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Development of Scaffolds using 3D Printing for Tissue Engineering

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ABSTRACT

The rapid growth of populations made it necessary to develop a new range of bio functional frameworks that could be tailored to restore the functionality of deteriorating tissues and improve patients' quality of life by using tissue-engineered scaffolds that could promote cellular adhesion, multiplication, and divergence. Given their inertness within the body and their inherent hardness and abrasion resistance, ceramic materials have been extremely significant in this context. They are also commonly utilised as biomaterials in bone replacement surgery. Its inherent brittleness still prevents it from being widely used in the biomedical industry. The development and integration of various 3D printing processes produced bioceramics or manufactured ceramics, which significantly increased their use. Because of their superior mechanical strength, exceptional resistance to wear, and low electrical conductivity, 3D ceramic scaffolds are the ideal choice even for the drug delivery industry. The bio glass alumina composite scaffold made of hydroxyapatite (HAp) has a porosity of 20–25% and high compressive and tensile strengths. The primary topics of this review are 3D ceramic scaffolds, including their manufacturing processes, the ceramic materials they are made of, their benefits, their uses, and their potential future developments.

1. INTRODUCTION

The bone defects are one of the orthopaedic most difficult problems and still there are many researches related with their treatment. Development of an improved method for ontogenesis of bone grafts and to reduce the auto logger bone is of paramount nature [1]. With the big breakthrough of the technology of additive manufacturing in bone tissue engineering, the research and development of bone regeneration has been greatly promoted. The most important 3D printing methods include three dimensional printing (3DP), stereo lithography, fused filament fabrication, and selective laser sintering. Those three essential properties, which are bioactivity, biodegradability and biocompatibility, are the major concerns in the search for an ideal tissue repair material. Biomaterials have potential economic and social values for use of an efficient and safe material for the repair of a bone defect by pottery. Thus, bone regeneration treatment by tissue engineering technology has an excellent potential. The aim of this writing is to present the main printing technologies used for the creation of 3D scaffolds and the popular biomaterials, also to discuss the fabrication and clinical application of scaffolds [2].

3D printing, also referred to as additive manufacturing, is a technique for fabricating three-dimensional objects by incrementally building them layer by layer. In contrast to conventional manufacturing processes that entail material removal through cutting or molding, 3D printing involves adding material to form the desired object. This method enables the direct fabrication of intricate shapes and geometries without the necessity for specialized tools or molds [3].

2. ROLE OF 3D PRINTING IN ADDITIVE MANUFACTURING

The process of 3D printing typically involves the following steps:

- Design
  The first step is to create a digital 3D model of the desired object. This can be done using 3D modeling software or by scanning an existing object using a 3D scanner. The model defines the shape, size, and details of the final object [4].
- Slicing
  The digital model is sliced into thin cross-sectional layers using specialized software. Each layer represents a thin 2D slice of the object.
- Printing
  The sliced model is sent to the 3D printer, which starts building the object layer by layer. Various materials can be used for 3D printing, including plastics, metals, ceramics, and even biological materials. The printer follows the instructions provided by the slicing software and deposits or fuses the material layer by layer, gradually building up the final object.
- Post-processing
  Once the printing is complete, some objects may require post-processing to improve their surface finish or mechanical properties. This can involve removing support structures used during printing, sanding, polishing, or applying additional coatings.

3. 3D PRINTING'S AND ITS APPLICATIONS ACROSS DIFFERENT FIELDS

Charles Hull invented three-dimensional printing technology in 1986. The foundation of 3D printing technology is the ability to create and print 3D images of objects with the use of computer software known as computer-aided design (CAD). Additive manufacturing is the new term for 3D printing because of the layer-by-layer addition. The fundamental idea of 3D printing is that the material solidifies under the influence of this software to create a three-dimensional item layer by layer [5]. This cutting-edge technology ensures less waste generation and produces intricate structures, customised goods, creative freedom, and automation. Under the International Organization for Standardization (ISO)/American Society for Testing and Materials (ASTM) 52900:2015, 3D printing categorised primarily into seven categories: (1) binder jetting; (2) directed energy deposition; (3) material extrusion; (4) material jetting; (5) powder bed fusion; (6) sheet lamination; and (7) vat photo polymerization [52]. The different 3D printing technique is shown in Fig. 1.

