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Surgery

3D PRINTER SUPPORTED IMPLANT PRODUCTION AND COATING METHODS

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ABSTRACT As today's technology advances rapidly, the advantages provided by 3D printing technology have also increased its usage in the medical field. This approach, which includes advantages in personalized patient care, has also made a breakthrough with the use of biocompatible materials. Although the history of implanted devices dates back quite some time, covering them with biocompatible materials has yielded new advantages.

KEYWORDS : 3D print, biocompatible materials, coating methods, personalized implant

INTRODUCTION

Advancing technology emerges as a dynamic phenomenon in all areas capable of enhancing quality of life and expanding people's comfort zones in the rapidly evolving world that we live in. This dynamism drives individuals towards continuous development, change, and innovation. The innovative and entrepreneurial nature of humans is an undeniable reality. Thanks to the entrepreneurial spirit, three-dimensional printing and bioprinting technologies have begun to occupy a significant place in our lives [1,2].

The process of three-dimensional printing involves obtaining three-dimensional solid objects from a three-dimensional file prepared in computer graphics design programs. In other words, it is the process of rapid prototyping that can transform three-dimensional objects into tangible entities. The machines that produce objects are called three-dimensional printers. A three-dimensional printer is a machine that converts computer data into a tangible, real, and touchable object [2].

To carry out the three-dimensional printing action, the implant to be produced must first be modeled and drawn in three-dimensional design programs. These modeling processes can be realized with computer-aided professional three-dimensional design software such as Blender, 3DS MAX, AutoCAD, or web-based design software such as Tinkercad, SketchUp [7,8]. After the model is designed and drawn, it is exported and saved to create a file on the computer. The file created by the model is usually saved as an OBJ or STL extension file and sent to the three-dimensional printer editing and slicing program. The model is sliced through this program, divided into layers, and a "gcode" file, which is the language understood by the three-dimensional printer, is created. Gcode is a software language that conveys a lot of information to the three-dimensional printer about which route to follow in the coordinate plane and at what speed, in other words, it converts our 3D model into a language that the machine will understand for three-dimensional printing. The generated gcode file is transferred to the three-dimensional printer via USB memory, memory card, or wireless network, and the printing process is carried out. In the three-dimensional printing process, the object is produced by stacking layers on top of each other [3,4].

Types of Three-Dimensional Printers

Currently, three different 3D printing technologies are widely used. These are FDM (fused deposition modeling), SLA (stereolithography), and SLS (selective laser sintering) technologies. FDM technology is the most widely used method in prototyping and final product production due to the convenience it provides in use and lower cost. FDM printers are a form of printing where the material (filament) is pushed forward with extrusion and sprayed from a thin nozzle, and the layers are stacked from bottom to top. The nozzle moves in the x, y, and z axes with the help of slides and shafts to create a solid object starting from the table. Nozzles can be of various shapes and sizes, but they all serve the same purpose. The most commonly used nozzle is 0.4 mm in size. There are different nozzle types that can grow up to 1.2 mm. The smallest nozzle diameters are 0.15 mm, which are difficult to calibrate and use but provide good results for very complex prints [3,4].

Historically, the first 3D printer was developed by Charles Hull using stereolithography (SLA) technology in 1984. Since 1984, the 3D printer technology has been rapidly advancing. It covers a wide range of areas ranging from automotive to the healthcare sector, from hobby products to medical materials.

Operation Method

The printing process in three-dimensional printers occurs when the 'extruder' part of the printer, which we can describe as the head section, reaches the required temperature. For the printing process to occur, the filament needs to reach sufficient temperature in the extruder and melt. When the filament flowing fluidly from the nozzle reaches the printer's table, it solidifies and takes on a solid form. This process continues layer by layer horizontally and vertically, and the 3D printing process is completed [3,5].

When a comprehensive research is conducted on three-dimensional printers, it is observed that they have a wide range of applications covering various fields. They are used in many different areas ranging from engineering to the healthcare sector, from hobby and entertainment to the education sector [6,7].

