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Fabrication of HA/PLLA Composite Scaffolds for Bone Tissue Engineering Using Additive Manufacturing Technologies

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1. Introduction

This chapter presents an overview of a research work carried out for the rapid manufacture of bioceramics (HA)/biopolymers (PLLA) composite scaffolds by means of Selective Laser Sintering (SLS) technique, to be used for bone tissue implantation aiming to replace and/or repair bone defects due to traumatised, damaged or lost bone.

SLS is an Additive Manufacturing Technology (AMT) that selectively sinters powders of engineering materials, from solid or surface models created by a CAD - 3D file, by means of a CO_2 laser and in a layer-by-layer basis.

HA (hydroxyapatite) is a bioceramic used since several years for medical applications although being mainly processed by conventional methods (cast, machined or manually produced).

In recent years ceramics and their composites are being used to augment or replace various parts of the body, particularly bone. Their relative inertness to the body fluids, high compressive strength, and aesthetically pleasing appearance led to the use of ceramics in dentistry as dental crowns. Some carbons have found use as implants, especially for blood-interface applications, such as heart valves. Due to their high specific strength as fibbers and their biocompatibility, ceramics are also being used as reinforcing components of composite implants and for tensile loading applications such as artificial tendons and ligaments.

Calcium phosphate based bioceramics have been in use in medicine and dentistry in the last thirty years, in several applications: dental implants, periodontal treatment, alveolar ridge augmentation, orthopaedics, maxillofacial surgery, and otolaryngology. Different phases of calcium phosphate ceramics are used depending upon whether a resorbable or bioactive material is desired. Porous hydroxyapatite has been studied for use in repairing large defects in bone. Implanted HA is slowly resorbed by the body over several years and replaced by bone. HA as the capability to form a direct chemical bond with hard tissues. On implantation of HA particles or porous blocks in bone, new lamellar cancellous bone forms within 4 to 8 weeks. Porous materials are used on bone compatible implants to encourage bony ingrowths. Therefore, pore size is of considerable biological importance.

PLLA (Poly-L-lactic acid) is a biodegradable polymer. The interest in biodegradable polymeric biomaterials for biomedical engineering has increased dramatically during the

past decade, because this class of biomaterials has two major advantages that non-biodegradable biomaterials do not have.
First, these biomaterials don't elicit permanent chronic foreign-body reaction due to the fact that the human body would gradually absorb them, and they do not permanently retain trace of residual in the implantation sites. Second, some of them have recently been found to be able to regenerate tissues (*tissue engineering*), through the interaction of their biodegradation with immunologic cells. Hence, surgical implants made from biodegradable biomaterials could be used as temporary scaffold for tissue regeneration.
This approach toward the reconstruction of injured, diseased, or aged tissues is considered one of the most promising fields for this century. One of the bone formation strategies is to construct bio-scaffold, which allows bone reformation once it is surgically placed in bone-defect. The bio-scaffold has to combine mechanical strength with biocompatibility and osteoinductiveness (induction of bone cells) and osteoconductiveness (cells attachment).
A key requirement in many biomedical applications, including artificial bones, is a property called connected porosity. Green parts produced by the chosen SLS technology inherently have this property. While HA has been used in bone replacement and grafting for more than 20 years, this material was a logical choice for this work. PLLA was chosen as a binder because it offers a higher degradation time and a low melting temperature when compared with other acid lactic biodegradable derivates. This biopolymer acts as a binder during the sintering operation, and afterwards improves the mechanical properties of the implants.
In this research work CAD/CAM/CAE systems, AMT, biomaterials and medical imaging techniques were integrated and this enabled the production of anatomical models. This approach provides a direct method of producing HA-based scaffolds suitable for bone replacement or bone tissue engineering.

2. Biomaterials

Biomaterials are natural or synthetic materials, used to replace part of a living system or to function in intimate contact with living tissue.
This group of materials includes:
- Metals (e.g. titanium and its alloys, Co-Cr alloys, stainless steels, etc.);
- Ceramics (e.g. alumina, zirconia, calcium phosphates, marine coral, nacre etc.);
- Polymers (e.g. polyethylene, polypropylene, polyvinyl, poly(lactide acid); poly(glycolic acid), etc.);
- Composites (e.g. carbon-carbon, wire or fibre reinforced bone cement, etc.).

Some of these biomaterials are *biodegradable or resorbable* (e.g. hydroxyapatite, polylactides, or composites of both).
The required properties of biomaterials, for artificial tissue engineering are:
- Biocompatibility (does not induces immune response or inflammation);
- Biodegradability (biodegrade for non-toxic components);
- Sterilizability (able to be sterilisable);
- Stability over timescales, allowing the growth of new tissues;
- Adequate mechanical and physical properties;
- Adequate manufacturing.

A description of materials for use in the human body is shown in Table 1:

Materials	Advantages	Disadvantages	Examples
Polymers (nylon, silicone rubber, polyester, polytetrafuoroethylene, etc.)	Resilient, easy to fabricate	Not strong, deforms with time, may degrade	Sutures, blood vessels, hip socket, ear, nose, other soft tissues
Metals (Ti and its alloys, Co-Cr alloys, stainless steels, Au, Ag, Pt, etc.)	Strong, tough, ductile	May corrode, dense, difficult to make	Joint replacements, bone plates and screws, dental root implants, pacer and suture wires
Ceramics (aluminium oxide, calcium phosphates including hydroxyapatite, carbon, etc.)	Very biocompatible, inert, strong in compression	Brittle, not resilient	Dental, joint replacements, coating of dental and orthopaedic implants
Composites (carbon-carbon, wire or fibre reinforced bone cement)	Strong, tailor-made	Difficult to make	Joint implants, heart valves

Table 1. Materials for use in the body (After Bronzino et al., 1995)

This section will mainly focuses on the biomaterials used in the experimental work of the research (bioceramics and biopolymers).

