Comprehensive Review on the Feasibility Study of Traditional versus 3D Bio-scaffold Synthesizing Process for Bone Cell Regeneration

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Abstract Scaffolds are three-dimensional (3D) porous, fibrous, or permeable biomaterials designed to increase intercellular communication, cell survival, and extracellular matrix (ECM) deposition with the least amount of toxicity, inflammation and itbiodegrades at a specific time.Bio-scaffolds need to satisfy a few criteria to allow osseointegration, Osseo-conductivity and Osseo-inductivity. A growing number of Traditional synthesizing processes and three-dimensional (3D) printing processes have been applied to tissue engineering. This project presents a feasibility study of traditional versus 3D-printing technologies for tissue-engineering applications, with particular focus on the development of a traditional synthesizing process versus computer-aided scaffold design system; the 3D printed methodology used here is Fused Deposition Modeling (FDM) and traditional methodology used here is Freeze casting.Inorganic materials and natural or synthetic materials are now used to develop a bone scaffold. The mechanical properties of the designed 3D scaffold were simulated and analyzed by using Ansys software where freeze casted scaffold was characterized by FTIR, Light microscope.

Keywords: Bio-scaffold, 3D, FDM, Freeze casting, Traditional Method, and Tissue engineering.

I. INTRODUCTION

The main objective of tissue engineering is to develop porous three-dimensional scaffolds to restore and enhance tissue function. By integrating cells, scaffolds, and bioreactors, it has shown promise in bone regeneration. A bone scaffold is a 3D matrix that enables and promotes osteoinducible cells to connect to and proliferate on its surfaces. Bone is a naturally occurring mineral composed of hydroxyl carbonate apatite and collagen. Building an "ideal bone scaffold" is difficult since the mechanical properties of bone vary substantially from cancellous to cortical.In addition to cells a dense intercellular substance, and numerous blood vessels, bone is a dynamic, specialized connective tissue. It provides mechanical support for the body and permits movement. Bone issues have grown to be a big concern as our society's median age has increased. Due to trauma, cancer, vascular necrosis, and/or infections, any missing bone must be replaced with an adequate functioning equivalent. The healing process usually begins with an inflammatory phase that lasts a few days after the fracture, during which the blood clot at the fracture site creates a sturdy foundation for new bone production. The clot is eventually replaced by fibrous and collagenous tissue, which forms a soft callus that hardens weeks after the fracture.Bone grafts have traditionally been used to repair injured bone. Bone graft substitutes made of synthetic biomaterials are now being employed. The biomechanical qualities of these biomaterials were originally used to choose them for structural rehabilitation. Currently, tissue engineering uses scaffolds (artificial supporting structures) to restore injured tissues and organs. These are used for the attachment and subsequent development. Scaffolds should be three-dimensional, highly interlinked porous networks with the right porosity, pore size, and pore shape for cell development and metabolic waste movement. An excellent scaffold has enhanced osteogenic differentiation, proliferation, vascularization, host integration, and, if necessary, load bearing capabilities. In order to provide injured or diseased bone with mechanical support during healing and regeneration, bone scaffolds are typically made of porous, biodegradable materials. In order to simulate cell/tissue

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development in vitro or in vivo, scaffolds must be biodegradable and have an adequate degradation rate.