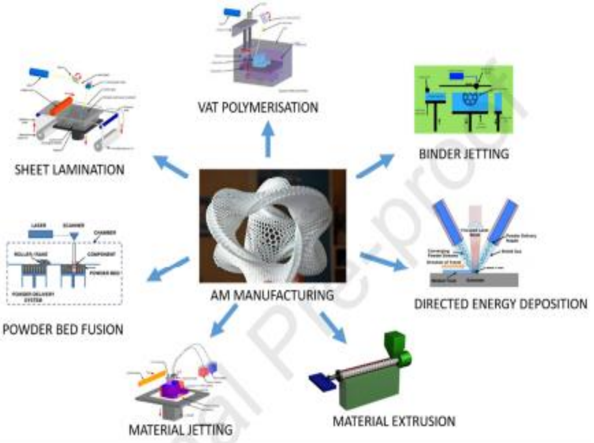

Fig. 1. 3D Printing technology based on ASTM standard ISO/ASTM 529000:2015 [6].

Overall, 3D printing is a transformative technology that offers immense versatility and potential for innovation, enabling the creation of complex and customized objects with ease [7]. It is being adopted across various industries, driving advancements in manufacturing, healthcare, aerospace, automotive, and more [8].

- Complex Geometries
  3D printing allows the creation of intricate and complex geometries that are often challenging or impossible to achieve with traditional manufacturing methods. This is particularly advantageous in fields like aerospace, automotive, and medical devices where complex designs can improve performance and functionality [9].
- Customization
  3D printing enables the production of highly customized and personalized products. This is valuable in healthcare for creating patient-specific medical implants, prosthetics, orthotics, and dental devices that precisely match individual anatomies.
- Rapid Prototyping
  3D printing facilitates rapid prototyping, allowing designers and engineers to quickly create physical prototypes for testing and validation. This speeds up product development cycles and reduces time-to-market for new innovations.
- Reduced Material Waste
  Traditional subtractive manufacturing methods often involve cutting away excess material, leading to significant waste. 3D printing is an additive process, meaning material is deposited only where needed, minimizing waste and reducing environmental impact.
- Cost-Effective Low-Volume Production
  3D printing can be cost-effective for producing low volumes of parts. This is particularly useful in industries where demand is limited or where customization is required, as it eliminates the need for costly moulds or tooling.
- Supply Chain Optimization
  3D printing can be used for on-demand manufacturing, reducing the need for extensive warehousing and inventory. This can help companies optimize their supply chains and respond quickly to changing demands.
- Tooling and Jig Production
  3D printing can be used to produce specialized tools, jigs, and fixtures for manufacturing processes. These tools can be designed and printed quickly, enhancing efficiency on the factory floor.
- Medical Applications
  In medicine, 3D printing has revolutionized surgical planning, allowing surgeons to visualize and practice complex procedures on patient-specific 3D models. It's also used to create implants, prosthetics, and medical instruments.
- Education and Research
  3D printing is a valuable tool for education and research, enabling students and researchers to create tangible models for experiments, demonstrations, and visualizations.
- Design Iteration
  With 3D printing, designers can easily iterate through different design variations and make modifications quickly based on physical prototypes, leading to better final product designs.
- Remote Manufacturing
  3D printing can be used to produce parts in remote or hard-to-reach locations, reducing the need for shipping and logistics.
- Reduced Lead Times
  By eliminating the need for tooling and reducing the steps in the production process, 3D printing can significantly reduce lead times for manufacturing.

Overall, 3D printing offers unprecedented design freedom, customization, and speed, making it a transformative technology across industries ranging from manufacturing and healthcare to aerospace and art.

4. ROLE OF SCAFFOLDS FOR TISSUE ENGINEERING

Scaffolds in the context of tissue engineering and regenerative medicine are three-dimensional structures that serve as templates to support the growth, organization, and differentiation of cells into functional tissues [10].

They mimic the extracellular matrix (ECM) of native tissues and provide a framework for cells to adhere, proliferate, and form new tissue [11]. Scaffolds are essential in tissue engineering because they guide the regeneration process, allowing the development of functional and viable tissues to replace damaged or lost ones [12].

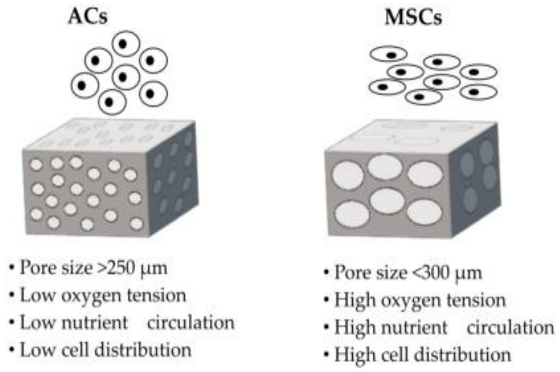

Fig. 2. General schematic demonstration of the scaffold properties for the appropriate growth of articular chondrocytes (ACs) and mesenchymal stem cells (MSCs) [13].