One of the most common uses of three-dimensional printing technology is in the medical and healthcare sector. In recent years, with the help of three-dimensional printers, even surgeries considered risky can be performed thanks to 3D models designed specifically for patients [6,7]. Files consisting of patient tomographies are scanned with various programs to convert them into three-dimensional files and obtain anatomical models. These models provide many benefits both for educational and practical purposes. With the help of these printers, personalized medical and surgical products such as prostheses for body parts like the face, arm, and leg can be made. In addition, dental implant applications in oral and dental health, dental alignment objects used in defective dental anatomy are among the commonly used applications. Moreover, three-dimensional printers are widely used in the production of materials such as soft tissue and cell printing, biomedical materials [8,9].

Materials Used İn The Production Stage

Filament is the raw material used by three-dimensional printers during printing. It is thermoplastic and there are many types of filament that require different temperatures and properties. The quality and diameter of the filament, even the humidity in the environment where it is located, are factors that directly affect the printing quality. Filaments have two preferred diameters, 1.75 and 2.85. The most preferred filament types for three-dimensional printing processes are PLA, ABS, Flex, TPU, and PETG types. Among these, PLA and ABS types are the most widely used.

PLA (Polylactic Acid) Filament

Polylactic Acid, abbreviated as PLA, is known as a filament type that originates from organic sources. PLA filament type is the most preferred material especially in home-type three-dimensional printers. PLA is more environmentally friendly than many other filament types, has a hard and durable structure. The printing temperature is in the range of 190-220 degrees Celsius. The printer bed temperature should be in the range of 60-70 degrees Celsius. Since PLA filament is not

harmful to health, it can be used in the printing of products that come into contact with the human body. It is also preferred for hobby products due to its attractive shiny surface [3,10].

ABS (Acrylonitrile Butadiene Styrene) Filament

ABS filament is another of the two most preferred filament types. Printing ABS is slightly more difficult than printing PLA. The reason for this is due to the properties of ABS filament type. However, ABS is a superior filament type compared to PLA in many aspects. It prints at high temperatures and has high durability. It has low elasticity and the printing temperature is between 230-260 degrees Celsius [3,10].

Biocompatible Materials Used in the Production Stage

Kitosan

Chitosan is a copolymer obtained from the alkaline deacetylation of chitin and used in the health field. Chitosan has excellent natural properties such as biocompatibility and biodegradability, being a non-toxic biopolymer. It has potential applications in biomedicine such as antimicrobial activity, hemocompatibility, and biodegradability. Chitosan and its derivatives are used as hemostatics in neurosurgery due to their mechanical and ionic coagulation effects in endoscopic surgery and brain hemorrhages. Positively charged chitosan induces hemostasis through the aggregation of negatively charged erythrocytes, followed by the activation of platelets. Hydrophobically modified chitosan (hm-C) forms a three-dimensional gel when in contact with blood, thus polymer chains form a self-supporting network. The hydrophobic interior of the blood cell membranes is anchored to modified chitosan hydrophobes, turning into a viscous gel to stop bleeding from small and severe injuries [11]. Another interesting approach is the development of a hemostatic wound dressing by adding asiclodextrin to chitosan-based materials [8].

Hydrophobically modified chitosan demonstrates good hemostatic activity. Chitosan, along with alkylation, possesses an easy clotting ability. It can rapidly convert all liquid blood into a gel form, thus stopping bleeding from both minor and severe injuries [9]. Chitosan has been modified into amphiphilic derivatives such as sulfo (hydrophilic) and lauroyl (hydrophobic) groups (lauroyl-sulfated chitosan), palmitic anhydride, succinyl groups, carboxymethyl groups, and quaternary ammonium groups. Modified chitosan has shown enhanced effectiveness for applications involving contact with blood, such as erythrocyte adhesion and platelet aggregation.

Cellulose

Cellulose is a natural, renewable, and biodegradable polymer with a linear structure of glucose units commonly encountered. Non-toxic cellulose-based products, especially surgical hemostats, wound dressings, tissue engineering, and potential biomedical applications such as drug delivery, are available in different forms such as sponges, hydrogels, films, and powders [12].

The hemostatic studies of cellulose have shown that it weakly inhibits the adsorption of fibrinogen and even slightly slows down the interaction between fibrin and fibrinogen. In contrast, oxidized cellulose (OC) has shown subsequent activation and adhesion of platelets and fibrin formation. Oxidation of cellulose improves its biological solubility, biodegradability, and biocompatibility with animal cells and tissues. OC activates hemostasis through contact activation pathways where the interaction of negatively charged surfaces and thrombin formation plays a significant role [13].

