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Overview of Rapid Prototyping for Fabrication of Bone Tissue Engineering Scaffold

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Abstract. The scaffolds of bone tissue engineering (BTE) are designed with complex interconnected pores for providing mechanical support, cell attachment and nutrition delivery, and can be directly fabricated via rapid prototyping (RP). Based on reviews on amount of papers, fundamental of BTE, including research procedure and biomaterials for scaffold are presented. And various RP methods for scaffold fabrication, including selective laser sintering (SLS), fused deposition modeling (FDM), 3 dimension printing (3DP), are introduced. The conclusions including existing problems and future researches about BTE scaffold fabrication are given at the end.

Introduction

Bone grafting is a large mount surgery in clinic, such as in the USA, over 1 million orthopedic operations involve bone repair for replacement surgery, trauma, abnormal development or skeletal deficiency, and in which over 250,000 bone grafts are performed annually [1]. But bone grafting, including autografting and allografting, have many defects which limit the use and quality of clinic application. For example, the bone grafts are avascular and rely on diffusion for survival, and the size of the defect and viability of the host bed can therefore limit their use. In large defects, the bone graft can often be resorbed before osteogenesis is complete. Addition, autologous bone grafts are also limited in supply. For these reasons, tissue engineering, a discipline typically involveing the combination of cells and biomaterials to form tissues with the goal of replacing or restoring physiological functions lost in diseased organs [2], offers great potential for the construction of new musculoskeletal tissues.

Tissue engineering is an interdisciplinary field including medicine, biology, and technology of design and manufacturing. Bone regeneration via tissue engineering techniques requires a number of components: stem cells such as bone marrow derived osteoblasts capable of differentiation into mature bone cells, a suitable carrier which aids in filling large sites for repair, can deliver cells to specific sites and then function as a scaffold for growth, and in some cases, a viable well vascualrised host bed. The biomaterial scaffolds, one of the most important components in BTE, include six primary requirements: (1) a three-dimensional (3D) and highly porous structure to support cell attachment, proliferation and exra-cellular matrix production; (2) an interconnected/permeable pore network to promote nutrient and waste exchange; (3) a biocompatible and bioresorbable substrate with controllable degradation rates; (4) a suitable surface chemistry for cell attachment, proliferation, and differentiation; (5) provide temporary mechanical support, and (6) enhance tissue regeneration through biologic delivery [3,4]. Thus, the scaffolds are designed with complex microstructures of interconnected pores, which can not be fabricated with general methods such as machining cutting, casting, even computer numerical cutting, and how to fabricate the complex structure of scaffold is a long concerned problem in tissue engineering research.

Fundamental for Scaffold Fabrication

In BTE, the scaffold provides a framework and initial support for the cells to attach, proliferate and differentiate, and form an extracellular matrix, and the design, fabrication and biological experiment are widely studied. The difficult of scaffold fabrication not only lies in complex structure, and other factors such as the properties of biomaterial, the procedure of surface bio-modification also limit the fabrication. Especially, the properties of biomaterial determine the selection of the fabrication method to one or several kinds.

Research Procedure of BTE Repairing. Tissue engineering, including BTE, is now still at the state of research in lab, even on animal, rather than clinic application. Scaffold is one of critical elements of the BTE, and the bone repairing procedure via tissue engineering is a complex procedure, among which, the scaffold fabrication is an important step. The overview of the whole procedure is given in Fig. 1.

