ADDITIVE MANUFACTURING OF POROUS TI-BASED ALLOYS FOR BIOMEDICAL APPLICATIONS – A REVIEW

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Abstract

Titanium (together with its alloys) has become 'king' among biometals and has demonstrated to function perfectly in the human body. Despite its well-known celebrated biocompatibility properties, it has a major drawback due to its relatively high Elastic modulus as compared to bony tissue. Using additive manufacturing (AM) methods to manufacture porous Ti-based implants by a process called porosification would greatly reduce the Elastic modulus to a value suitable for biomedical applications.

Varying the processing parameters of AM methods could lead to production of graded pore implants. Scanning speed was identified as the major influencing parameter which could be varied to produce pore-graded implants. Even though the fundamental principles of manufacturing porous Ti-implants are very well grounded in literature, the optimum pore size and corresponding mechanical properties for bone ingrowth are yet to be determined.

Keywords: additive manufacturing, graded or gradient pores, implants, porosity, Ti-based alloys

1. INTRODUCTION

Loosening of prosthetic joints is the main reason for implants failure, due to the high Elastic modulus of metallic biomaterial (80-120 GPa) (Niinomi, Narushima, & Nakai, 2015). The Elastic modulus of human cancellous bone is <3 GPa and that of compact bone is between the ranges of 3-30 GPa (Long & Rack, 1998; Wen, Yamada, Nouri, & Hodgson, 2007; Parthasarathy, Starly, Raman, & Christensen, 2010); as a result of this Elastic modulus mismatch, when a metallic implant is planted into a living bone, the metallic material bears the load without transmitting the load to the surrounding bone *(stress shielding effect)* which leads to implant failure (Barbas, Bonnet, Lipinski, Pesci, & Dubois, 2012).

Metals are considered the optimum choice for biomedical applications because of their structural advantages as compared to other biomaterials, with Ti-based alloys as the most preferable, due to its excellent specific strength, exceptional corrosion resistance, low weight, low toxicity, etc. (Niinomi, 2003; Zhou, Niinomi, Akahori, Nakai, & Fukui, 2007; Niinomi, 2008; Mohammed, Khan, & Siddiquee, 2014; Kulkarni, Anca, Patrik, & Aleš, 2014).

Despite the outstanding biomechanical, physicochemical and bio-functionability properties of Ti and its alloys, it has a major drawback as a clinical biomaterial due to its high Elastic modulus which would induce bone resorption (Hermawan, Ramdan, & Djuansjah, 2011).

However, there is a process called porosification of metal, which involves the introduction of a considerable number of interconnected pores in to the material by additive manufacturing (AM) methods, in an attempt to reduce its Elastic modulus (Niinomi *et al.,* 2015).

Another alternative to develop implants with low Elastic modulus is the production of beta-rich Ti-based alloys, which have demonstrated a low Elastic modulus value of about 80 GPa. Liquid foam Ti-based alloys have also been produced with a low Elastic modulus between 40-60 GPa, but all these alternative results are still higher than the Elastic modulus of bone tissue (Mohammed *et al.,* 2014; Niinomi *et al,* 2015). However, Van Bael, Chai, Truscello, Moesen, Kerckhofs, Van Oosterwyck, Kruth, & Schrooten (2012) employed SLM technology to produce porous Ti-based (Ti-6Al-4V) implants with pores measuring between 500µm and 1000µm in size with Elastic modulus ranging from 0.4 - 11 GPa, demonstrating that AM methods are possibly the only promising technology of producing implants with low Elastic modulus that can mimic bone tissue.

Implants with such low Elastic modulus are recommended for areas of low bending stresses to ensure homogenous load transferred stress stimulation of the bone. Such characteristic would serve the analogous function of epiphysis and metaphysis found in the human limbs (Liu & Webster, 2007). The experimental work of Wieding, Jonitz, Bader (2012) reveals that a low Elastic modulus implants could stimulate the growth of bone cells due to mechanical stimulus by physiological load application.