Polymers can be both bioactive and biodegradable. Commonly used natural polymers for bone tissue engineering are collagen, fibrin, alginate, silk, hyaluronic acid, and chitosan. These polymers are utilized as a material for traditional bone scaffolding. During cell proliferation, the scaffold gradually degrades, and the end result is a new tissue with the correct shape and qualities. Freeze-casting, also known as ice-templating or freeze alignment, it is a process that uses highly anisotropic solidification behavior of a solvent (usually water) in well-dispersed slurry to generate a directionally porous ceramic in a controlled manner. The ability of freeze casting to transport fluids through aligned pores has led to its use in biomedical applications such as bone scaffold materials. In freeze cast structures, the alignment of pores also results in extremely high heat resistance in the direction perpendicular to the aligned pores.Fused deposition modeling (FDM) is a popular additive manufacturing technique for 3D modeling, prototyping, and production. Fused Deposition Modeling (FDM) creates three-dimensional things directly from three-dimensional CAD data.It's necessary to developing a matrix with mechanical characteristics (stress, strain and displacement) that are similar to those of the tissue in the defect's close surroundings. To check the mechanical strength of bone scaffold, it is simulated using Ansys software. Scaffolds with the right surface chemistry and qualities encourage cell adhesion, proliferation, and differentiation, and a 3D scaffold that replicates the extracellular matrix works well (ECM). To offer indistinguishable 3D microstructures for the damaged locations, the cells should generate their own extracellular matrix (ECM) while consuming for scaffold biodegradation.Over the past few years, research institutions have concentrated on creating scaffold using bio-fabrication techniques to enable quick, accurate, and affordable automatic manufacture of these structures. Numerous studies examine the ability of biomaterials to regenerate bone cells, but no one has determined which method is most effective for creating 3D bone scaffolds. In order to determine which technology gives the most advantages, we compare and contrast the traditional and 3D methods of bone scaffolding in this study.

II. MATERIALS & METHODS

Hydroxyapatite, Polypropylene, Sodium chloride (NaCl), PEEK (polyetheretherketone) and Double distilled water.

A. Preparation of bone scaffold using traditional method

The traditional method for bone scaffolding was done using freeze casting technology. Freeze casting is a fabrication process which includes four steps such as material preparation, mold filling, freezing and freeze drying. In this method a suspension of solid and liquid particles is frozen to produce distinctive micro structural characteristics. As the solvent or liquid phase, of the material freezes, the solidifying growth front separates the particles of the solid phase particles, segregating and templating the particles into a specific pattern. The frozen solvent is sublimated away after the suspension has fully solidified. Without going through the liquid phase, a substance can be directly converted from its solid to vapor phase by sublimation. A porous structure remains where the ice was produced after the solvent has been completely eliminated.

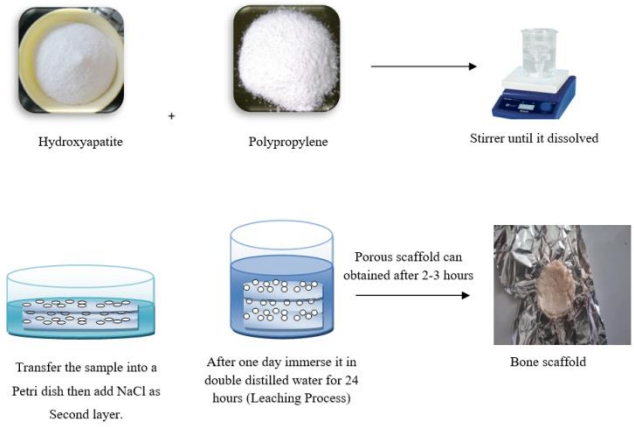

Fig1. Schematic Diagram of Traditional 3D Bone Scaffold

B. Characterization

Porosity of scaffold by traditional method were seen by optical microscope. The optical microscope, also known as the light microscope, magnifies an image using a combination of light and lenses. The greatest magnification power of an optical microscope is 1,000.

C. 3D technology for bone scaffolding

3D printed bone scaffold was done using Fused Deposition Modeling Technique. It is a cost effective additive manufacturing method.The design part was started with the computer aided design for 3D porous scaffold architecture using rhinoceros' software and simulation using ANSYS software. Once the 3D printing part is finished the 3d scaffolds were cool down at room temperature and removed from the bed. The FDM printing process begins with the import of a model's STL file into a pre-processing programme.