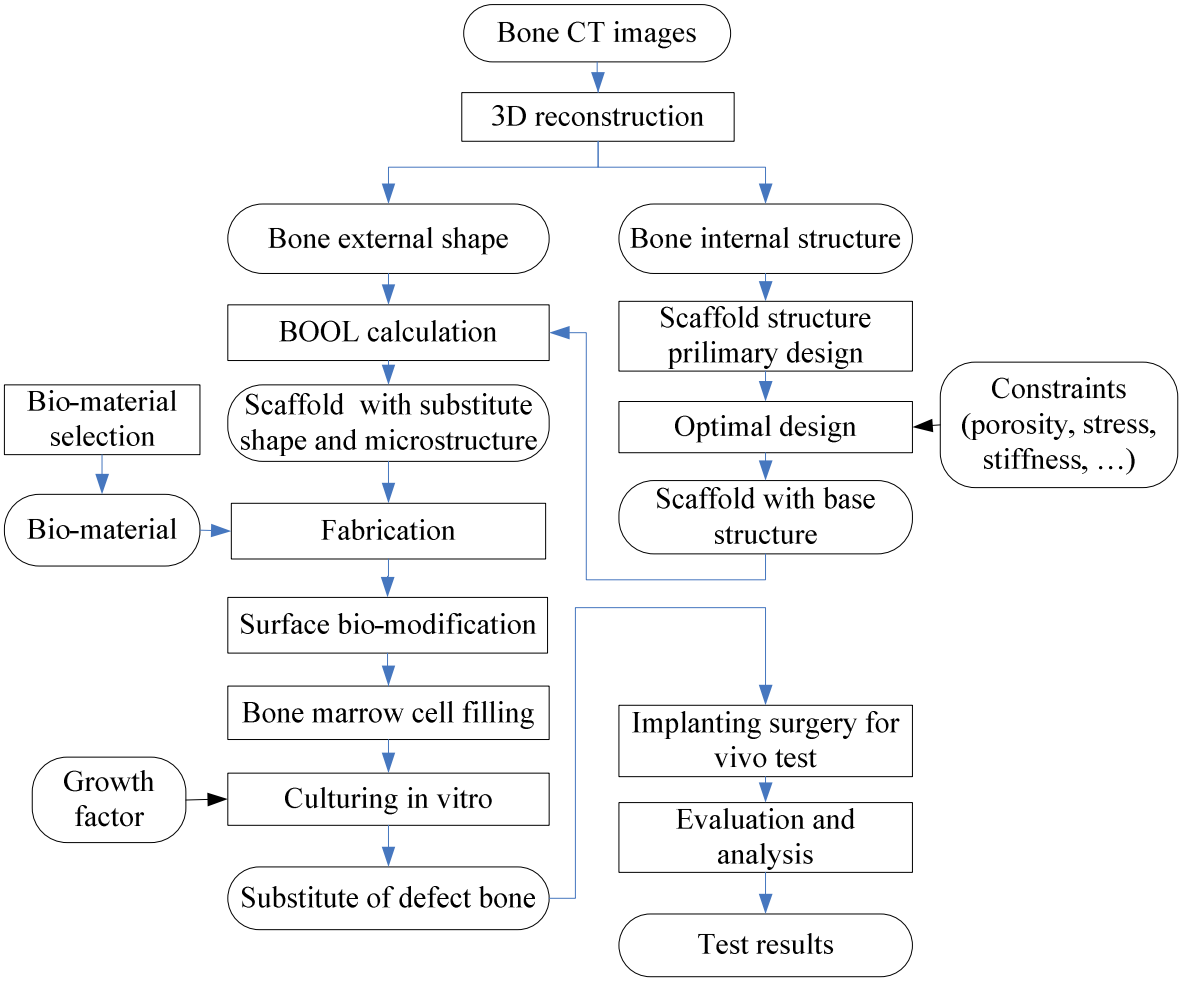


Fig. 1 Procedure of BTE study and experiment

First, the scaffold structures including internal porous and external personalized bone shape are designed regarding to the anatomic structure of defected area. Then, select appropriate biomaterial and fabrication method to produce the scaffold. After post-processing of surface bio-modification for cell attachment conveniently and better biocompatibility, the scaffolds are cultured in vitro with growth factors and bone marrow cell. The culturing scaffolds will biodegrade and guide new bone formation at the same time, and this process will proceed further in vivo through clinic operation after vitro culturing past enough time to make the bone-scaffold system sufficient mechanical property to sustain evolution in vivo. At the end, the research results can be concluded through evaluation and analysis of bone-scaffold system via some instruments including CT (computed tomography) scanner and SEM (scanning electron microscope).

