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Title	Laser sintering for the fabrication of tissue engineering scaffolds
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Publication Date	2012
Publication information	Stefan Lohfeld and Peter E. McHugh (2012) 'Laser Sintering for the Fabrication of Tissue Engineering Scaffolds' In: Michael A. K. Liebschner(Eds.). Computer-Aided Tissue Engineering. New York Dordrecht Heidelberg London : Springer Science+Business Media.
Publisher	Springer Science+Business Media
Link to publisher's version	http://link.springer.com/protocol/10.1007%2F978-1-61779-764-4_18
Item record	http://hdl.handle.net/10379/5523

Laser Sintering for the Fabrication of Tissue Engineering Scaffolds

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Abstract

Laser Sintering (LS), also referred to as selective laser sintering (SLS), is a rapid prototyping/manufacturing technique utilising a laser to fuse or sinter powder particles to form solid objects. Two major manufacturers of these machines are 3D Systems, USA, (Figure 1) and EOS GmbH, Germany. The abbreviation SLS[®] is a registered trademark of 3D Systems, therefore EOS refers to their system as a laser sintering machine [1]. Laser sintering allows the production of complex shapes like other rapid prototyping (RP) techniques, such as stereolithography, fused deposition modelling, 3D printing, etc. Closed volumes are possible, however unsintered powder will be trapped in the volume.

Key Words: Laser Sintering, Tissue Engineering, Scaffold, Composite Materials

1. General Aspects of Laser Sintering

As with the other rapid prototyping methods, volumetric models are divided into slices with thicknesses that are determined by the sintering process, typically in the region of 0.10 to 0.15 mm, and which are subsequently transferred to the scanner unit of the machine. Based on the cross sectional image of the sliced part, the laser scans selective areas of the preheated powder bed, where the powder particles melt and solidify quickly to form a dense part. To establish fusion with the current layer, the laser energy also partially liquefies the previous layer.



Figure 1: DTM (now 3D Systems) Sinterstation 2500plus

A typical machine has a part cylinder and one or more feed cylinders (Figure 2). After each slice is scanned, the part piston is lowered by a predefined increment (slice thickness) and the feed piston is raised by the required amount to provide sufficient powder to the part bed. A roller picks up the material from the feed cylinder and distributes it over the part bed.

The sintered parts are supported by the unsintered powder surrounding them, i.e. there is no need to build support structures simultaneously as in some other RP processes.

LS machines usually are quite costly to run and a high throughput is necessary to justify the cost. The build volumes are fairly large and the laser spot diameter is focussed to 400 to 500 μm to allow quick sintering of large areas with sufficient fine details.

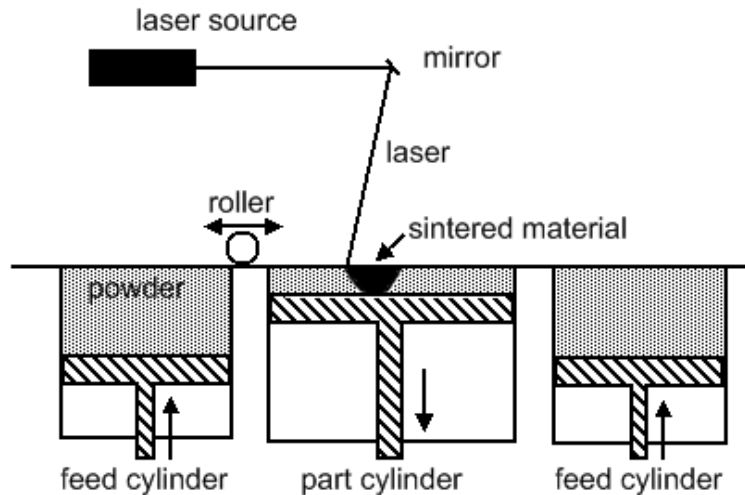


Figure 2: Laser sintering schema

2. Laser Sintering for Tissue Engineering Applications

The minimum feature size, which directly depends on the laser spot diameter, slightly limits the usability of the machines for tissue engineering (TE) scaffolds, where in general highly porous constructs are desired, with pores bigger than the struts within the scaffold. However, a significant advantage of the SLS process over some other rapid prototyping techniques is that no toxic solvents or binders are needed.