Calcium phosphate based bioceramics have been in use in medicine and dentistry in the last thirty years, in several applications: dental implants, periodontal treatment, alveolar ridge augmentation, orthopaedics, maxillofacial surgery, and otolaryngology. Different phases of calcium phosphate ceramics are used depending upon whether a resorbable or bioactive material is desired.

Apatite is a natural calcium phosphate containing a little fluorine (Ca_4 (Ca F) $(PO_4)_3$) or chlorine (Ca_4 (Ca Cl) $(PO_2)_3$). It is found in granular limestone, igneous rocks and metalliferous ores.

Hydroxyapatite (HA or HAp) is a complex phosphate of calcium (Ca $(PO_4)_3OH$) that occurs as a mineral and is the chief structural element of vertebrate bone. It is a very important material for bioceramics.

One of the important research issues concerning HA is its mechanical behaviour limitation. In fact, brittleness, poor fatigue resistance, low tensile strength, and low fracture toughness value precludes HA from use in load bearing situations.

Dense, porous, or particulate forms have been prepared. However, porous HA as an implant material, is preferred. The pores (100-300μm) allow bone to grow into implant, promoting mechanical fixation with the natural bone. Nevertheless, porosity and pore size can reduce the mechanical properties of HA ceramic. The minimum pore size of approximately 100-150μm has been established as necessary for the continued health of bony ingrowths.

Porous hydroxyapatite has been studied for use in repairing large defects in bone. Implanted HA is slowly reabsorbed by the body over several years and replaced by bone.

HA has the capability to form a direct chemical bond with hard tissues. On implantation of HA particles or porous blocks in bone, new lamellar cancellous (soft) bone forms within 4 to 8 weeks (Zan et al., 2010).

Porous materials are used on bone compatible implants to encourage bony ingrowths. Pore size can be of considerable biological importance. Studies have shown (Hench, 1991; Chelule, 2002) that with pore sizes ≥ 150μm, in orthopaedic implants, bony ingrowths into the pores occur, and this is useful to anchor the implant. It was found experimentally that pores smaller than 75μm did not permit the ingrowths of bone tissue. Moreover, it was difficult to maintain fully viable osteons within pores in the 75-150μm size range. This large pore size is needed so that capillaries can provide a blood supply to the in-growth of connective tissues. Vascular tissues do not appear if pores < 150μm. If the micro-movements occur at the interface of a porous implant, the capillaries can be cut off, leading to tissue death, inflammation and destruction of interfacial stability (Hench, 1991).

When a porous material is implanted in bone, the pores become filled first with blood, which clots, then with osteoprogenitor mesenchymal cells, then after about 4 weeks, bony trabeculae. The ingrowths bones then become remodelled in response to mechanical stress. The bony ingrowths process depends on a degree of mechanical stability in the early stages. If too much motion occurs, the ingrowths tissue will be collagenous scar tissue, not bone.

The porous and dense HA materials show excellent biocompatibility after implantation. The porous material can only be used to replace those places in the skeleton which are not loaded or are loaded mainly in compression. The dense sintered material does not convert to natural bone after implantation (Chelule, 2002).

Synthetic polymeric materials have been widely used in medical disposable supplies, prosthetic materials, dental materials, implants, dressings, extracorporeal devices encapsulates, polymeric drug delivery systems, and orthopaedic devices such as metal and ceramics substitutes.

The most natural polymer is demineralised bone matrix (DBM), which is produced by decalcifying pieces of bone. Other popular synthetic biodegradable polymers are poly (lactide acid) (PLLA) and poly(glycolic acid) (PGA) (Gibson, 2003).

The required properties of polymeric biomaterials are similar to other biomaterials, which are given in Table 2:

Properties	*Description*
Biocompatibility	Noncarcinogenesis, nonpyrogenicity, nontoxicity, nonallergic response.
Sterilizability	Autoclave, dry heating, ethylenoxide gas, radiation.
Physical property	Strength, elasticity, durability.
Manufacturability	Machining, moulding, extruding, fibre forming.

Table 2. Requirements for biomedical polymers (After Bronzino et al., 1995)

The biomedical applications of polymeric biomaterials are very large, as shown in Table 3.

For implant applications special attention have be given to polyethylene (PE) and polymethylmetacrylate (PMMA).

The effect of implantation on the behaviour of biocompatible polymers is given in Table 4.

The interest in biodegradable polymeric biomaterials for biomedical engineering has increased dramatically during the past decade, because this class of materials has two major

Synthetic Polymers	I. Applications
Polyvinylchloride (PVC)	Blood and solution bag, surgical packaging, dialysis devices, catheter bottles, connectors, and cannulae.
Polyethylene (PE)	Pharmaceutical bottle, no woven fabric, catheter, pouch, flexible container, and orthopaedic implants.
Polypropylene (PP)	Disposable syringes, blood oxygenator membrane, suture, no woven fabric, and artificial vascular grafts.
Polymethylmetacrylate (PMMA)	Blood pump and reservoirs, membrane for blood dialyser, implantable ocular lens, and bone cement.
Polystyrene (PS)	Tissue culture flasks, roller bottles, and filter wares.
Polyethylenterephthalate (PET)	Implantable sutures, mesh, artificial vascular grafts, and heart valve.
Polytetrafluoroethylene (PTFE)	Catheter and artificial vascular grafts.
Polyurethane (PU)	Film, tubing, and components.
Polyamide (nylon)	Packaging film, catheters, sutures, and mould parts.