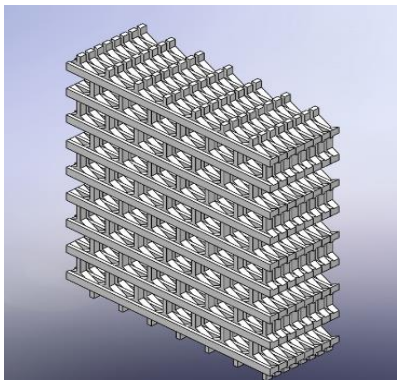

Fig2.3D Bone Bio-Scaffold Design

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This model is aligned and mathematically split into horizontal layers with thicknesses ranging from 0.127 mm to 0.254 mm. Depending on the shape and position of the pieces, a support structure is built where it is required.The data is downloaded to the FDM machine after it has been reviewed and tool paths have been generated.The model is drawn in the X, Y, and Z axes one layer at a time by the system. This procedure is similar to how melted glue beads are extruded from a hot glue gun. After completed the bone scaffold was printed using Polyetheretherketone, or PEEK, it is a high-performance semi-crystalline engineering thermoplastic that exhibits very tough chemical resistance, very little moisture absorption, strong fire performance, great mechanical strength across a wide temperature range, and good dimensional stability.

D. Mechanical stimulation

The programme ANSYS was utilized for stimulation. ANSYS is a finite-element modeling programme that may be used to numerically solve a variety of mechanical issues. These difficulties include those related to fluid, heat transport, static/dynamic, structural analysis, static/dynamic, acoustic, and electromagnetic obstacles.

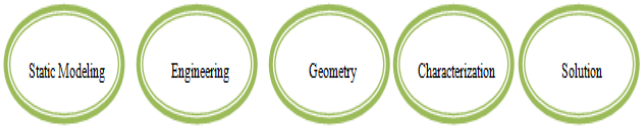

Fig3.Simulation Process Flow chart

Using the Ansys program's static structural option, the planned model's mechanical properties were initially examined. The engineering data needed to be updated as a second stage. The model was then added to the geometry column. The force distribution throughout the surface of the suggested model needed to be uniform during the mesh technique, which was the third step. The fourth stage involved setting up each characteristic, including total deformation, equivalent elastic strain, maximum shear elastic strain, equivalent stress, and maximum shear stress.When the procedure is complete, a button that displays the solution to the developed model will appear. The results of the simulation were examined and summarized below.

III. RESULT AND DISCUSSION

A. Surface morphological image of bio scaffold

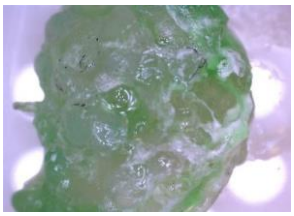

Fig4. 3D Different Phase angle of Bioscaffold.

The three-dimensional porous scaffold is critical since it influences the mechanical properties, cellular fate, nutrient supply, vascularization and tissue in growth. The pore size is usually in the range of 100 – 1500 µm. although the perfect size has been estimated around 350 µm [Murphy et al., 2010], it's believed that larger pore sizes support deeper cell proliferation and tissue penetration [Muschler et al., 2004]. Concerning the pore structure, the geometry are often dictated by the fabrication process (for instance within the case of biological based scaffold), or Figure shows a synthesized scaffold. Most of the bio-scaffolds are homogeneous permeable media with isotropic properties. Considering the most recent advancement in the fabrication techniques (e.g. 3D-printing, stereo lithography), it's visiting be possible to produce controlled pore size scaffolds with hierarchical microstructures and oriented channels to guide the patterns of cell migration, fluid flow and dispersion through the constructed scaffold [Hutmacher, 2000; Khademhosseini et al., 2006; Sprio et al., 2011]. Finally, the nano-structural architecture of the scaffold should be considered since the substrate rigidity and rugosity is known to influence cell adhesion, differentiation and migration [Engler et al., 2006; Yoon et al., 2012].

B. Scaffold design

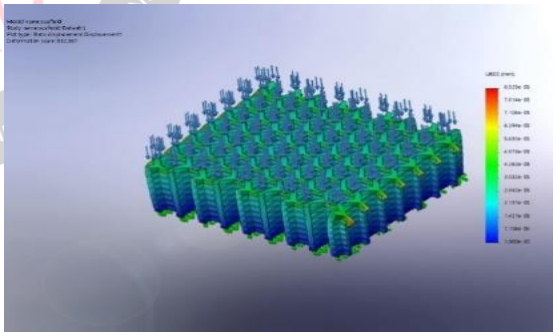

Fig5. Shows the results of fabricated designs with different pore size and radius for PEEK scaffold.

