

REVIEW ON MATERIALS AND RAPID PROTOTYPING TECHNIQUES FOR CARTILAGE IMPLANTS

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Abstract— The human tissue is a regular interconnected pore structure. Mechanical material properties and hydro gel lubrication characteristic can bring implant structures closer to the form that we can find in natural cartilage. Laser is used in a wide variety of materials to fabricate complicate 3D structures and that is way they have chosen it for closer analysis. In our days there are more and more biomaterials discovered and in use for the long term implant to substitute damaged tissues. In this paper some of the widely used synthetic implant materials and laser based fabrication methods are featured; why they would be ideal for this cartilage implant and for this laser based manufacturing method.

Keywords—Tissue, Cartilage, Composite, Implant, Rapid Prototyping

I. INTRODUCTION

Osteoarthritis or traumatic disorders can cause cartilage degeneration followed by pain and loss of motion of affected joints. By now, there is no successful long term treatment for this serious medical problem affecting people in all ages. Needful approach could be found in a biomaterial or biomaterial combination, which would repair full thickness defects. This could diminish the need of total joint replacements and provide a long term solution to release pain.

When comparing an artificial biomaterial to a natural body tissue some disadvantages appear. In composite material, where different materials are divided into layers, materials should mimic the surrounding tissue separately and together. Even if this way mechanical property of the implant can be tailored close to the properties of the host tissue, biomaterials do not have the ability to adapt their structure and properties according to the environmental factors.

Manufacturing process of the implant should be nontoxic, should not leave residues into the material and should be suitable for the selected materials. Basic idea

of the laser is to focus a high power source, laser beam, into the specific point and create a melted pool of material. Particles weld together and create a wanted structure.

The review presents the conclusions concerning materials and the compatibility of the processing methods. All of the presented materials are synthetic materials, which are used for permanent replacement of the tissue. They should be biocompatible and bring benefit to this composite implant used in cartilage.

II. STRUCTURE OF KNEE AND CARTILAGE

A. Cartilage

Articular cartilage is a living material composed of a relatively small number of cells known as chondrocytes surrounded by a multicomponent matrix. Mechanically, articular cartilage is a composite of materials with widely differing properties. Approximately 70 to 85% of the weight of the whole tissue is water. The remainder of the tissue is composed primarily of proteoglycans and collagen [1].

B. Composition

Chondrocytes are the cells that make up cartilage. The number of chondrocytes in cartilage is less than 10% of the full tissue volume. Chondrocytes produce an extra cellular matrix (ECM) which is composed of a dense network of collagen fibers and proteoglycans (PGs). The collagen content in cartilage is about 10-30% while the PG content is 3-10% (wet weight). The remaining component is water. Other compounds are inorganic salts and small amounts of other matrix proteins, glycoproteins and lipids. It is the collagen and PGs that provide the structure for the tissue and together with water determine the biomechanical properties and functional behavior of cartilage.

The articular cartilage can be divided into different zones consisting of a superficial tangential zone (10-

20%), a middle zone (40-60%) and a deep zone (30%). There is also a calcified zone close to the bone [2].

C. Knee

While there are four bones that come together at the knee, only the femur (thigh bone) and the tibia (shin bone) form the joint itself. The head of the fibula (strut bone on the outside of the leg) provides some stability, and the patella (kneecap) helps with joint and muscle function. Movement and weight-bearing occur where the ends of the femur called the femoral condyles match up with the top flat surfaces of the tibia (tibial plateaus).

Inside the knee, there are two shock-absorbing pieces of cartilage called menisci (singular meniscus) that sit on the top surface of the tibia. The menisci allow the femoral condyle to move on the tibial surface without friction, preventing the bones from rubbing on each other. Without the menisci, the friction of bone on bone would cause inflammation, or arthritis. Bursas surround the knee joint and are fluid-filled sacs that cushion the knee during its range of motion. In the front of the knee, there is a bursa between the skin and the kneecap called the prepatellar bursa and another above the kneecap called the suprapatellar bursa (supra=above). Each part of the anatomy needs to function properly for the knee to work. Acute injury or trauma as well as chronic overuse both cause inflammation and its accompanying symptoms of pain, swelling, redness, and warmth [3].