Table 3. Biomedical applications of polymeric materials (After Bronzino et al., 1995)

Polymers	II. Effects of Implantation
Polyvinylchloride (rigid)	Tissue reaction, plasticizers may leach out and become brittle.
Polyethylene (PE)	Low-density ones absorb some lipids and lose tensile strength; high-density ones are inert, and no deterioration occurs.
Polypropylene (PP)	Generally no deterioration.
Polymethylmetacrylate (PMMA)	Rigid form: crazing, abrasion, and loss of strength by heat sterilization. Cement form: high heat generation, unreacted monomers during and after polymerisation may damage tissues.
Polyethylenterephthalate (PET)	Susceptible to hydrolysis and loss of tensile strength.
Polytetrafluoroethylene (PTFE)	Solid specimens inert; if fragmented, irritation will occur.
Silicone rubber	No tissue reaction, very little deterioration.
Polyamide (nylon)	Absorb water and irritate tissue, lose tensile strength rapidly.

Table 4. Effect of implantation on polymers (After Bronzino et al., 1995)

advantages that non-biodegradable biomaterials do not have. First, these biomaterials don't elicit permanent chronic foreign-body reaction due to the fact that the human body would gradually absorb them, and they do not permanently retain trace of residuals in the implantation sites. Second, some of them have recently been found to be able to regenerate tissues (tissue engineering), through the interaction of their biodegradation with immunologic cells. Hence, surgical implants made from biodegradable biomaterials could be used as temporary scaffold for tissue regeneration.

This approach toward the reconstruction of injured, diseased, or aged tissues is considered one of the most promising fields of this century (Stevens, 2002).

The most commercially significant biodegradable polymeric biomaterials are originated from:

- Glycolic acid (e.g. polyglycolide (PG), polyglycolic acid (PGA));
- Lactic acid (e.g. polylactide (PLA), poly-L-lactide (PLLA)).

Their biomedical applications have been limited to mainly orthopaedic surgery, drug control/release devices, coating materials for suture, vascular grafts, and surgical meshes to facilitate wound healing after dental extraction.

PLLA is a biodegradable semi-crystalline polymer derived from lactic acid ($C_3H_6O_3$).

Lactic acid is a natural organic acid. Long before it became commercially available lactic acid was formed by natural fermentation in products such as cheese, yoghurt, soy sauce, meat products, pickled vegetables, beer and wine. Animal and human bodies also produce significant amounts of L (+) lactic acid during daily activities such as walking and running**.**

Today, lactic acid, its salts and esters are extensively used in food, industrial, cosmetic, medical and pharmaceutical industries**.** It is produced by fermentation of sugar and water or by chemical process and is commercially sold as a liquid. Lactic acids are optically active compounds including L-and D- forms.

Applications of this polymer in medicine and pharmacy include wound closure products, drug delivery systems and surgical implant devices. The main advantages of these polymers are their mechanical strength, combined with biodegradability and biocompatibility. The biodegradation of PLLA takes place by random hydrolysis, being the final degradation products eliminated by natural way.

Fig. 1. PLLA image (Designinsite, 2001)

PLLA presents an extremely slow biodegradation rate at body temperature (> 24 months). This biopolymer has a Tm = 170°C and a Tg = 56°C. The high Tg is mainly responsible for the mentioned slow degradation rate. It resembles clear polystyrene as can be seen in Figure 1.

Recently, biodegradable polymers, e.g. polylactic acid (PLA) have been used to treat minimally loaded fractures, thereby eliminating the need for a second surgery for implant removal.

Because metals are too stiff to prevent stress protection, polymers tend to be too flexible and to weak to meet the mechanical demands for an internal fixation device, and bioceramics (e. g. HA) are to brittle and have unfavourable mechanical properties where weight bearing is concerned, composite materials should be considered for this purpose.

Composite materials are solids that contain two or more distinct constituent materials or phases, on a scale larger than the atomic.

Natural composites include bone, wood, dentin, cartilage and skin. In biomaterials, e.g. HA/PLLA composites, each constituent of the composite must be biocompatible. Moreover, the body environment should not degrade the interface between constituents.
Composite materials can be made having carefully tailored properties for specific engineering performance and design requirements whether these are mechanical, biological, chemical, or electrical.
The property of the composite is related to the properties and proportions of the composite constituents and the interface between those constituents. Composites can be produced with a high specific modulus and an advantageous strength-to-weight ratio. Composites can also often have superior toughness since the filler fibres or particles can deflect or stop the process of a crack. This is reflected in a higher strength of the composite compared to that of the matrix material alone. In addition, the filler can confer certain biological properties, such as bioactivity, when incorporated into the composite in appropriate amounts. Bioactive materials, e.g. hydroxyapatite and various bioactive glasses and glass-ceramics, are generally renowned for low toughness and tensile strength.
The properties of the composites (density, stiffness, chemical activity, and possibly biological activity) are determined by the Rule of Mixtures.
Many of the synthetic biocomposites are used in orthopaedics to reconstruct or augment living bone.
In Table 5 the classes of materials that can be used in biocomposites are shown:

Possible matrices	Possible fillers
Thermoplastics	Glasses
Thermosets	Carbon
Ceramics	Ceramics
Metals	Metals
	Polymers

Table 5. Classes of materials that could either be used as fillers or matrices (After Yamamuro et al., 1990)

For bone reconstruction different composites can be used, as shown in Table 6.
Because metals are to stiff to prevent stress protection, polymers tend to be too flexible and to weak to meet the mechanical demands for an internal fixation device, and bioceramics (e. g. HA) are to brittle and have unfavourable mechanical properties where weight bearing is concerned, composite materials should be considered for this purpose. Recently attention has been paid to the application of HA in combination with a polymeric substance. The use is still confined to the field of the filling of bony defects and as drug carrier. Polyethylene, polybyturate and PLLA are the most frequently used polymers in such composite materials.
Recently attention has been paid to the application of HA in combination with a polymeric substance. The use is still confined to the field of the filling of bony defects and as drug carrier. Polyethylene, polybyturate and PLLA are the most frequently used polymers in such composite materials.
Composites of HA / PLLA combines bioresorption (PLLA) with bone bonding potentials (HA) resulting in a potentially bioactive and bioresorbable composite with higher strengths and stiffness than the unfilled polymer (Ignjatovic et al., 1999; Kesenci et al., 2000).

Type of system	Composite
Stable systems	Epoxy resin / carbon fibre
	Polysulfone / carbon fibre
	Epoxy resin / alumina / stainless steel
	Polymethylmethacrilate / polyaramid
	Polyethylene / carbon fibre
	Carbon fibre-reinforced carbon
Bioactive systems	Epoxy resin / Bioglass®
	Collagen / hydroxyapatite
	Polyethylene / hydroxyapatite
	Polymethylmethacrilate / phosphate / silicate / apatite (CPSA) glass fibre
	Polymer / phosphate glass
	Hydroxyapatite / collagen + gelatin - resorcinol - formaldehyde
Degradable systems	Polylactic acid / glycolic acid / with self-reinforcement
	Polyhydroxybutirate / hydroxyapatite
	Polylactic acid / glycolic acid / hydroxyapatite

Table 6. Composites for bone reconstruction (After Yamamuro et al., 1990)

Figure 2 shows new bone formation surrounding an implant of HA/PLLA after 32 weeks:

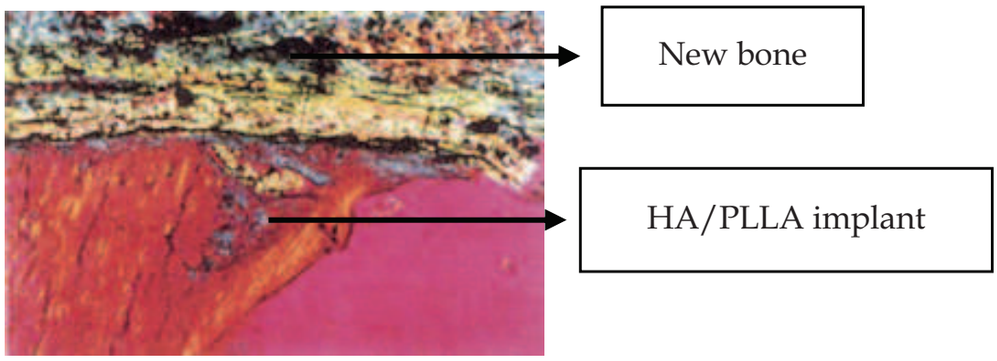

Fig. 2. HA/PLLA implant (Biocomposites, 2001)

3. Selective Laser Sintering

The Selective Laser Sintering (SLS) process belongs to the solid-based Additive Manufacturing Technologies, which primarily use powder as the basic medium for manufacture. The objects are built layer by layer by sintering / interfusing thin layers of powder. Each layer fuses to the previous one creating a physical object.

Thus, the Selective Laser Sintering process creates three-dimensional objects, layer by layer, from powdered materials, with the heat generated by a CO_2 laser within the apparatus (Sinterstation System). First, three dimensional CAD data must be output in the industry-standard .STL (Standard Triangulation Language) format.

The process comprises 4 phases:

- As the selective laser sintering process begins, a thin layer of the heat-fusible powder is deposited into the part build chamber;

- An initial cross-section of the object under fabrication is selectively "drawn" (or scanned) on the layer of powder by a heat-generating CO_2 laser. The interaction of the laser beam with the powder elevates the temperature to the point of melting, fusing the powder particles and forming a solid mass, i.e., sinters the powder particles (heats and bonds selected portions of each layer). The intensity of the laser beam is modulated to melt the powder only in areas defined by the object's design geometry;
- An additional layer of powder is deposited, via a roller mechanism, on top of the previously scanned layer;
- The process is repeated, with each layer fusing to the layer below it. Successive layers of powder are deposited and the process is repeated until the part is complete.

After the building the part is removed from the build chamber and the loose powder falls away. Parts may then require some post-processing, such as sanding, depending upon the intended application.

There is no need to create support structures with the CAD design prior to or during processing and, therefore, no support removal is needed when the part is complete.

The software components of the Sinterstation System include a Unix operating system and proprietary application software.