As noted in the experimental study of Xu, Weng, Wang, Huang, Zhang, Muhammad, Ma, & Liao (2013), there is little research on porous Ti-based alloys for biomedical applications. Therefore, this review seeks to augment and synthesize the existing literature by reporting on the current efficient and effective methods of producing porous Ti-based implants by AM technologies.

2. POROSITY AND MECHANICAL PROPERTIES OF POROUS TI-BASED BIOMEDICAL OBJECTS

Mour, Das, Winkle, Hoenig, Mielke, Morlock, & Schilling (2010) defined porosity of a material as “the percentage of void space in a solid material”. They also grouped the pores created in medical devices into three categories: closed pores *(pores that do not permit transportation of fluid through them),* blind pores *(pores that terminate inside the fabricated part)* and through pores *(pores that permit complete transportation of body fluid)* (Figure 1).

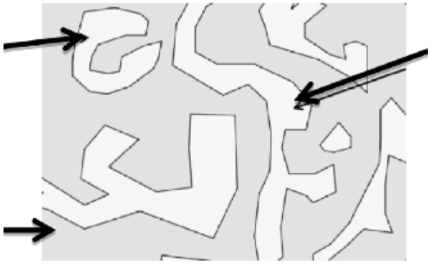


Figure 1: A schematic diagram of different types of pores (Stoffregen, Fischer, Siedelhofer, & Abele, 2011)

The blind and open pores permit the transportation of fluid cells and bacterium between the implant and the surrounding tissues, but closed pores are surrounded by fully dense material and do not permit transmission of fluid (Mour *et al,* 2010; Stoffregen *et al.,* 2011).

The review work of Miao and Sun (2009) and Li, Yang, Zhao, Qu, Li, & Li (2014) reveals that porosity between the range of 1–100 microns is mostly observed in bone structures and is needed for optimum functionability, those in the range of 100–350 microns are usually for bone ingrowth, and those between the range of 350–1,000 microns has the function of reducing Elastic modulus, while those in the range of 350–3,500 microns are normally useful during the surgical procedures for wiring-like sutures. The larger pores also provide a great surface area for cell attachment and a good medium of transportation of nutrients and metabolic waste out of the pores. The small pores would also enhance cartilage ingrowth. Mour *et al.* (2010) also noted that pore sizes of more than 100 µm are considered suitable for rapid bone ingrowth.

As noted by most of the previous reviews (Miao & Sun, 2009; Hannink & Arts, 2011; Wally, van Grunsven, Claeyssens, Goodall, & Reilly, 2015), the optimum pore size value for bone ingrowth and fluid transportation is yet to be determined. Nevertheless, there is an upper limit on porosity set by constraints associated with mechanical properties; hence any arbitrary increase in porosity of an implant would adversely affect its mechanical properties (Figure 2).

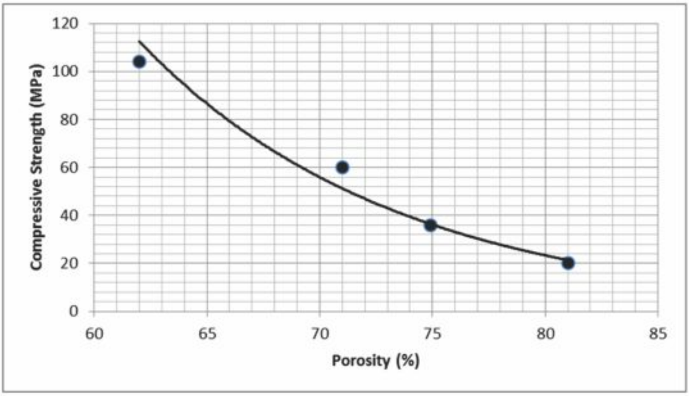


Figure 2: A graph of compressive strength decreasing as porosity increases (Data from- Mullen, Stamp, Brooks, Jones, & Sutcliffe, 2009).