Cellulose's chemical modification provides better control over the material's biocompatibility, biodegradability, and clotting properties. Chemically modified cellulose has shown enhanced hemostatic activity by activating clotting factors through electrostatic interaction and concentrating plasma and platelets.

The combination of physical adsorption and physiological hemostasis governs the hemostatic activity of oxidized regenerated cellulose (ORC). ORC can absorb most of the liquid in the blood to form a viscous material to increase the concentration of blood in minor and severe injuries.

The chemical modification of cellulose provides better control over the material's biocompatibility, biodegradability, and clotting properties. Chemically modified cellulose, especially carboxymethyl and carboxyethyl modified cellulose, has shown enhanced hemostatic activity by activating clotting factors through electrostatic interaction and concentrating plasma and platelets.

Composite with other biopolymers has gained increasing interest in designing new hemostats with superior final adapted properties than each individual component. ORC-based materials do not remove all blood from the surgical field and are ineffective in preventing tissue adhesion in the presence of blood or body fluids. Therefore, they have limited application in adhesion-based hemostats. In general, the micro/nano porous structure of hemostats contributes to the rapid adsorption of blood. In addition, the small pore size of the material increases the adsorption of blood cells to provide synergistic clotting [14].

Alginates

Alginate is a natural polysaccharide obtained from the cell wall of seaweed. Alginate forms a viscous gel denser than water and has an excellent water absorption capacity. This property of alginate provides moisture management in the wound bed, prolongs the dressing effect, and facilitates the autolysis of necrotic tissue in the wound. It exhibits good thickening behavior and stabilizing properties by forming a mild gel with divalent cations such as Calcium. Alginates and their derivatives have structural similarities to extracellular matrices of living tissues. They can be applied for the delivery of drugs, proteins necessary for wound healing and hemostasis, and even bioactive agents like live cells. One of the important criteria for alginate composition is pore size and degree of swelling; it depends on molecular weight (MW) and the ratio between mannuronic (M) and guluronic acid (G) residues (M/G ratio); it cross-links with cations. Generally, G blocks have a higher affinity for cations than M blocks. Alginates with a higher M/G ratio produce more permeable alginate gel matrices, while a lower M/G ratio leads to stronger structures. Pore size and degree of swelling are important hemostatic properties of a biomaterial for hemostat design.

The porosity of alginate-based material depends on its nature and the degree of cross-linking changes with cations. A higher content of G partly reduces the available space (porosity) for molecule spreading and thus leads to greater resistance to spreading in alginate. Additionally, high M content results in stiffer gels that can affect the inflammatory response to the implanted material. A high G content alginate with low molecular weight interacts more with cations to form stable clear gels, resulting in materials with smaller surface area, volume, and pore size. Calcium alginate is a calcium salt of alginic acid prepared by alkaline extraction of seaweed cell walls.

Calcium alginate dressings have been shown to increase hemostatic activity. Upon contact with body fluids, alginate fibers exchange ions, converting insoluble calcium alginate to soluble sodium alginate and releasing calcium ions.

The presence of calcium at the injury site supports prothrombin activation. It stimulates platelets and clotting factors such as VII, IX, and X in the clotting cascade necessary for increased hemostasis. Additionally, the reticular gel layer on the wound surface enhances the effectiveness of blood clotting. Therefore, calcium alginate-based hemostats are widely used in dental applications to control bleeding in tooth sockets. Calcium alginate has also been applied in Grade I and II spleen injuries associated with intra-abdominal adhesion formation. Calcium alginate has been observed to reduce intraoperative bleeding after spleen injury [15].

Hydrophobically modified (hm) alginate is widely used in wound healing applications due to its natural hemostatic properties. Hm products can form a three-dimensional gel upon contact with blood, necessary for blood clotting [16].