In Figure 3 a schematic view of the Sinterstation Process Chamber is present:

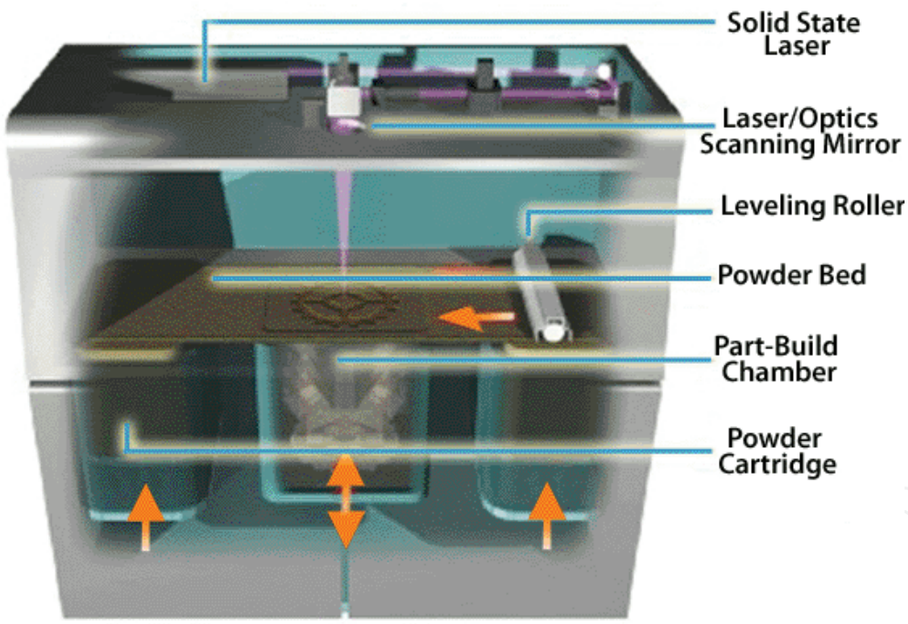

Fig. 3. Process Chamber of the SLS Sinterstation System

The main aspects to be considered in the SLS technology are the properties of the powders used in the process and the fabrication parameters. The fabrication parameters depend strongly on the materials used, and have significant influence in the mechanical properties (e.g. tensile strength, surface hardness and density), dimensional accuracy and surface quality (i.e. roughness) of the parts produced. With SLS it is not possible to achieve the best quality in appearance with the best mechanical properties. Maximum density of the parts is only achieved with parameters that result in excess powder sticking to the surface and low speed of construction (which is time-consuming). Using the correct combination of coating

and finishing in post-processing, the mechanical properties and surface of SLS parts can be improved.
A large range of materials is available for this process. Basically, any substance that can be grounded to a fine powder may be employed. At present there are 12 commercially available powders that can be used in the SLS process. The most used are nylon (polyamides), nylon composites (glass fibre nylon), polystyrene and polycarbonate. They are non-toxic, safe, and can be sintered with relatively low power lasers (10-20W).
The main SLS process variables are: part bed temperature, laser power, scan size, scan spacing, slice thickness, and part position and orientation (3D Systems, 2003).

4. Experimental work

In this section an overall view of the experimental work is presented.
Based on previous screening trials, a choice of 40% ratio of PLLA by weight has been made. This choice was based on the fact that adding lower than 30% wt. of PLLA to HA will not add significantly for the biodegradation or to enhance the ductility properties, and higher than 50 % wt. the implant could be too plastic and therefore not behave as bone tissue (Cruz, 2005).

4.1 Materials

The materials used in this work (in powder form) were as follows:
- HA: Captal® 120 grade – sintering powder, supplied by Plasma Biotal Limited (UK), with mean particle size (D50) of 111±5µm, melting point of 1250 (-0 +50) °C and 1.30 g/cm^3 of density (~£300 /Kg);
- PLLA: Purasorb® L, supplied by PURAC (The Netherlands), with mean particle size (D50) of 163±5µm (after sieving), melting range of 182.4 – 192.3°C and 0.47 g/cm^3 of density (after sieving) (~£1700 /Kg).

4.2 Equipments

The experiments were performed on a SLS Sinterstation 2000 (3D Systems™, USA) apparatus installed at CRDM (Centre for Rapid Design and Manufacture), High Wycombe, UK.
This apparatus was modified, namely the feeding envelopes and the part platform, to allow operating with non-standard materials (as the standard material is nylon), and with small amounts of HA/PLLA (1Kg instead of the standard 20Kg) due to cost control of testing.
In Figure 4 a general view of the SLS apparatus used in the experimental work is presented.

4.3 Method

The aim of the first phase of the experimental work was to identify those factors (process parameters) that have large effects on the response variables (physical properties of the parts produced). In this phase a screening experimental design and analysis, based in the fractional factorial design technique, was applied to determine the most influential factors of interest on fabrication of HA/PLLA models by SLS. A DoE (Design of Experiments) methodology was used (Montgomery, 1997).
The results obtained in the tests were focused on three (3) response variables (density, geometric accuracy and surface quality of the parts produced).
The results obtained in the screening analysis show that the three factors with most influence on the physical properties of the parts produced by SLS were laser power, scan

speed and scan space, i.e., the Applied Energy Density (AED). In fact, these three factors together constitute the Andrew's Equation (Cruz, 2005), corresponding to the energy density applied to the powder bed, which determines the scanning strategy during the SLS operation.