Parthasarathy, Starly, Raman, & Christensen (2010) evaluated the mechanical properties of porous Ti-based implant fabricated by the electron bean melting (EBM) process. The manufactured patient-specific custom porous implants have porosity ranging from 50%–70% with effective stiffness values ranging from 0.57 (±0.05)–2.92 (±0.17) GPa. The authors concluded that the mechanical properties of the implants are very suitable for craniofacial applications. The experimental work of Lin, Wirtz, LaMarca, & Hollister (2007) led to the manufacture of porous Ti implants with average compressive modulus of 2.97±0.90 GPa, which is comparable to bone tissue.

The work of Harrysson, Cansizoglu, Marcellin-Little, Cormier, & West (2008) focused on design and fabrication of titanium hip stems by the EBM process with tailored mechanical properties that will reduce stress shielding effect. The porous Ti bone substitute structure has porosities ranging from 60% to 96.2%, with average Elastic modulus of 12 GPa which were close to the mechanical properties of compact bone.

Yavari, Wauthlé, van der Stok, Riemslag, Janssen, Mulier, Kruth, Schrooten, Weinans, & Zadpoor (2013) experimented with fatigue behaviour of porous titanium alloy manufactured by the selective laser melting process. Four different porous microarchitectures were produced with porosities between 68 and 84% and the fatigue S–N curves of the four bone substitutes were determined. The authors found that generally, given the same absolute stress level, the fatigue life is much shorter for more porous structures.

3. CURRENT AM METHODS OF PRODUCING POROUS TI-BASED BIOMEDICAL OBJECTS

Some of the AM methods which have been used recently to manufacture porous bone substitute are: selective laser melting (SLM), selective laser sintering (SLS), direct laser forming (DLF), electron beam melting (EBM), and laser engineered net shaping (LENS) (Barbas *et al.,* 2012; Niinomi *et al.,* 2015). AM technology is a revolutionary technology which could be used to produce intricate structures with great control over the mechanical properties and good surface finishing that may not require any further finishing processing (Yadroitsev & Smurov, 2011; Niinomi *et al.,* 2015).

Kim, Yue, Zhang, Jones, Jones, & Lee (2014) and Niinomi *et al.*(2015) explained that the SLM and SLS methods of manufacturing use a computer-aided design to direct a laser that melts/sinters a powder bed of Ti and its alloys to directly build Ti structures with controlled porosity, which makes it a prime choice. Yadroitsev, Shishkovsky, Bertrand, & Smurov (2009) emphasized that, by controlling the processing parameters, the porosity of the manufactured samples could be tailored to precisely predetermined dimensions. The ability to control the processing parameters would permit greater control over the final structure of very complex interconnected strut designs to produced customized tailored pore and strut sizes for a specific medical application. SLM technology enables a continuous connected pore network to be produced throughout the manufactured parts which is probably impossible with the traditional methods of fabrication. By controlling the pore size, shape, pore size distribution and interconnectivity the mechanical properties of the porous fabricated objects can be greatly tailored to desired values (Cheng, Humayun, Cohen, Boyan, & Schwart, 2014).

The fundamental difference between the SLM/SLS and EBM process is that the SLM/SLS process uses a laser to melt/sinter the metallic powders while the EBM process uses an electron beam for the melting process. The EBM process has the advantage of higher electron beam energy density compared to the laser energy density which leads to reduced build times and consequently reduced manufacturing cost for EBM manufactured bone substitute (Parthasarathy *et al.,* 2010; Nakano, Fujitani, Ishimoto, Lee, Ikeo, Fukuda, Kuramoto, 2011). Both methods can be used to manufacture patient-specific implants to suit the patient morphology which does not required plastic deformation during surgery, contrary to implants manufactured by the conventional methods (Barbas et al., 2012). Implants manufactured by these methods have the advantage of graded composition and macrostructure in a controllable manner for a specific biomedical application (Stamp, Fox, O'neill, Jones, & Sutcliffe, 2009).

Although there are many routes for producing porous Ti-based biomedical objects, this review is confined to relatively new areas of AM such as SLM, SLS and EBM methods of producing homogenous pore and heterogeneous pore Ti-based alloy implants.