4.1 Fabrication of Scaffolds

Scaffolds can be manufactured using various techniques, and the choice of method depends on the material, desired structure, and intended application. Some common manufacturing methods include [14].

3D Printing allows precise layer-by-layer deposition of material to create complex and customized scaffold structures. Materials are often in the form of powders, filaments, or liquid resins [15].

- Electro spinning
  Electro spinning involves using an electric field to create ultrafine fibers from a polymer solution or melt. The fibers can be collected to form a scaffold with a high surface area-to-volume ratio.
- Salt-Leaching
  A soluble salt (such as sodium chloride) is mixed with a polymer solution, and after solidification, the salt is leached out, leaving behind a porous scaffold structure.
- Solvent Casting and Particulate Leaching
  A polymer solution is mixed with porogen particles. After casting, the porogen is removed, leaving behind pores in the scaffold.
- Gas Foaming
  Gas bubbles are introduced into a polymer solution, and the solvent is removed. The resulting foam structure contains interconnected pores.
- Freeze-Drying
  A solution or suspension containing the polymer is frozen, and the solvent is sublimed under vacuum, resulting in a porous scaffold.
- Phase Separation
  A polymer solution is induced to undergo phase separation, forming two distinct phases—one becomes the scaffold material, and the other is extracted to create pores.

4.2 Applications of Scaffolds

Scaffolds find applications in various fields, primarily in tissue engineering and regenerative medicine. Some key applications include [16]:
Scaffolds can be designed to promote bone regeneration by providing a scaffold for osteoblasts to attach and mineralize, aiding in the repair of bone defects and fractures [17]. Cartilage Tissue Engineering: Scaffolds support the growth of chondrocytes, facilitating the regeneration of cartilage tissue in damaged joints. Skin Regeneration: Scaffolds can be used to regenerate skin in cases of burns, wounds, and chronic ulcers, providing a platform for skin cells to grow and heal. Organ Transplantation: Scaffolds can serve as a support structure for growing functional organs, addressing the shortage of donor organs for transplantation. Neural Tissue Engineering: Scaffolds facilitate nerve cell growth, aiding in nerve regeneration after injury or disease. Cardiac Tissue Engineering: Scaffolds can be used to engineer heart tissue, potentially assisting in repairing damaged cardiac tissue after a heart attack. Vascular Tissue Engineering: Scaffolds can support the development of blood vessels, addressing challenges in vascular grafts and cardiovascular diseases. Dental Tissue Engineering: Scaffolds aid in regenerating dental tissues such as enamel, dentin, and periodontal ligament [18].

Scaffolds play a crucial role in these applications by providing a structure that guides cell behaviour and tissue development, ultimately contributing to the restoration of function and health in damaged or diseased tissues [19].

Biomaterials and Tissue engineering is a field that aims to create functional biological tissues by combining cells, biomaterials, and growth factors. Biomedical materials play a crucial role in tissue engineering as they provide the structural framework, support cell attachment and growth, and facilitate the development of new tissue. Here are some commonly used biomedical materials in tissue engineering [20].

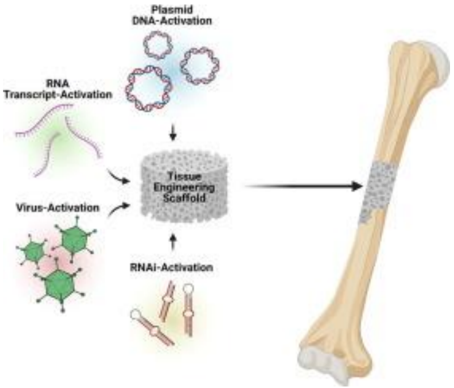

Fig. 3. Use of Scaffolds for tissue engineering [20].