Fig. 4. The SLS Sintersation 2000 apparatus (Courtesy of CRDM)

After this preliminary stage of the experimental work, the next step was focused on the measurement of the ultimate compressive strength and the elastic modulus in compression, as well as the bending strength and modulus of the parts produced, by means of a 2^k full factorial design and analysis, in order to achieve more detailed information about the most influent factors selected in the previous phase.

A 2^3 full factorial design was applied (Montgomery, 1997). The objective was to obtain a mathematical equation to express the effects of the AED in the ultimate compressing strength, bending and density of HA/PLLA specimens.

A design consisting of sixteen (16=8+8) experiments (i.e., a 2^3 experimental design: 3 independent variables at 2 levels each, with one (1) genuine replicate added to the design) was conducted in a randomised sequence.

The experimental design was conducted according with the data presented in Table 7 (Cruz, 2005):

	Levels	
Factors	*Low*	*High*
Coding	–1	1
Laser power (W)	5	7.5
Laser scan speed (mm sec^{-1})	200	300
Laser scan spacing (mm)	0.10	0.15
Applied energy density (cal cm^{-3})	2.66	8.96

Table 7. Data for the 2^3 factorial design

To investigate the degradation behaviour of the HA/PLLA parts produced by SLS, namely its PLLA component, in vitro tests were performed. To study the in vitro degradation mechanism of the HA/PLLA specimens, an aqueous media (physiological fluid) – saline phosphate buffer (SPB, pH=7.4) was used. This media has been taken as a model of biological fluids (Taddei et al., 2002). The study was conducted on their physical properties, namely their mass loss along the time (six months).

5. Results

In the following Table 8 and Figures 5 to 7, the main results obtained are summarized (Cruz, 2005):

	Compression		*Bending*		*Density* ($g\ cm^{-3}$)
	σ_c (MPa)	E_c	σ_c (MPa)	E_c	
Cortical bone (hard bone)	200 ± 36	23 ± 4.8 GPa	35–283	5–23 GPa	1.7–2.1
Cancellous bone (soft bone)	1.5–38	10–1570 MPa	–	<1 GPa	0.14–1.1
HA/PLLA (laser sintered)	2.4–4.6	17.2–40.8 MPa	1.6–4	140–257 MPa	0.78–1.1

Table 8. Comparison of properties between HA/PLLA parts and human bone

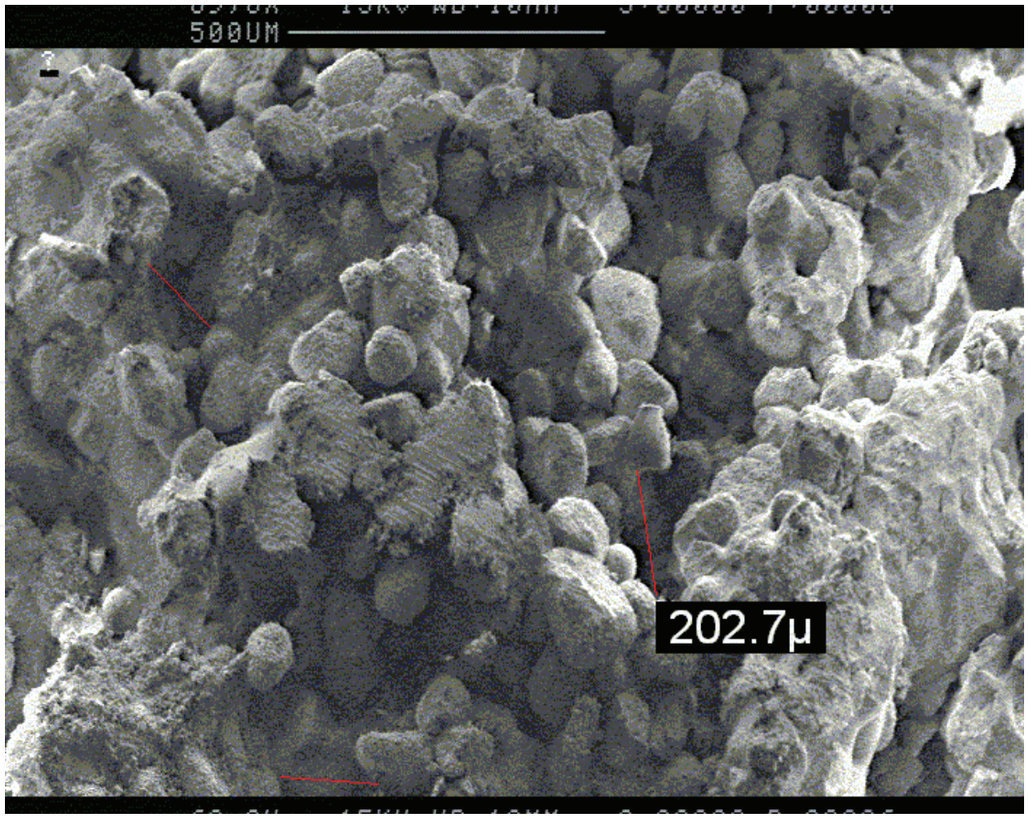

Fig. 5. SEM image of a HA/PLLA part with measurement of internal porosity (Example in the Z direction - magnification 100x)