4. MANUFACTURING OF POROUS TI-BASED BIOMEDICAL OBJECTS BY SLM/SLS AND EBM

SLM/SLS and EBM technologies have proven to manufacture highly porous micro-topography Ti-based alloy bone substitute with several hundred micrometres' accuracy (Fukuda, Takemoto, Saito, Fujibayashi, Neo, Pattanayak, Matsushita, Sasaki, Nishida, Kokubo, & Nakamura, 2011), which made available a large surface area for better bone-implant-contact (BIC) micro-interlocking (Liu, Han, Pan, Ge, Feng, Shen, 2015) without affecting the biocompatibility of the implant.

Pattanayak, Fukuda, Matsushita, Takemoto, Fujibayashi, Sasaki, Nishida, Nakamura, & Kokubo (2011) used the SLM method to manufacture porous Ti metals structure similar to that of human cancellous bone with different porosities by using cancellous bone image data obtained from a CT scan to create three-dimensional CAD models of porous metallic structures. The SLM machine used had a Yb fibre laser with a nominal beam diameter of 100 μm and a maximum power of 200 W which could move at a maximum speed of 7000 mm s^{-1} in an argon gas environment. To obtain optimum process parameters, a boundary contour beam of 58.5 W power was followed by a hatch beam of 117 W while a hatch space of 180 μm and a hatch offset of 20 μm were used. With a constant powder deposition layer of 30 μm thickness, the hatch lines were rotated with respect to the previous layer by 66.7° to melt the powder completely at a constant scanning speed of 225 mm s^{-1}. With powder particle size less than 45 μm, the biomimic Ti-6Al-4V cancellous-like structures manufactured have a porosity of 75–55% and a compressive strength of 35–120 MPa which were found similar to some bone structures in the body.

To establish basic data for developing a porous osteoinductive Ti alloy implant, Fukuda *et al.* (2011) melted Ti powder with a Yb fibre laser at a power of 117 W, a scanning speed 225 mm s^{-1}, a hatch spacing 90 μm and a hatch offset 20 μm in an argon gas atmosphere. With a powder deposition thickness of 30 μm, they manufactured four cylindrical implants with lengths of 15 mm and diameters of 3.3 mm. The implants were made with longitudinal square channels acting as pores with different diagonal widths of 500, 600, 900, and 1200 μm. These were implanted in the dorsal muscles of eight mature beagle dogs (weight 10–11 kg), for periods of 16, 26, or 52 weeks.

It was evident that the amount of bone formation increased with time and the total induced bone formation showed a tendency to increase with increasing pore size at 52 weeks. They also evaluated variations in the location, quantity, and time-course of the bone formed in each pore size and represented the results in terms of the amount of bone formation from the end of the pores. The record showed osteoinduction might occur at approximately 5 mm from both ends at 16 weeks and continue to 7 mm at 52 weeks, which is far above 2.5–3 mm noted in the research work of Fujibayashi, Neo, Kim, Kokubo, & Nakamura (2004), Habibovic, Li, Van Der Valk, Meijer, Layrolle, Van Blitterswijk, & De Groot (2005), and Takemoto, Fujibayashi, Neo, Suzuki, Matsushita, Kokubo, & Nakamura (2005 and 2006), probably due to the relatively bigger diameter (5-6 mm) but shorter length (10-11mm) of their experimental implants. They concluded that the longer length (15 mm) of their implant is what made the difference; hence a wider pore throat might be necessary for larger implants.

Barbas *et al.* (2012) used the SLM method to produce porous titanium with a particular periodic internal architecture close to the mechanical properties of bone. Mechanical anisotropy of bone was their focus, and by adopting a porosity of 53% and pore sizes in the range of 860 - 1500 μm, they produced porous CP Ti implants mimicking the orthotropic properties of the human bone following several mechanical and geometrical criteria which could possibly permit bone ingrowth. Their efforts led to the manufacturing of porous CP Ti with mechanical properties mimicking those of human bone.