D. Collateral Ligaments

Collateral Ligaments prevent hyperextension, adduction, and abduction. Superficial MCL (Medial Collateral Ligament) connects the medial (inner) epicondyle of the femur to the medial condyle of the tibia and resists valgus (bending out) force. Deep MCL (Medial Collateral Ligament) connects the medial (inner) epicondyle of the femur with the medial meniscus. LCL (Lateral Collateral Ligament), entirely separate from the articular capsule, connects the lateral (outer) epicondyle of the femur to the head of the fibula and resists varus (bending in) force [4].

III. CURRENT TREATMENT METHODS

The high demands on the weight-bearing joint make treatment of articular cartilage injuries and restoration of the injured joint surfaces critically important to facilitate a physically active lifestyle. Maintaining an active lifestyle has significant medical benefits, such as reducing the risk of serious medical conditions like heart disease, hypertension, and diabetes. Since injuries to articular cartilage have been shown to present one of the most common causes of permanent disability, their management has important long-term implications. Treatment of articular cartilage injuries has traditionally

presented a significant therapeutic challenge. However, development of first-generation surgical techniques has created considerable clinical and scientific enthusiasm for articular cartilage repair. Based on the source of the cartilage repair tissue, these new surgical techniques can generally be categorized into three groups: marrow-stimulation-based techniques, osteochondral transplantation techniques and cell-based repair techniques [5].

IV. MATERIALS

A. Biomaterials and Cartilage Repair

Biomaterials are of great importance in applications concerning tissue engineering therapies. The purpose of the biomaterial is to provide biochemical, mechanical and organizational cues for cells to attach, grow, differentiate and form new tissue. The chemical identity of the biomaterial, its surface characteristics and the methods of material processing can also influence cell behavior. The scaffold should have mechanical properties similar to the replacing tissue, be able to withstand variable mechanical loads and its rate of biodegradation should match the rate of the tissue regeneration. Furthermore, the final byproducts of the degradable scaffold must be nontoxic and have low antigenicity. Various types of biomaterials have been used in generating tissue engineering scaffolds that usually are divided into two major classes: synthetic and natural materials. A number of fabrication and surface modification methods have been employed to create scaffolds in various architectures that can enhance cellular behavior, generate suitable environments for tissue growth and allow manipulation through the incorporation of biomolecules [6].

1) Natural Materials

A wide range of natural materials including cellulose, alginate, chondroitin sulfate, gelatin, chitosan, agarose, HA, fibrin and collagen are commonly used in cartilage tissue engineering. These types of biomaterials have the capability of interacting with cells via specific surface receptors, which in turn facilitate cell motility, proliferation and protein production. However, these materials may elicit an immune response due to this constant interaction. Additionally, natural biomaterials may be unsuitable for long-term loading applications due to their susceptibility to enzymatic degradation [6].

2) Synthetic Materials

Synthetic polymers are often used to prepare tissue engineering scaffolds because of their abundance, cost and ease of preparing biomaterials/scaffolds with tunable and custom-made properties (i.e. degradation kinetics,

hydrophilicity, crystallinity, strength, bioactivity, etc.) Some of the most common synthetic polymers currently used for cartilage engineering include polyethylene glycol (PEG), poly(NiPAAm), poly(α -hydroxy esters), poly(propylene fumarates), and polyurethanes. Still all of these biomaterials need to be functionalized to a certain degree with signaling molecules in order to interact with their surrounding biological environment in a tissue responsive manner [6].

B. Polymers

Poly(α -hydroxy esters) are the most commonly used synthetic polymers in cartilage tissue engineering because of their biodegradability and the approval from the US Food and Drug Administration (FDA) for clinical. Specifically, poly(glycolic acid) (PGA), poly(lactic acid) (PLA), and their copolymer poly(lactic-co-glycolic acid) (PLGA) have been investigated for use as cartilage tissue engineering scaffolds. Both, *in vitro* and *in vivo* studies have demonstrated the maintenance of chondrocyte phenotype and the production of cartilage-specific extracellular matrix (ECM) in these scaffolds. In addition, PLGA is used as a scaffold material for matrix-based autologous chondrocyte transplantation clinically for more than 3 years [7].