To directly manufacture a scaffold for tissue engineering via rapid prototyping, the material not only has to be biocompatible to ensure suitability for tissue growth *in vivo* or *ex vivo*, and possibly other properties such as biodegradability, but it also has to be suitable for the chosen rapid prototyping technique. While the laser sintering technique suggests that in principle any powder material can be processed, only a small range is commercially available. In addition, only few biocompatible materials have been used successfully to produce scaffolds via laser sintering. A major limitation of the materials holding the most promise for tissue engineering is their suitability for laser sintering. Polycaprolactone (PCL) is investigated most extensively for scaffolds fabricated via laser sintering [2-6]. Other materials include poly(methyl methacrylate) (PMMA),

polyetheretherketone (PEEK) [7], polylactide acid PLA [8] and poly(lactic-*co*-glycolide) (PLG) [9].

Tissue engineering scaffolds generally require small features to achieve small diameter strut networks with high porosity. Accuracy and minimum feature size are influenced by both the laser and the powder. Coarse powder particles will lead to a rough surface. The particle size should be around 50 to 100 μm for satisfactory surface quality on general macroscale parts. For TE scaffolds, the surface roughness is significant in relation to the overall dimensions of the part. The laser beam spot size limits the minimum feature size. With a diameter of 400 μm to 500 μm for a typical machine, in practice the minimum feature size is at least 500 μm . When using powder particles with a size of 50 to 100 μm , this feature, e.g. a strut of the scaffold, is just five to ten particles thick.

Parts may be overly porous and brittle if the degree of sintering is too low. On the other hand, growth, where the feature is bigger than the actual sintered area, may become extensive if the laser adds too much energy to achieve a dense part. For tiny features as required in scaffolds it can be difficult to find settings that lead to dense sintered areas that are still within their intended dimensions. Williams et al. [5] experienced this when manufacturing PCL scaffolds with various designs and porosities, that were consistently 27 % lower than those of the corresponding CAD designs. A dense cylinder, in contrast, had a designed porosity of 0 %, but an actual one of 17.8 %. The heat gradient in the powder surrounding the sintered area caused growth and decreased the size of the designed pores. The porosity of the cylinder, on the other hand, shows that although the laser energy caused growth, the sintering settings applied were still insufficient to achieve a dense body. As an example, Figure 2 shows the cross section of a strut of a PCL scaffold. Clearly visible is the area that was liquefied during sintering with a laser spot diameter of 410 μm . While the sintered area still contains pores and is just over 300 μm wide, the overall thickness with all particles connected to the surface already exceeds 500 μm .

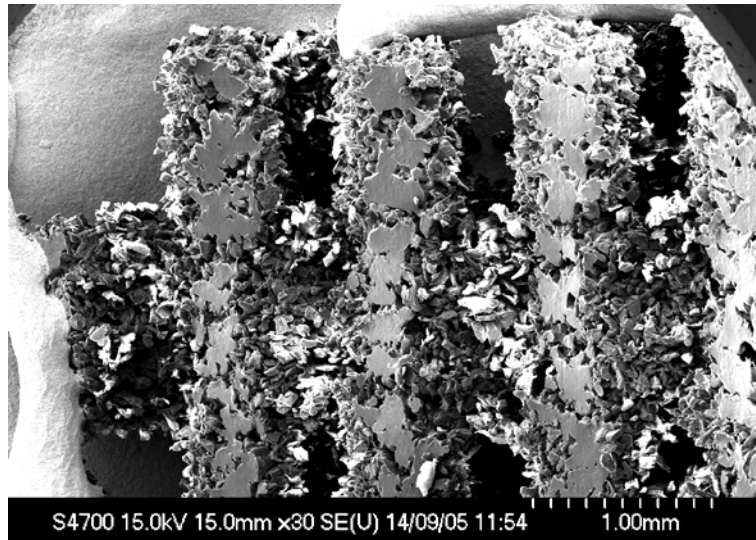


Figure 3: Cross sectional view of a PCL scaffold strut, produced at NUI, Galway on a DTM Sinterstation 2500^{plus}, powder particle size 50-110 μm , laser spot diameter 410 μm