Biomaterials for BTE Scaffold. The scaffold fabrication method is determined by the different properties of used biomaterial. Biomaterial used for BTE scaffold must own some properties including appropriate mechanical properties, biodegradation, and biocompatibility, and main three types material are used: polymer, bioceramics, and composites [5]. The polymers, including natural polymers and synthetic polymers, have good biodegradable and biocompatible properties. But the natural polymers, such as collagen, fibrin, chitosan, and starch are limited to use due to their very low mechanical stability. Recent years, the synthetic polymers, such as polycaprolactone (PCL), poly lactic acid (PLA) and poly glycolic acid (PGA), are widely studied and used for BTE scaffolds for their tremendous versatility via various RP methods [6]. Bioceramics, such as hydroxyapatites (HA) and tricaclcium phosphate (TCP) and biphasic calcium phosphates (BCP, which contains HA and TCP in different proportions), resemble the mineral phase of bone and are characterized as biocompatible, bioactive and osteoconductive, and are studied and used for BTE scaffold widely too. But these organic ceramics biodegrade slowly in body environment and is too brittle which limit the use for BTE scaffold [7, 8]. To utilize the advantages and balance the shortages of above two material comprehensively, many researchers attempt fabricating the BTE scaffold with composite consisting of bioceramics and polymers, and some experiments proved its effectiveness [9, 10]. But the fabrication procedure with composite become longer and the process become more complex, and the internal microstructure of scaffold become no controllable. From comprehensive analysis, organic synthetic polymers such as PCL and PLA are hotspots currently on the researches of BTE scaffold material.