Polymers are formed by chemical reactions in which a large number of molecules called monomers are joined sequentially, forming a chain. In many polymers, only one monomer is used. In others, two or three different monomers may be combined. Polymers are classified by the characteristics of the reactions by which they are formed. If all atoms in the monomers are incorporated into the polymer, the polymer is called an addition polymer. If some of the atoms of the monomers are released into small molecules, such as water, the polymer is called a condensation polymer. Condensation polymers are made from monomers that have two different groups of atoms which can join together to form, for example, ester or amide links. Polyesters are an important class of commercial polymers, as are polyamides (nylon) [8]-[9].

As early as 1973, it was shown that the polyester poly(ϵ -caprolactone) degrades when disposed in bioactive environments such as soil. This and related polyesters are water resistant and may be melt-extruded into sheets, bottles, and various shaped articles, marking these plastics as primary targets for use as BPs. Several biodegradable polyesters are now in the market or at an advanced stage of development [10].

Polymers are used as engineering materials in the neat form, i.e., as the pure material, or in combination with a large diversity of additives, both organic and inorganic. These additives may be, among others, plasticizers

which reduce the rigidity or brittleness of the material, fillers which increase strength and load deflection behavior under load, or stabilizers which protect the polymer against ultraviolet radiation [11].

C. Titanium and Titanium Alloys

Titanium and its alloys are used primarily in two areas of application where the unique characteristics of these metals justify their selection: corrosion-resistant service and strength-efficient structures. For these two diverse areas, selection criteria differ markedly. Corrosion applications normally use lower-strength "unalloyed" titanium mill products fabricated into tanks, heat exchangers, or reactor vessels for chemical-processing, desalination, or power-generation plants. In contrast, high-performance applications such as gas turbines, aircraft structures, drilling equipment, and submersibles, or even applications such as biomedical implants, bicycle frames, and so on, typically use higher-strength titanium alloys. However, this use is in a very selective manner that depends on factors such as thermal environment, loading parameters, corrosion environment, available product forms, fabrication characteristics, and inspection and/or reliability requirements. Desired mechanical properties such as yield or ultimate strength to density (strength efficiency), fatigue crack growth rate, and fracture toughness, as well as manufacturing considerations such as welding and forming requirements, are extremely important. These factors normally provide the criteria that determine the alloy composition, structure (α , α - β , or β), heat treatment (some variant of either annealing or solution treating and aging), and level of process control selected or prescribed for structural titanium alloy applications [17].

V. APPLICATIONS OF BIOMATERIALS IN CARTILAGE REPAIR

The idea of promoting cartilage repair at the earliest possible time is the goal of any therapeutic approach for cartilage regeneration. For a tissue engineering approach to have a successful outcome, variables such as scaffold architecture and properties, tissue characteristics (i.e. ECM, cell type) and enabling signaling molecules require careful consideration. Earlier tissue engineering approaches were focused on singular parameters (i.e. scaffold architecture or cell type), but recently a multicomponent approach is sought where a biomaterial/scaffold is combined with cells and/or signaling molecules. The following sections outline a number of proposals for cartilage repair, ranging from the use of scaffolds, cell therapy, growth factors and hybrid constructs [6].

A. Scaffolds

Scaffolds are generally considered as a mechanical substrate, but when placed in a physiological environment, scaffolds may interact with cells and the surrounding tissue via specific chemical interactions (i.e. ligand-receptor binding) as well as mechanical stimulation. These interactions need to be dynamic and concomitant in order to guarantee a regenerative response. As a result the main purpose of a scaffold is to support cell seeding, infiltration, proliferation, and in some cases differentiation due to signaling molecules and mechanical stimuli. Scaffolds can be classified depending on their morphology as hydrogels, fibrous constructs and porous scaffolds [6]-[7]-[8].

B. Porous Scaffolds

Porous scaffolds have certain characteristics that will help dictate their behavior in a physiological setting; these characteristics include pore size, porosity and interconnectivity. Where porosity determines the surface area for cell adhesion, pore size and interconnectivity will affect cell behavior, and nutrient/ metabolite transport within the scaffold. Porous scaffolds have been developed through different methods and biomaterials, resulting in different geometric conformations that may influence cellular behavior. The addition of biological factors (e.g. growth factors, cytokines), cells or pharmaceuticals via encapsulation or surface modification could further facilitate cartilage repair [6].