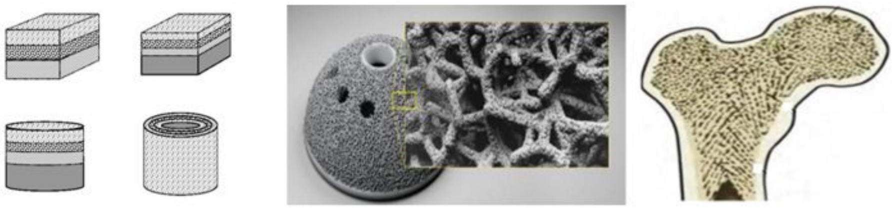
In the quest to determine the bone mass and bone density of newly formed bone, Nakano *et al.* (2011) conducted bone regenerative test by embedding novel unidirectional interconnected porous cylindrical implants of Ti-6Al-4V alloy manufactured by EBM method in rabbits. An Arcam, EBM S12 device with accelerating voltage, 60 kV; beam current, 2 mA; beam scan rate, 100 mm/s; lamination pitch, 0.1 mm with grating wall thickness of 0.73±0.11 mm was adopted. The porous manufactured implant has the ability to attach to bone over a long period of time without causing bone resorption. Parthasarathy *et al.* (2010) also focused on evaluating porous Ti-6Al-4V parts fabricated by EBM for use in craniofacial applications for cortical bone and load-bearing reconstruction. With porosity between 50% to 70% and pore sizes from 500 – 2000 μm respectively, well-interconnected porous implants which can facilitate tissue ingrowth were manufactured with Elastic modulus values ranging between 0.57 to 2.92 GPa.

Recently, Matena, Petersen, Gieseke, Kampmann, Teske, Beyerbach, Escobar, Haferkamp, Gellrich, & Nolte (2015) also demonstrated that bone formation is strongly dependent on fast vascularization of fluid through the interconnected pores of the implants by using SLM technology to manufacture Ti-6Al-4V implant of pore size 250 μm to enable vessel ingrowth. "The development of a scanning strategy for the manufacture of porous biomaterials by selective laser melting" was experimented by Stamp *et al.*

(2009) which they termed the "beam overlap" process. This process was used to demonstrate that the porosity (pore size, pore distribution and interconnectivity) and mechanical properties of manufacture porous implants can be greatly controlled to a tailored value. It was also mention that altering pore width of a Ti-based implant manufactured by SLM can help tailor the mechanical properties of the implant for a particular biomedical application.

SLM technology was used by Wang, Shen, Wang, Yang, Liu, & Huang (2010) to produce a Ti alloy implant with high porosity (~ 70 %), interconnected Ti walls and open porous structures with macroscopic pores (~ 200 - ~ 500 μm). The laser power and scanning speed were 1000 W and 0.02 m/s respectively. The authors noted that as the scanning speed increased from 0.01 to 0.03 m/s, the porosity increased, but then decreased when the scan speed increased further to 0.05 m/s, which they attributed to laser input energy.

In order to investigate the influence of different porous structures on osteoinduction, Fujibayashi *et al.* (2004) manufactured porous metallic bioactive Ti structures by plasma sprayed or powder sintered method in 2004. Realizing that the conventional method does not produce well-defined concavities such as precise control porosity, pore size and interconnectivity as required for biomaterial objects, they performed another experiment in 2011 using an AM method, which resulted in well-defined concavities (Fukuda *et al.* 2011), demonstrating that AM methods can produce substitutional porous bone structures with well-defined concavities (Figure 3b and Figure 6).



a) b) c)

Figure 3:
(a) Different types of graded pore structures (Miao & Sun, 2009)
(b) Micro porous acetabular hip cup (Austin-Morgan, 2015)
(c) Porous nature of cancellous bone (Bankoff, 2012)

5. USING AM METHODS TO MANUFACTURE GRADED PORE TI-BASED POROUS STRUCTURES

As explained by several published articles (Simske, Ayers, & Bateman, 1997; Keaveny, Morgan, & Yeh, 2004; Miao & Sun, 2009; Choi, Zhang, & Xia, 2009), it can be learned from nature that the architectural nature of the human bones are of graded or gradient pores (Figure 3c), and it is only a similar graded or gradient implant that can suitably replace any affected part of the body.