To increase the overall porosity of a scaffold to a value desirable for tissue engineering, Huang et al. [2] mixed 80 wt-% of NaCl to PCL. The NaCl was leached out with water and a porosity of 89 % was achieved in the scaffold with a branching and joining 3D diameter-varying flow-channel network. While PCL is mainly used for hard tissue applications, the scaffold described by Huang et al. was considered as an evolutionary step in the development of a scaffold for tissue engineering of a liver.

While in the process of laser sintering no solvents are needed that could have negative consequences for tissue engineering applications, it has to be kept in mind that the heat of the laser in the standard laser sintering process can influence the molecular weight of the polymer, hence degrading it. To confront this problem and to be able to expand the range of materials that can be processed via laser sintering, surface selective laser sintering (SSLS) was introduced [8, 10]. SSLS uses a diode laser with a wavelength of 0.97 μm , whose laser radiation is not absorbed by the polymer particles, which are therefore not heated. Only biocompatible carbon microparticles, that were added in a very low ratio to the actual scaffold material and which settle on the powder particle's surfaces, take up the radiation. They cause local melting, leaving most of the bulk particle cold. This technique allows the processing of thermally unstable polymers such

as polylactides or polylactoglycolides and to obtain polymeric structures with bioactive proteins [8, 10]. In the present case, ribonuclease was mixed to PLA, and carbon microparticles were added to absorb the laser radiation. Struts with a thickness of approximately 200 μm and a separation distance of 500 μm were sintered with a layer thickness of 200 μm . Raman spectroscopy showed no significant difference in sintered and untreated material. Degradation of the polymers was only detectable when a considerable high laser energy density of 250 W/cm^2 was chosen for sintering.

A similar method to fabricate constructs from materials usually not suited for laser sintering is to mix them with a binder phase. For instance, a ceramic or metallic phase with a sintering temperature too high for the laser sintering machine is blended with a polymer to fabricate a green body. During laser sintering, only the polymeric phase is sintered. The polymer will be removed from the green body by burning it out at an elevated temperature, while the ceramic or metallic particles will be sintered in a subsequent step at a further increased temperature. Examples of this procedure were published by Goodridge et al. [11], who added up to 15 % of an acrylic binder to an apatite–mullite glass ceramic, and Lin et al. [12], where an epoxy resin/nylon blend was used as a binder for tricalciumphosphate.

3. Composites

The previously described powder mixtures can be referred to as composite powders, blended for the purpose of processing a material that cannot be laser sintered on its own. Composites scaffolds consist of two or more phases after the final manufacturing step. In this case all phases have a function beyond simple bonding of material; however, only one phase is sintered. Starting with a biocompatible polymer, a second phase may be added when the polymer is bioinert or has low mechanical properties. A bioactive phase is then added to enhance cell attachment, bone ingrowth, etc., or to increase the stiffness, especially when the scaffold is likely to be loaded after implantation. Hydroxyapatite (HA), for instance, is known for its bioactive behaviour and osteoconductivity. HA has been blended with PCL, PE, PEEK, and polyvinylalcohol (PVA), and the compound powders have been processed via laser sintering [6, 7, 13, 14].

In the 1990's, i.e. at an early stage of selective laser sintering, Lee et al. [15, 16] worked with PMMA-coated HA particles to develop bioceramic scaffolds via selective laser sintering. The drawback of the technique using coated particles was the involvement of organic solvents used in the production process of the powders. Any remnants of the solvent would cause inflammation. To avoid the necessity of solvents, Tan et al. [7] later used a physical blend of PEEK and HA powders. As PEEK is bioinert, HA was used to increase the bioactivity of the implant. Composite powders with up to 40 wt.-% of HA were sintered successfully.