Natural materials have also been used to prepare porous scaffolds. Kuo et al. hybridized chitin and chitosan through genipin crosslinking and subsequently freeze-dried the constructs. The resultant scaffold was then coated with HA to modify the surface chemistry, and therefore enhance the chondrocytic attachment and growth. The study demonstrated that the scaffold's mechanical properties, pore sizes and pore number depended on the freezing temperature, and the concentration of the components. Additionally, the use of HA generated positive effects on the cell number, the content of GAG and the collagen level over a 28 day incubation period. Silk fibroin has become a suitable option as a biomaterial substrate, due to its capabilities to support greater proliferation and chondrogenesis than collagen scaffolds. Hofmann et al. prepared silk fibroin scaffolds through salt leaching. The scaffolds were seeded with human bone marrow - derived MSCs and incubated for 21 days. The silk scaffolds supported greater cell proliferation and the expression of GAG, collagen type II and aggrecans was higher than the control collagen scaffolds [12]-[13]-[14].

VI. LASER BASED FABRICATION

The Rapid Prototyping Laboratory (RPL) supports internal design, manufacturing, and process

development with three rapid prototyping (RP) technologies: Stereolithography (SL), Selective Laser Sintering (SLS), and 3D Printing (3DP). Rapid prototyping uses advanced computer and laser technologies to produce complex three-dimensional prototypes in a fraction of the time required by more traditional technologies. The rapid prototyping process begins with a CAD solid model output to the appropriate RP file format. The file data is sliced into cross sections of 0.003 to 0.010 in. thickness. The cross sections are then fabricated in a layer additive process using one of the three available RP technologies [19].

Many of the rapid prototyping methods are used to create biomaterial implants. Laser is said to be nontoxic, fast, accurate and cheap manufacturing method for many medical appliances and instruments. When using a layer by layer manufacturing process some facts have to be considered. Each layer thickness can not be chosen individually and steps at the edge of a layer will affect the completed object. The shrinkage of different materials can vary [15]-[16]-[18]-20].

A. Selective Laser Sintering

Selective laser sintering is a Material Accretion Manufacturing or Rapid Prototyping (RP) technology. It produces parts in a layer-by-layer fashion. The SLS technology allows a direct coupling with the CAD-model of the product, in which successive cross sections are calculated, to produce three dimensional parts without dedicated tools, like dies, as used in conventional sintering. Total production time and cost can hence be reduced.

K.U. Leuven aims at the development of the SLS process to make metal parts directly from commercially available powders, without using a polymer binder or a specially developed metal powder. Some successful applications have been made to high strength powder mixtures, like Fe-Cu, WC-Co and TiC-Ni. In order to master well the process, it is necessary to investigate the influence of processing and material parameters, such as laser power, scan speed, mixture ratio and particle size [21].

Layer Manufacturing (LM) technologies like Selective Laser Sintering (SLS) were developed in the late 80's as techniques for Rapid Prototyping (RP). Today, SLS - as well as its derived technology Selective Laser Melting (SLM) - is used as well for prototyping, tooling and manufacturing purposes. This widening of applications is caused mainly by the possibility to process a large variety of materials, resulting in a broad range of physical and mechanical properties [22].

1) Selective Laser Sintering Materials

Developing new materials for SLS machines is costly.

To fill an SLS machine with the current industry-standard Duraform powder costs several thousand dollars. Polymer companies typically produce test quantities either below 10lb. (too little to test in an SLS machine) or above 1 ton (a large amount before the SLS processing traits are understood). Few polymers are produced directly as powders and must be ground and classified to appropriate particle size distributions. Long-term changes in material behavior and machine operating conditions must be characterized if a material is to be used commercially [23]-[24].

a) Nylon 12 (Polyamide PA2200)

By far the most common material used in SLS, parts have good long term stability, offering resistance to most chemicals. It is harmless to the environment and safe to use with foodstuff. Complexity is irrelevant and the material delivers the impact strength and durability required for functional testing. Tensile and flexural strength combine to make tough prototypes, with the flex associated with many production thermoplastics. It is able to emulate living hinge designs, certainly to 20+ cycles. The material is non-hygroscopic, thereby negating the requirement to seal the surface on components being used with liquids [25].