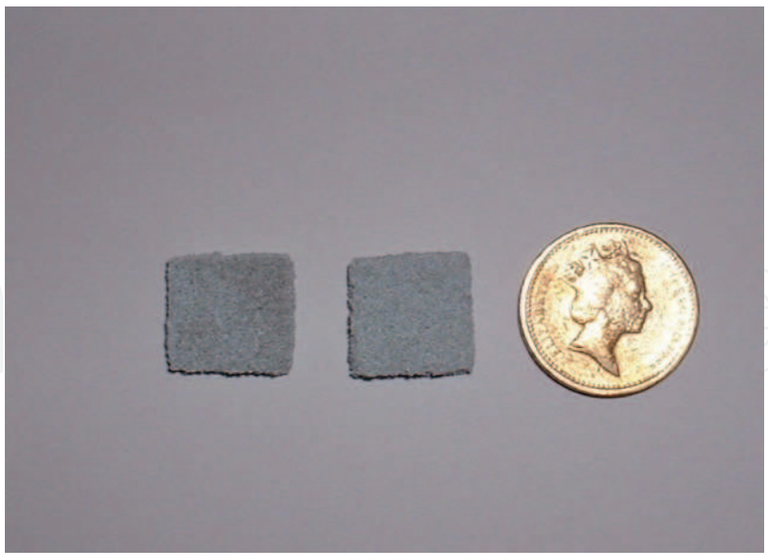

Fig. 6. HA / PLLA scaffolds as SLS produced

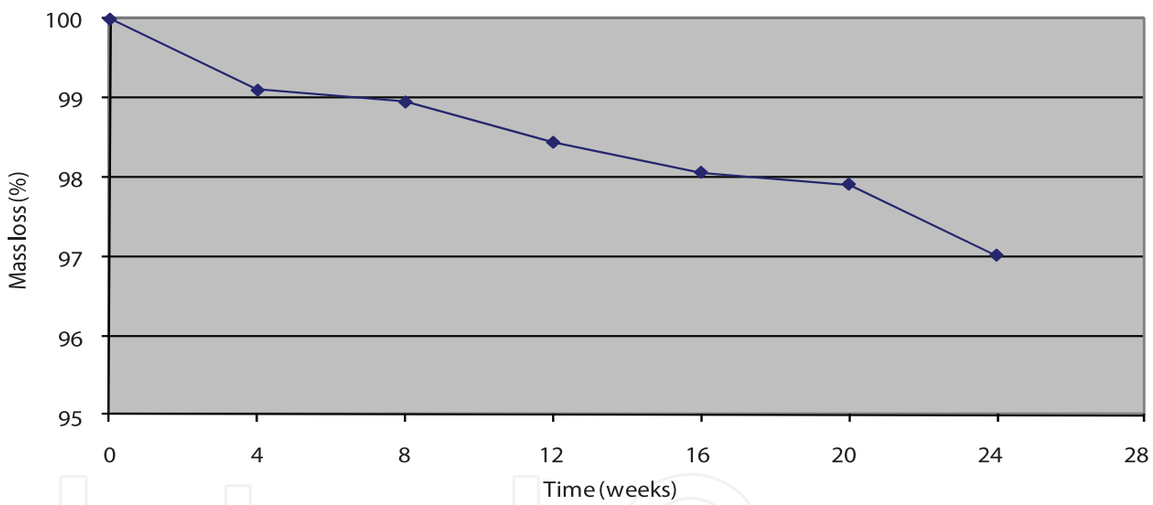

Fig. 7. Percentage of mass loss versus time

6. Discussion

The main goal of the experimental work was to demonstrate the feasibility of producing HA/PLLA parts by selective laser sintering. The results were successful in proving that feasibility.

In fact, the main results of the trials performed, have shown that:

- It is possible to produce bioceramic parts (HA based) by means of AMT - Additive Manufacturing Technologies, namely the Selective Laser Sintering (SLS) process, using a biocompatible/biodegradable polymer as binder;
- For that purpose it is necessary to use a polymeric binder (40% wt.) to promote the agglomeration of the ceramic particles during the laser operation (sintering). The component, in this phase, is the so-called "green body";

- In the case of using a biocompatible binder (e.g. PLLA), the blend HA/PLLA produces a part that can be used directly in the body without removal of the binder (green body). This technique is a direct route to fabricate laser sintered HA based ceramic parts for medical purposes;
- Thus, this route allows the production of parts directly, without the need of post-process operations, therefore reducing the time and cost of production;
- In such a case the mechanical properties of the parts produced constitutes a major limitation, allowing their application only in non-load bearing situations or supported load bearing uses;
- The internal porosity of the HA/PLLA parts produced (mean value >150μm) is suitable to promote the growth of new tissues in the implant. In fact, this condition is essential to allow extensive blood supply of the new bodies, providing a rich supply of cells, growth factors and other nutrients needed to make bone grow. Moreover, these small holes allow access of bone marrow elements from the host tissues to the bone graft, providing nutrients for bone healing;
- The density of the HA/PLLA sintered parts (mean value = 0.883 g/cm^3) is within the density range values for the cancellous bone (0.14 to 1.10 g/cm^3) as previously referred. It can be seen that the green density in nearly the same of the powder bed.
  This result is important because, in principle, the higher the density of bone implant, the larger its strength.

The results obtained by applying the full factorial design have shown that the mechanical properties of the HA/PLLA parts as SLS produced are relatively poor when compared with other biomaterials (σ_c between 2.44 and 4.57 MPa / E_c between 17.19 and 40.80 MPa), but, even so, the Ultimate Compressive Strength and the Elastic Modulus lie in the lower limits of reported values for cancellous bone (1.5 – 38 MPa and 10 – 1570 MPa, respectively).
These results confirm the low mechanical strength of the HA/PLLA parts, as SLS produced, thus constituting a limitation for the applications in load-bearing situations.
The mechanical properties of the HA/PLLA sintered parts by SLS are expected to rise with the optimisation of the various parameters involved, particularly the energy density applied and the grain dimension of the starting powder.