- Biodegradable Polymers
  These polymers can break down over time, gradually releasing cells and growth factors as the tissue regenerates. Examples include poly(lactic-co-glycolic acid) (PLGA), poly(caprolactone) (PCL), and poly(lactic acid) (PLA).
- Hydrogels
  Hydrogels are water-swollen networks that can mimic the natural extracellular matrix. They provide a hydrated environment conducive to cell growth and can be engineered to possess specific mechanical properties. Examples include alginate, agarose, collagen, and hyaluronic acid-based hydrogels.
- Natural Extracellular Matrix (ECM) Components
  These materials closely resemble the native tissue's ECM and provide cues for cell attachment, migration, and differentiation. Examples include collagen, fibronectin, and laminin.
- Synthetic Polymers
  Synthetic polymers can be tailored for specific properties such as mechanical strength, degradation rate, and surface chemistry. Examples include polyethylene glycol (PEG) and polyurethane.
- Ceramics and Ceramic Composites
  These materials are often used for bone tissue engineering due to their excellent biocompatibility and osteoconductive properties. Examples include hydroxyapatite (HA) and tricalcium phosphate (TCP).

The choice of biomedical material depends on the specific tissue being engineered, the required mechanical properties, degradation rate, and biocompatibility, among other factors. Researchers often tailor these materials to create scaffolds that closely mimic the native tissue's environment, fostering successful tissue regeneration.

3D printing, is integral part of additive manufacturing, has revolutionized the fabrication of scaffolds for tissue engineering due to its ability to create complex and customized structures. Here are some commonly used biomedical materials for the manufacture of scaffolds using 3D printing techniques [21]:

- Polycaprolactone (PCL)
  PCL is a biodegradable polyester that is frequently used for 3D printing.
- Poly(lactic-co-glycolic acid) (PLGA)
  Printing scaffolds due to its ease of printing, biocompatibility, and tunable degradation rate. PLGA is another biodegradable polymer that combines the properties of both lactic acid and glycolic acid. It's widely used for its controlled degradation and biocompatibility.
- Polyethylene glycol (PEG)
  PEG hydrogels are often used for 3D printing due to their ability to encapsulate cells and provide a hydrated environment. They can be modified to have tunable mechanical and degradation properties [22].
- Hydroxyapatite (HA) and Tricalcium Phosphate (TCP)
  These ceramic materials are commonly used in bone tissue engineering and can be incorporated into polymer matrices to enhance mechanical strength and bioactivity.
- Gelatin
  Gelatin-based materials are derived from collagen and offer good biocompatibility. They can be crosslinked to improve mechanical stability.
- Chitosan
  Chitosan is a natural polysaccharide derived from chitin and is used for its biocompatibility and potential to support cell adhesion and growth.
- Silk
  Silk proteins can be processed into hydrogels or other printable forms. They are known for their mechanical strength and potential to support cell attachment.
- Cellulose-based Materials
  Cellulose derivatives can be used for 3D printing, offering a biocompatible and biodegradable option.

- Alginate
  Alginate hydrogels are commonly used for cell encapsulation due to their ability to form a gel in the presence of divalent cations.
- Decellularized Extracellular Matrix (DECM)
  DECM can be processed into printable forms to provide a natural microenvironment for cell growth.
- Composite Materials
  Blends of different materials, such as polymers and ceramics, can offer a combination of properties suitable for specific tissue engineering applications.
- Bioceramics
  Various ceramic materials, such as hydroxyapatite and calcium phosphate, can be incorporated into 3D-printable formulations [23].

5. CONCLUSION

One appealing kind of substrate for fully using ceramic materials is mirrored in the biomedical field. In addition to its widespread application in tissue engineering, ceramic materials have been introduced in drug delivery applications, highlighting the essential and inevitable role that these substances play in our daily lives. One of the most unique and inventive inventions made by hominids, additively built bioceramic scaffolds expands the field of use and is now being studied. They can be applied to drug delivery applications that are inspired by nature (biomimetics) or even illnesses related to the bones. Ceramic scaffolds have a long history that began with clays (which are hardly employed in biomedical applications), and it continued with polymers, composites, biopolymers, ceramics, and, more recently, the usage of bioactive glass (BAg). The development of ceramic scaffolds has produced artificial material that may demonstrate its usage in a wide range of contexts. For example, ceramic scaffolds are utilised in tissue engineering and targeted drug delivery, and they can display biomimetics with comparable materials. The porosity, inertness, and biocompatibility of scaffolds are improved by the addition of ceramic material. The application of bioceramics in the manufacture of biomedical scaffolds has enabled scientists to create specialised, inert, superior mechanical, and porous products. Only a small portion of bioceramic scaffolds for biomedical applications are currently in use due to the laborious process of fabricating them and testing them; additionally, the lengthy safety and efficacy testing required for medical device approval delays market approval.

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