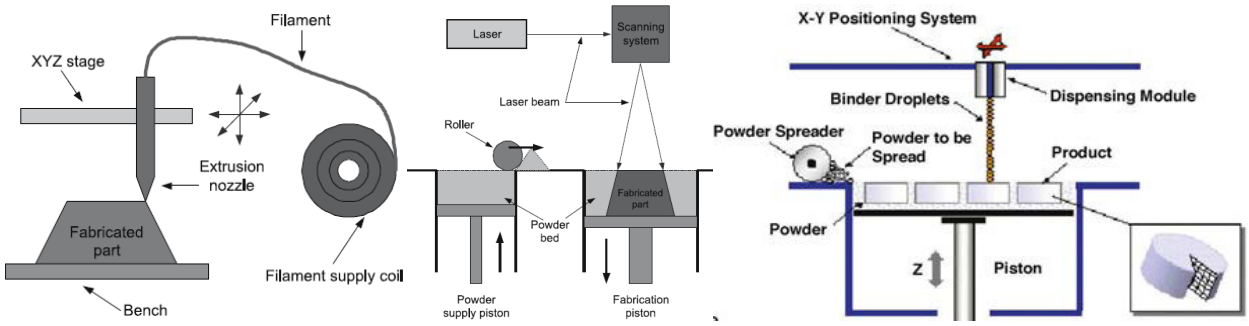
RP Methods for BTE Scaffold Fabrication

Conventional scaffold fabrication methods include fiber bonding, solvent casting, particulate leaching, membrane lamination, melt molding, temperature-induced phase separation, and gas foaming. These methods are limited in how they regulate scaffold parameters such as pore size, pore shape, pore interconnectivity, and pore wall thickness. This lack of fine control has led to the development of new techniques to produce scaffolds directly from a computer-aided design model [5]. RP technologies, also known as solid free-form fabrication (SFF), are the most widely applied and known fabrication methods in medicine that are based on additive fabrication principles, and they can be used to manufacture physical model of tissue, personalized implant and surgery aid tool, and tissue engineering scaffold [11]. Some of the major RP technologies used for scaffold fabrication are SLS, FDM, and 3DP. Other RP methods, such as stereolithography (SLA), are limited to create anatomical models for surgical planning or teaching in the biomedical industry for their shortcomes such as curing and shrinkage after post-processing [12]. What makes RP particularly appealing for scaffold fabrication is the fact that compared to alternative manufacturing technologies, like for instance CNC machining, RP systems can fabricate parts of almost any geometrical complexity in relatively lower time and with without significant requirements in technical expertise [13].

FDM. FDM is a fabrication method via fusion and deposition the bio-material from a nozzle layer by layer, as shown in Fig. 2(a) [14]. By altering the direction of material deposition with each layer, scaffolds with complex internal organization can be formed. FDM is restricted to the use of thermoplastic materials with good melt viscosity properties; cells cannot be encapsulated into the scaffolds during the fabrication process. So, the material used in this method mainly limited to polymer, such as PCL, which has the appropriate fusion temperature. But in oder to improve the mechanical properties of BTE scaffold of polymer, studies of adding bio-ceramic, such as the composites PCL/HA, PCL/TCP, have been done, and good results of favorable mechanical and biochemical properties were acquired [15].

SLS. This method constructs scaffolds from 3D digital data by sequentially fusing regions in a powder bed layer by layer, via a computer controlled scanning laser beam, as shown in Fig. 2(b) [14]. Unused powder released form the scaffold yields high porosity and surface area while retaining mechanical integrity. Compare to other SFF methods such as FDM, SLS does not require supports,

which are complex to design and remove from fabricated model usually in FDM. Additionally, SLS has good capable on material, theoretically, any biomaterial that will fuse without decomposing under a laser beam can be used to fabricate scaffold, even it may be easier to incorporate multiple materials. So bioceramic and polymer can be used in SLS. For example, scaffold with PCL via SLS is presented by Williams in 2005 firstly [16]. Even, the two materials can composite and be used to fabricate hybrid scaffold via SLS with only one fabrication process [17]. The pattern resolution of SLS is limited by the diameter of the laser beam diameter to about 400μm [18], and maximum pore size is about 50μm, due to the powder particle size [19].



(a) FDM (b) SLS (c) 3DP

Fig. 2 Schematic of RP methods

3DP. 3DP technology became one of the most investigated SFF techniques in tissue engineering and drug-delivery applications. An advantage of 3DP is that it can perform in an ambient environment. As shown in Fig. 2(c), the 3D printer constructs the 3D model by first spreading a layer of fresh powder over a building platform. An "inkjet" print head prints or deposits the binder solution onto the powder bed. Multiple layers can be fabricated and stacked with dimensions one the scale of polymer particle size (approximately 200-300μm) [20]. The drawbacks of 3DP include difficulties in removing the support powder form complex architectural features deep within the scaffold and the complete removal of the organic solvent. Polymers, such as polylactic acid (PLLA) and poly (DL-lactic acid-co-glycolic acid) (PLGA) have been used to fabricate scaffolds by printing chloroform onto a bed of these particles. The chloroform acts to swell, partially dissolve the polymer and eventually bind adjacent particles once the solvent has evaporated [21]. And ceramics such as β-TCP have been used to fabricate BTE scaffold via 3DP too [22].

Conclusions

Scaffolds, as a key element of BTE, have acquired much attention from fields of bioengineering and mechanical engineering recent years. The scaffold fabrication methods, as well as bio-material used, are widely studied and will be done continue in future. Although scaffolds of various biomaterial, fabricated via RP methods including SLS, FDM and 3DP have been proved the effectiveness with culturing experiments in vitro or vivo, the fabrication parameters and procedure need to research more to make the pore size smaller and the porosity higher. And the microstructure design and biomaterial development will receive more attention too.

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