Using a physically blended powder mixture with up to 30 wt.-% HA, Chua et al. [14] successfully processed PVA/HA composites via laser sintering. As with most materials, the variation of process parameters settings for successful sintering, such as preheat temperature, laser scan speed and laser power, was very limited, and in general a considerable amount of time has to be dedicated to find the most suitable parameters when investigating the suitability of a new material for laser sintering. Outside the established window, in [14] the constructs were found to be either too brittle or suffered from burning of the material due to an excessive energy density applied.

Experiments with two different types of HA blended with PCL were conducted by Wiria et al. [6]. Depending on the type of HA (either "reactor" or "sintered" powder, which differed significantly in their particulate surface areas) and depending on the amount of HA, the process parameters had to be adjusted. A range of possible setting combinations to sinter PCL with various amounts of HA was established. In vitro cell culturing showed the suitability of the processed material for cell ongrowth. A bioactivity analysis and mechanical testing of laser sintered material complemented the investigations showing the potential of this composite for tissue engineering.

Simpson et al. [9] investigated laser sintering of composites of 95/5 poly(L-lactide-co-glycolide) (PLG), hydroxyapatite and tricalciumphosphate (TCP). Solid constructs with mechanical properties similar to those of trabecular bone were successfully manufactured. However, dimensional inaccuracies occurred due to shifting of previously sintered layers when the roller passed to spread new material, creating difficulties to manufacture scaffolds with accurate shapes and dimensions. As this phenomenon may partly be

caused by the non spherical shape of the PLG particles, this problem may be rectified by an optimised powder preparation technique.

In any case, in general it is found that the amount of the second phase is limited. If the polymer content is too low, the sintered constructs may be too brittle to handle. In their publication on PVA/HA composites, Chua et al. [14] also reported on laser sintering of HA particles coated with PVA in a spray dry process, which unlike the blended powder mixture couldn't be sintered successfully. It appeared that this was rather due to the high HA content than to the nature of the composite powder, as in this case the HA content was 80 wt.-% and the amount of polymeric binder phase was too small to generate bonding between the particles. Maximum concentrations of hydroxyapatite (HA) in composites were investigated by Hao et al. [13], Savalani et al. [17], and Zhang et al. [18]. Polyethylene and polyamide were used as binders, and concentrations of up to 50 % of HA were achieved. Not all of the fabricated constructs were found suitable for tissue engineering due to the material choice, however, the research showed promising results in achieving mechanically stable, HA rich composites.

In summary, a limited number of materials, including composites, have successfully been evaluated thus far; however, from the present results laser sintering of selected biocompatible materials for tissue engineering is promising. The build chamber size of industrial laser sintering machines allows for the production of a reasonably large number of scaffolds at the same time. A reduction of the laser beam spot size to meet the requirements regarding minimum feature size of TE scaffolds would permit finer details and higher porosities. Machines developed especially for TE purposes, such as the SLS machine, already take this into account. As the materials investigated are non standard materials for the industrial laser sintering process, powder preparation currently is an important issue. Both size and shape of the particles are crucial for successful processing, and the preparation of the material can be a costly step in the entire process of manufacturing scaffolds for tissue engineering. In addition, when the particle size of a second phase is too small, the particles may settle on the surface of the polymeric phase and shielding can occur, also observed by Simpson et al. [9]. This shielding prevents the polymeric particles establishing connection to each others and forming a mechanical stable construct. Hence a similar particle size for both phases seems favourable, so that the second phase does not severely impair the sintering behaviour of the polymeric phase. It has

been proven that with careful process control the thermal degradation of the polymeric phases during laser sintering can be kept either superficial or at least not too severe, so the biocompatible nature of the materials remains unchanged. Selection of the material depends on the task and intended site of the scaffold, and the addition of bioactive phases caters for improved performance of the scaffold in tissue engineering.

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