Hyaluronic Acid (HA)

Hyaluronic acid is a component of the extracellular matrix that plays a significant role in tissue regeneration processes. It contains numerous carboxyl and hydroxyl groups responsible for excellent hydrophilic properties. It is a biocompatible, biodegradable, and non-immunogenic biomaterial that can assist in tissue hydration. Identified as a fundamental component in wound healing applications due to its hemostatic activity, inflammation regulation, and promotion of re-epithelialization [17]. HA is found in extracellular tissues throughout the body and represents a major component of connective tissues. During wound healing, HA secretion initiates the healing process through the formation of an initial blood clot, which is vital for fibrinogen accumulation and cessation of bleeding. Hyaluronic acid plays a significant role in the hemostasis mechanism. Its molecular structure initiates physiological processes such as lubricating joints,

regulating vascular permeability, promoting cell proliferation, and accelerating wound healing. HA-based wound healing dressings have been used as dermal replacements. They can remain in the wound for an extended period and perform scaffold-like functions. HA is involved in all stages of wound healing, including inflammation, hemostasis, proliferation, and remodeling, by promoting fibroblast proliferation, stimulating angiogenesis, and regulating collagen synthesis [18].

With advancements in engineering and rapidly growing 3D printing technology, the ability to produce patient-specific and customized medical implants, products, and equipment offers a significant advantage, especially in biomedical applications such as tissue engineering. Current and future research areas in 3D printing of biomedical products include tissue or organ fabrication, customized structural scaffolds and prostheses, implants, and anatomical models. Additionally, the 3D printing technique can be flexible to adapt to the relevant tissue surface and prepare prints suitable for hemostasis in complex tissue organs [19].

In future research, 3D structures combined with new optical biosensors and stimuli-responsive materials can be used to produce materials for surgical applications that can release active agents suitable for wound healing, thus reducing hospitalizations and shortening surgical procedures. A next-generation 3D biocompatible implant will be beneficial for minimizing hospital stays and shortening surgical duration.

Biocompatible Implant Coating Methods

1. Hydroxyapatite Coating on Titanium Implants

a. Sol-Gel Technique

The aim is to coat titanium (Ti) metal substrate with bioactive calcium phosphate (CaP) using the sol-gel technique. Ammonium hydroxide (NH4OH), calcium nitrate tetrahydrate [Ca(NO3)24H2O], and ammonium dihydrogen orthophosphate (NH4H2PO4) were used as the source of Ca and P for the initial sol-gel solution formation and pH adjustment in the solution.

Calcium nitrate was mixed with ethanol at 70°C for 4 hours to form the sol-gel for the calcium source. Ammonium dihydrogen orthophosphate, as the P source, was continuously stirred in double-distilled water at 70°C for 4 hours. The resulting solutions were matured for 24 hours and hydrolyzed. The ammonium phosphate solution was prepared by continuously stirring the solution at 70°C for 3.5 hours at a rate of 5 ml/min. The coated samples were dried at 100°C and sintered in air atmosphere at 750°C-900°C. The characterization of the coatings was performed using X-ray diffraction (XRD) technique with Cu Kα radiation. Additionally, the coatings obtained from cross-sections and surfaces were examined using a scanning electron microscope (SEM) [20].

b. Promimic Liquid Technique

Two different titanium surfaces were evaluated: the processed surface used as the control group, where no surface treatment was applied to the samples after processing, and the surface modified with hydroxyapatite (HA) using the Promimic nano HA method, where the surfaces were conditioned by acid etching followed by accumulation with nano-sized HA particles (nano group) [21]. The method involves creating a liquid crystalline phase in a water solution containing calcium, phosphorus, and a surfactant and placing the phase in an ammonia environment to form nano-sized crystals. The surfactant is then removed by solvent extraction, and the nano-sized crystals are collected to obtain powder. The liquid crystalline phase treated with ammonia is diluted with a hydrophobic organic solvent to create a microemulsion of nano-sized crystals in water. The surface coated with oxide layer is immersed in the microemulsion, or alternatively, the application of ammonia to the liquid crystalline phase can be deferred until after the surface is immersed in the microemulsion. Finally, the coating is removed from the surface by removing the organic solvent and surfactant, allowing the coating to be deposited [22].

