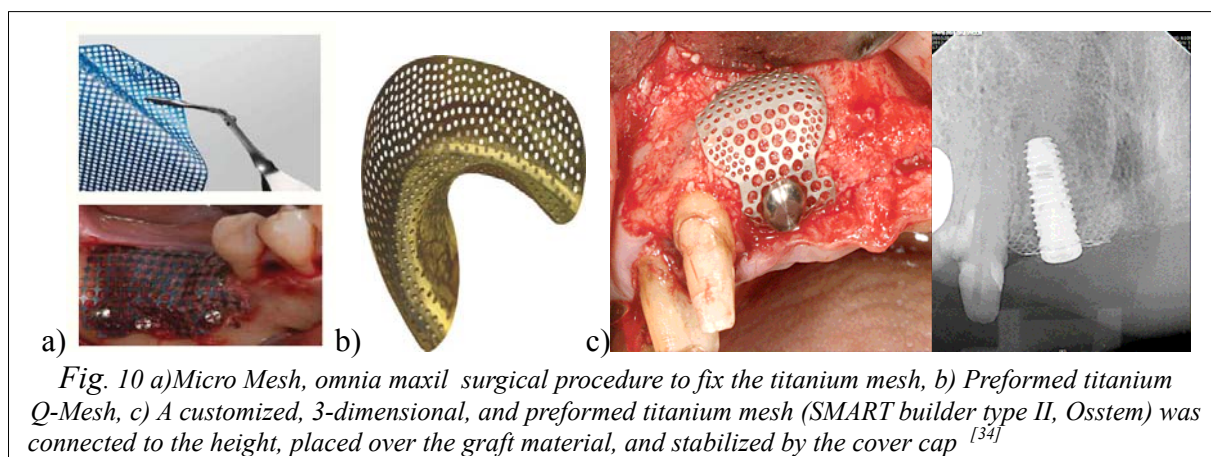

Fig. 9 a) Cranial Implant made of composite β-TCP / PDLLA, Fraunhofer Generative EuroMold 2012,
b) Zygomatic bone implant made from PA 2200 manufactured by SLS process in DME

Fig. 10 a)Micro Mesh, omnia maxil surgical procedure to fix the titanium mesh, b) Preformed titanium Q-Mesh, c) A customized, 3-dimensional, and preformed titanium mesh (SMART builder type II, Osstem) was connected to the height, placed over the graft material, and stabilized by the cover cap [34]

international premier because, so far such customized titanium implants were used only to reconstruct the mandible. The surgery team of doctors was conducted by Dr. H. Rotaru. The result of the surgery was a success, and after four months the implant was perfectly integrated in the body without any signs of rejection [31]. Psychological condition of the patient was also greatly enhanced by reintegrating into the community.
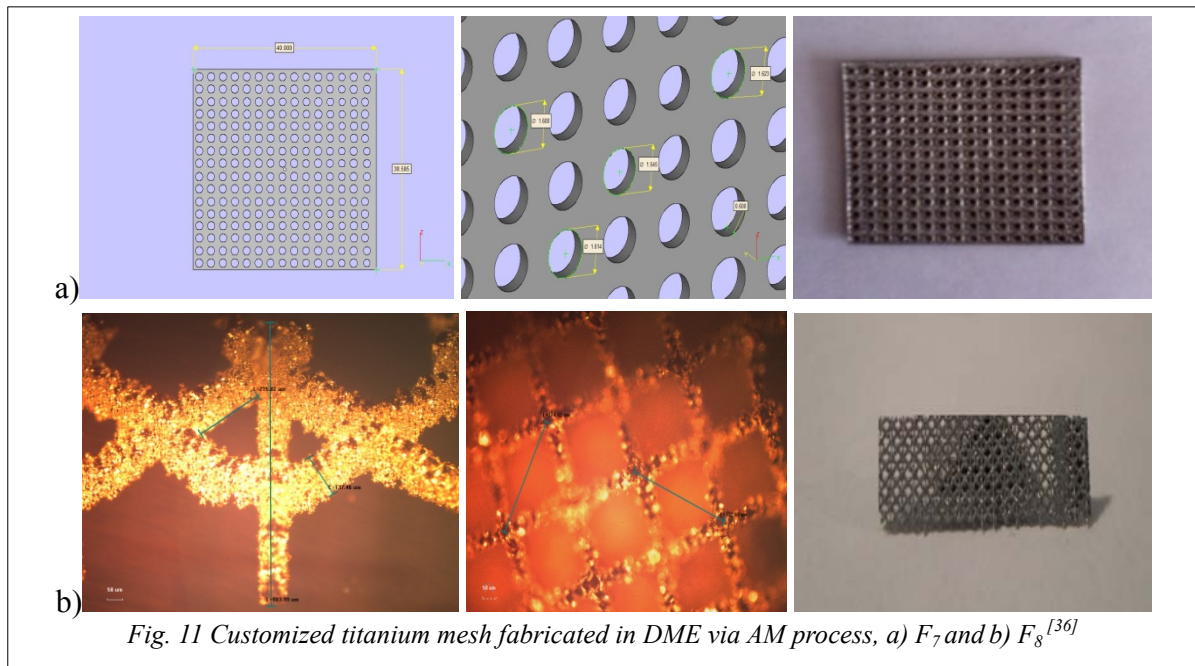
Titanium customized mesh