7. Recommendations

It is believed that the investigation carried out can give guidance for other researchers interested in this subject. For successful SLS with HA powder and binder, the following care must be taken:

- Particle size is very important as it decides good powder spread with dense structure for component strength;
- When using coarse particles the friction between successive layers is higher, not allowing the correct spreading of the powder in the part platform during the build. In some cases a kind of "powder wave" can originate the displacement of the part being built;
- Also, the higher the particle size the higher the surface roughness and the lower the surface definition and the strength of the components;
- To avoid those phenomena it is recommended that powders be used with grain size in the range 80–120 μm, though the grinding of ductile polymers is problematic.

Therefore, an investigation into methods for reducing PLLA raw granules in order to obtain particles in that size range is necessary. The use of a ball mill for ground blends of HA coated with PLLA (produced using emulsions) is a possible solution;

- Although no references have been found in literature, and in testing, the possible existence of carbon in the HA matrix, as a result of the burning from the laser of the organic portion of the PLLA binder, is a concern. The effect of carbon on the behaviour of the implant is not fully understood, but some researchers suggest that it can have a possible negative influence either on the living tissues around the implantation area (eventual inflammation) or by the generation of hard spots in the implant matrix (eventually promoting a fragile structure). The thermal analysis performed didn't indicate any signs of carbon. The use of high temperature DSC (Differential Scanning Calorimeter) is therefore recommended for that purpose. The use of such equipment was not possible during the time of this research.

8. Conclusion

The major contribution of this research is the establishment of data and formulation of guidelines for the rapid manufacture of hydroxyapatite based components, by means of the SLS technology, to be used for bone tissue implantation, to replace and/or repair bone defects, due to traumatised, damaged or lost bone.

The overall feasibility of producing hydroxyapatite based bone shapes, from SLS, has been established.

While potentially very biocompatible, the porous calcium phosphate/poly-lactide implants are probably not strong enough for load bearing applications, such as artificial hips, bone screws, or dental implants. This is a limitation of the SLS technology, due to the fact that this process cannot produce directly full-density implants because it always yields porous parts.

This bioactive and resorbable composite (HA/PLLA) can be a potential improvement of the currently used internal fixation devices in orthopaedic surgery, because bone healing is a dynamic process and such a material should be resorbable to insure a progressive stress transfer to the bone.

This approach will allow the promotion of autograft (i.e., the patient's bone reconstruction), bone reconstruction, eliminating the need of using allograft bone graft substitutes (i.e., cadaver bone obtained from a tissue bank), thus reducing the chance of remote risk of disease transmission that all forms of allograft carry. A synthetic replacement is a major contribution for eliminating such problems.

The use of biodegradable polymers is, nowadays, still quite expensive, which can constitute a major drawback for the application of this type of products in bone reconstruction, although the good potentialities presented for that purpose.

The main advantages of RM (Rapid Manufacturing) of medical implants are: to reduce the number of patient visits prior to the surgery, remove time consuming operations, and reduce prostheses construction times.

The research has shown that the additive fabrication of biomaterials is possible with an adequate accuracy, strength and geometry of the models produced. The main advantages of using AMT to produce medical implants include the reduction of patient's visits prior to the surgery, remove time consuming operations, and reduce prostheses construction times. The mechanical properties (i.e., the compressive strength, compressive elastic modulus, bending strength and bending modulus) of the sintered SLS specimens produced in this research are

lower than that of cortical bone and pure solid sintered HA, but acceptable when compared with the mechanical properties of cancellous bone. *In vitro* studies have shown a slow degradation rate, and a good biocompatibility of the parts, as SLS produced, meaning that the implants can act as a good scaffold for bone ingrowths.

Thus, this bioactive and resorbable composite (HA/PLLA) can be a potential improvement of the currently used internal fixation devices in orthopaedic surgery, because when bone healing is a dynamic process such a material should be resorbable to insure a progressive stress transfer to the bone.

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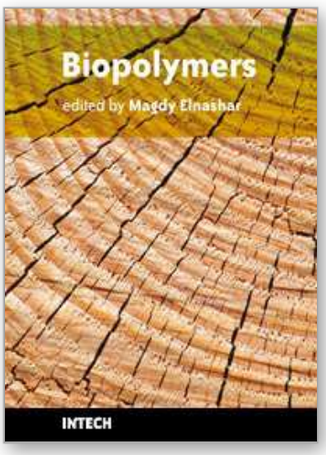

Biopolymers

Edited by Magdy Elnashar

ISBN 978-953-307-109-1

Hard cover, 612 pages

Publisher Sciyo

Published online 28, September, 2010

Published in print edition September, 2010

Biopolymers are polymers produced by living organisms. Cellulose, starch, chitin, proteins, peptides, DNA and RNA are all examples of biopolymers. This book comprehensively reviews and compiles information on biopolymers in 30 chapters. The book covers occurrence, synthesis, isolation and production, properties and applications, modification, and the relevant analysis methods to reveal the structures and properties of some biopolymers. This book will hopefully be of help to many scientists, physicians, pharmacists, engineers and other experts in a variety of disciplines, both academic and industrial. It may not only support research and development, but be suitable for teaching as well.

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