c. Dip Coating Technique

In this study, natural HA (CAM implant company, produced in the Netherlands), MgO nanoparticles (98% pure, 30-70 nm), sodium chloride (NaCl), and GN polymer (98% purity) were obtained from Merck company. The initial material, HA, was ground with MgO nanoparticles for 60 minutes using a planetary high-energy ball mill (HEBM) under argon atmosphere to form different weight fractions of MgO nanoparticles (0%, 5%, 10%, and 15%). The ball-to-powder ratio (BPR) was selected as 10:1 in the HEBM process. The drawing of the process for producing bio-nanocomposite scaffold structures using the space holder (SH) technique is added. NaCl particles, constituting 65-70% of the total weight of the material, are used as spacer type particles. The homogeneous mixture (HA, MgO, and NaCl) is compressed together with cooking vegetable oil (2% by weight of sunflower oil) into cubic steel molds with dimensions of 14x15x6 mm and subjected to 120-160 MP pressure. The resulting Ha-MgO scaffold structures are immersed in deionized water for 12 hours to remove the remaining NaCl particles. The samples are then coated with 15% IBO loaded 85% GN polymer using the dip coating technique for 1 hour. GN is dissolved in 100 ml of hot water at 60°C on a hot plate stirrer at 1000 rpm for 2 hours, then 1.5 g of IBO is added to GN. The produced scaffold structures are immersed in GN-IBO solution for 25 minutes using the space holder (SH) technique. The samples are placed on aluminum foil and incubated for 24 hours. Compression strength, fracture toughness, hardness, and stress-strain analysis are performed on cubic samples at a loading rate of 2 mm/min using the SANTAM STM50 machine. The elastic modulus of the bio-nano composite scaffold structure is calculated from the slope of the stress-strain curve obtained. Poisson's ratio and mass density values are determined using the Hounsfield tensile testing machine. Biological behaviors such as biocompatibility, drug release, dissolution rate, antibacterial response, and wettability of the samples are experimentally estimated by immersing them in SBF for 21 days under bench conditions (pH=7.4 and T=37°C). The biological response is visualized based on chemical changes [23].

2. Gold Coating on Titanium Implants

Magnetron Sputtering Technique

Implants and gold coating technique. In this study, 20 custom-made titanium alloy implants with plasma-sprayed porous coatings of Ti-6A1-4V surfaces were used. The rough surface coating was applied gently with Biomet (Warsaw, IN). Each implant was cylindrical with a diameter of 8.0 mm and a length of 10 mm. The company determined the average pore diameter to be 480 μm, the porosity rate to be 44%, and the coating thickness to be 1.6 mm. Two endplates with a diameter of 11.0 mm at both ends of the implant had created a standard 1.5 mm gap around each implant. Half of the porous Ti-6A1-4V surfaces were then coated with a thin pure gold layer of 40-80 nm thickness using a non-reactive physical vapor deposition (PVD) process called magnetron sputtering. Magnetron sputtering is a deposition technique that utilizes a magnetic field placed above the spray configuration. The magnetic field placed above applies an additional force to charged particles. The force is perpendicular to the velocity direction, forcing the charged particles to spiral rather than move straight towards the gold target where the gold is deposited during the coating process. A longer trajectory increases the number of collisions between electrons and ions, allowing the plasma to self-sustain at lower operating pressures. The higher collision energy between the target and the charged gas ions will apply higher energy to the sprayed gold [24].

3. Silver Coating on Titanium Implants

Thermal Spraying Coating Technique

Currently clinically used AMS HA Cup and 910 PerFix Fullcoat D body (KYOCERA Medical, Osaka, Japan) were used as the base material. This implant is a cementless type THA implant. The cup's bone-facing surface and the body's portion for intermedullary insertion were coated with HA. The neck and joint-facing cup surfaces were not coated. Ag-HA was prepared by adding Ag2O powder (Kanto Chemical, Tokyo, Japan) to HA powder (KYOCERA Medical, Osaka, Japan). Ag-HA was thermally sprayed as a coating material to obtain Ag-HA coated implants. TiO2 nanotubes were formed on porous Ti rods using an electrochemical anodization method.

The anodization setup included titanium rods with porous cp-Ti, platinum wires serving as anode and cathode, respectively, suspended with platinum wires, and deionized (DI) water containing 1% hydrofluoric (HF) acid. A DC power supply (Hewlett Packard 0–60 V/0–50 A, 1000 W) was used to apply a continuous voltage of 20 V throughout the process. Silver electrodeposition (accumulation) was performed using a 0.1M silver nitrate (AgNO3) solution with porous Ti rods as cathode and platinum foil as anode following the same arrangement. For silver plating (accumulation), a DC current was applied for 30 seconds at a fixed voltage of 3V and for 3 minutes at two different silver loading amounts. After coating (accumulation), excess silver was washed with DI water, and the coated samples were heated at 500°C [25].

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