The capability of AM methods to manufacture a biomimic bone substitute of graded porosity was demonstrated by Lin, Starr, Harris, Zandinejad, & Morton (2013), who used SLS and SLM strategies to produce cylindrical Ti-6Al-4V specimens with "dense outer skin + porous inner core" structure to reflect the natural geometrical nature of bones. With a laser power of 170 W, they produced fully melted outer skin of their biomimic implant samples and with laser power ranging from 43 - 85 W they produced sintered (partially melted) a graded porous inner core to form fully dense skin and gradient pore inner core prototype implants. According to them, the Elastic moduli of the samples were close to that of human bone. They explained that, the technique of manufacturing a graded or gradient porous structure by AM technologies depends on the laser energy; comprising laser power, scanning velocity, spacing between scan lines and powder layer thickness, which combine to determine the quantity of energy input into the material during the fabrication process. The variation of these fabrication parameters would control the solidification and cooling process to produce varied porosity. It is revealed that there are no automation universal optimum processing parameters. Careful selection of the principal processing parameters for specific desired mechanical properties is crucial. If the amount of laser energy injected into the powder bed is too high, there would be excessive melting. On the contrary, if it is too low the powder would not melt completely (Yadroitsava, Els, Booysen, & Yadroitsev, 2015; Spears & Gold, 2016).

However, Li, Liu, Shi, Du, & Xie (2010) did not use Ti-based alloy: they demonstrated that SLM can be used to produce graded pore metallic implants by using 316L stainless steel. The investigation reveals that the porosity gradients depend majorly on the scanning speed; as the scanning speed increases, porosity increases (Figure 4).

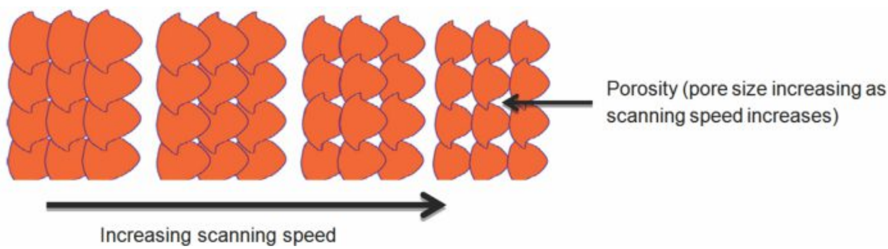


Figure 4: Schematic representation of porosity increasing as scanning speed increases (Li *et al.,* 2010)

By selecting scanning speeds of 50 mm/s to 1000 mm/s and laser beam power in the range of 20 W to 195 W, Emmelmann, Scheinemann, Munsch, & Seyda (2011) manufactured Ti-6Al-4V implant with osseointegrative surface using the SLM method. Porosity between 68 % - 87 % was obtained with powder deposition layers of 30 microns, as a result of change in the energy inputs per unit length from 0.3 - 1.0 J/mm leading to change in beam diameter, which triggered the change in porosity (graded pore). According to them, the manufactured implants have the capacity to avoid the stress shielding effect since their Elastic modulus ranges between 0.4 GPa – 1.2 GPa.

Traini, Mangano, Sammons, Mangano, Macchi, & Piattelli (2008) investigated the possibility of using SLS technology to manufacture functional porous isoelastic dental implants by using graded master alloy powder (Ti–6Al–4V) with a particle size of 1–10 μm to produce a dense core implant with porous surface. They concluded that the Elastic modulus of the graded dental implant porous surface is comparable to that of bone tissue. Tolochko, Savich, Laoui, Froyen, Onofrio, Signorelli, & Titov (2002) also manufactured dental root implants by selectively melting Ti powders to produce a dense core and selectively sintering an irregular porous Ti powder shell on the dense core. By using EBM Murr, Quinones, Gaytan, Lopez, Rodela, Martinez, Hernandez, Martinez, Medina, & Wicker (2009) also produced open cellular porous cells with different cell wall structures (Figure 6a). As expected, the Elastic moduli of the porous structures decrease with increasing porosity (Figure 5).