b) Glass Filled Nylon 12 (Polyamide PA3200)

This is the Glass Filled variant of PA2200. Providing greater rigidity, the glass-filled blend is perfect when prototyping rigid parts intended for production in advanced engineered thermoplastics, and is the right choice for functional testing. Form, fit and functional testing can now be completed without sacrifice. The filler is glass bead and not fibre, hence the part predominantly increases in stiffness but not strength. Filler ratios approximately 40%. The material is non-hygroscopic, thereby negating the requirement to seal the surface on components being used with liquids [25].

2) Manufacturing Implants with Selective Laser Sintering

A method for fabricating artificial calcium phosphate bone implants by the Selective Laser Sintering (SLS) process was developed that can fabricate complex and delicate calcium phosphate bone facsimiles from a variety of data inputs including Computed Tomography(CT) files [26].

Spray dried material were processed using a beta test workstation SLSTM Model 125 equipped with modulated 25 W CO₂ laser. Laser output power, beam scan speed, scan spacing and powder bed temperature were controlled to optimize the green strength according to the shape of the implants. Optimal settings for Energy Density were found to be in the range of 1 to 1.5 cal/cm² [26].

Testing of cartilage immediately after laser treatment shows three characteristic deformation regions. First, a region of small strain deformation ($\epsilon \leq 0.05$) corresponds to a two-fold decrease of Young's modulus compared to initial values. Second, a region of expansion with ϵ increasing from 0.05 to 0.4 shows a negligible change of Young's modulus. Third, in compression, Young's modulus is an order of magnitude higher than that for expansion. During laser irradiation, Young's modulus decreases by approximately two times. The mechanical properties (e.g., Young's modulus) of the irradiated specimens return to initial (non-irradiated) values after immersing the laser irradiated cartilage specimen for ten minutes in physiologic saline [27].

B. Stereolithography

Stereolithography has become a well known technique in the rapid prototyping sector. In preoperative model planning and surgery simulation, this technique has been used in the field of craniofacial surgery, tumour surgery, reconstructive surgery, orthognathic surgery, preprosthetic surgery and dental implants.

The technique of colour stereolithography was developed very recently. This technique allows the selective colouring of structures in the three dimensional (3D) solid model. The 3D information of a solid model combined with the extra information from the selective colouring of certain anatomical structures both combine as an ultimate diagnostic and preoperative planning tool [28]-[29].

VII. CONCLUSION

It was detected in the review how combination of titanium, polymer and hydrogel composite in cartilage implant is a novel application. This kind of implant is not directly found in literature. However, combination of these materials' good qualities could provide the needed solution for cartilage repair. Titanium or titanium alloy could provide attachment to the subchondral bone, whereas polymer could lower composites elastic modulus. Wear properties has to be considered carefully in long lasting tripobair application. To reduce the wear of the implant, hydrogel surface or coating could bring the solution. Properties of ultrahigh molecular weight polyethylene with polyHEMA coating have already been investigated. When combining these two materials in the implant some of the existing results could be utilized.

Laser based manufacturing of this multimaterial implant is a novel approach. All except hydrogels, have been separately used in some extend in laser based manufacturing. 3D plotting is the only solid freeform fabrication investigated for hydrogels. This method does not include laser, so hydrogel application fabricated by

laser based manufacturing, remains unsolved. All materials react differently to laser beam. This can be problematic if using only one fabrication method to all three separate materials. For example, when exposed to too high laser power polymers can start to degrade and lose their properties. Meanwhile production of titanium parts would need much higher laser power than polymer parts.

Laser Engineered Net Shaping was developed to overcome obstacles founded with high density materials like titanium. An interesting fact about the process is the possibility to vary processing parameters during fabrication, which could enable the use of different materials in the same implant.

The answer to the research question was not totally explicit. The lack of a specific investigation for reviewed materials and especially reviewed fabrication methods led only to assumptions that the cartilage implant might be able to be manufactured from reviewed materials with laser based manufacturing method.

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