Meshes and membranes of titanium are used as protection for bone reconstruction and they are available in different sizes and thicknesses to could adapt for any bone defect (figure 10 a and b). The 0.2 mm thick meshes ensure a better stabilization in case of serious bone defects, whereas 0.1 mm thick meshes are easier to adapt to any kind of bone defect. For mesh stabilization is used titanium micro-screws with 1.5-1.7 mm diameter.

Figure 10 c) presented a customized, three-dimensional, and preformed titanium mesh used in combination with autologous bone induced successful bone regeneration in peri-implant defects occurring after implant placement. Even in the cases of titanium mesh exposure, this preformed titanium mesh produced reliable outcomes as a barrier membrane. This preliminary study shows histologic evidence of satisfactory vital bone formation in the augmented area. Preformed titanium mesh supports the grafted space for new bone formation,

makes application and removal convenient, and minimizes the risk of mesh exposure in the reconstruction of peri-implant alveolar bone defects [33]. In order to this study and other in this field [34, 35] it was designed and manufactured 2 types of mesh named F_7 and F_8 (figure 11) and they had the thickness 0.2 mm and 0.6 mm. F_8 mesh was designed with different diameters of holes   (ø1.5 mm to ø1.7 mm) to see the accuracy of SLM equipment.

Factors such as osteogenic potential of the host residual bone, systemic health of patients, and morphology of the defects, will delimit the ideal bone substitute for each situation. For example in sinus augmentation, allografts, xenografs and synthetic calcium phosphates have been used as alternative to autografts with high rate of implants success and survival. To improve the osseointegration all the implants have special surface treatments. Among these are infiltration of hydroxylapatite (HA), β-TCP, enzymes, growth factors or other drugs and biomimetic coating.

Fig. 11 Customized titanium mesh fabricated in DME via AM process, a) F_7 and b) F_8 [36]

4. Conclusions

There are different researches attempts being performed along the world in order to obtain new findings applicable to new biomedical implants and for supporting the biomedical industry. These days, the main object is to combine porous medical applications manufactured by SLM technology with a variety of surface modification techniques developed in orthopedics and they have been successfully adapted to implants.

Engineers and surgeons are leading towards the emergence of a new specialization as bio CAD/CAM that will make possible emergence of patient specific implants that will replicate not only form as it is today but also have mechanical, chemical and physiological properties similar to native tissues they replace and provide an environment for cell differentiation and growth.

Further researches will include in vivo test, to check the proliferation of bone cells and the ingrowth osseointegration process on these porous implants made by SLM process. The mechanical properties of titanium and its alloys can be adapted to the requirements of patients to be more friendly.

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