Further, scaffold made up of PEEK with radius of pipe 0.2 mm and size of pore 2mm were analysed by using ANSYS software to study and compare its mechanical properties.

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C. Stimulation design

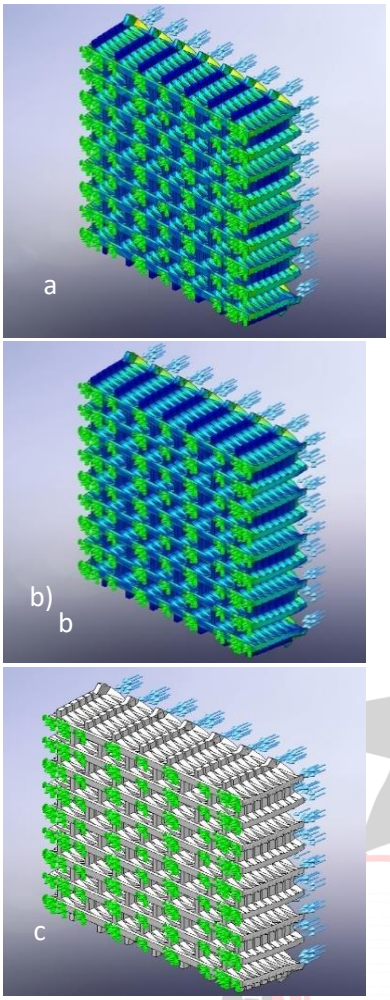

Fig6.a) Stress, b) Strain, c) Displacement

D. Stimulation calculation

The values are ranging from minimum 0N to maximum 27N

1kg = 9.8N, 3.0kg = 29.4N (Rat), We took value which is equivalent to 27N.

When a compression force of 27N is applied, the scaffolds' overall deformation is shown in Figs. 6.Roohani-Esfahani, et, al suggests that the comparative with the other pore-shapes, scaffold with hexagonal or pentagonal pore patterns showed the most noteworthy compressive strength at any obtained porosity. This expands from 90 MPa at ~70% porosity to 180 MPa at ~50% porosity. This is credited to higher contact region between printed struts prompting to enhanced load transfer as well as the highly anisotropic design of hexagonal or pentagonal designed frameworks. Others have associated high qualities to anisotropic architecture of scaffolds. For instance, Deville et al. prepared a hydroxyapatite scaffold with a lamellar architecture utilizing freeze casting procedure with a compressive strength of 65 MPa at 56% porosity. They showed that lamellar design and pore shape anisotropy can lead in unusual high compressive strength for scaffolds.The predicted pore diameter across were inside the permeable porous range of 100-550 mm. Virtual representations of a CAD-demonstrated bone scaffold model and future bone growth in the scaffold environment were compared.

IV. CONCLUSION

In the traditional method, shape and porosity of the bio-scaffold is a major concern; normally we use a different type of structure like beakers, Petri dish or conical flask for synthesis a traditional processing scaffold and that can be the only shape obtained of the scaffold.A significant advantage of 3D printed scaffolds is their capacity to construct the structure for porous material with total control over the geometrical parameters. We compared to 2 different material for 3D fabricated scaffold PETG, PEEK (Polyetheretherketone) is easier to print and its biocompatible nature, resistant to thermal and ionizing radiation, and resembles cortical bone biomechanically. With a GPa of 3.6 and a tensile strength of 90 to 100 MPa, PEEK is a robust material. According to our research, the overall deformation of the PEEK scaffold is smaller than that of the PETG scaffold, making PEEK the material of choice for more analytical tests. When it comes to creating porous scaffolds with increased strength for tissue engineering, 3D printing technology has a lot of promise. The porosity was uneven when we synthesised a 3D scaffold using the traditional method; this was characterized using an optical picture. The shape and porosity is also a significant drawback because we could only obtain the beaker's shape and uneven porosity using the traditional method.The 3D method is more efficient in terms of evaluation process of the scaffold. The traditional method will take longer to produce our findings than the 3D strategy. Therefore, the created 3D-printed bone scaffold may be enhanced and used as a suitable scaffold for bone tissue engineering and as a synthetic graft material in the restoration of bony defects.

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