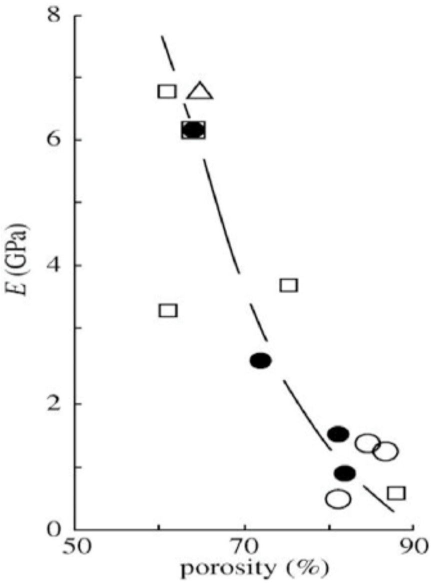


Figure 5. A graph demonstrating reduction in elastic modulus as porosity increases (Murr, Gaytan, Medina, Lopez, Martinez, Machado, Hernandez, Martinez, Lopez, Wicker, & Bracke, 2010)

Most of the porous implants produced currently are of dense core with porous surface (Figure 6b) (Ryan, Pandit, & Apatsidis, 2006; Mangano, Chambrone, Van Noort, Miller, Hatton, & Mangano, 2014), but Miao & Sun (2009) propose several structures for porous (gradient pore and non-gradient pore) metallic implants as represented in Figure 3a.

Simske *et al.* (1997) have declared in their review work titled "Porous materials for bone engineering" that "an area of future clinical research will be the construction of implants with gradients of porosity". They also mention that "the ultimate porous bone implant, perhaps, is yet to be designed; however, there is reason to believe that such a material is not long in coming".

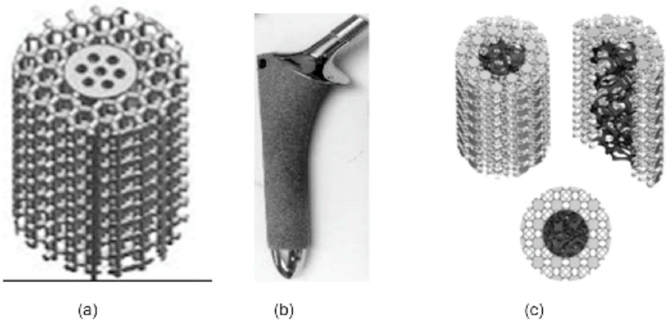


Figure 6:
(a) Porous Ti-6Al-4V implant manufactured by EBM method (Li *et al.,* 2010)
(b) Dense core implant with porous surface (Murr *et al.,* 2010)
(c) CAD model of graded porous implant (Murr *et al.,* 2010)

6. CONCLUSION

The current research data has emphatically pointed out that porous Ti-based implant could be manufactured by AM methods. There is a perceived idea presented in the literature that, the fundamental principles of producing graded or gradient porous implants by AM methods has come to maturity. But more needs to be done to harness the various ideas to reality, by practically using AM methods to manufacture reproducible non-homogenous porous implants, possibly in one step at "affordable" cost for biomedical applications. Micromechanical interlocking fixation improvement could be achieved by bone tissue growing into and through a porous matrix of metal to ensure a stronger BIC which would enhance rapid osseointegration and a suitable Elastic modulus. Pore-graded implants are more desirable than homogenous pores, due to their ability to mimic natural bone tissue. Despite the significant progress made, as a result of many researchers trying to propose an optimum pore size value for bone ingrowth, there are still divergent results concerning the optimum pore size for bone ingrowth.

7. ACKNOWLEDGEMENT

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