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Manufacturing of Biodegradable Scaffolds using 3D Printing: A Review

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Abstract: Additive Manufacturing is an advanced manufacturing process which is not only cost efficient, but is also completely customizable. With the aid of CAD/CAM and 3D printing technology in Biomedical Science, variety of organs can be generated. Bone being structurally strong and porous, scaffolds with approximate porosity can be made using 3D Printing technology. As accidents are on a rise, the demand for organs is also increasing. To tackle the problem, 3D printing of Biomaterials can be taken into account, following which numerous patients can be treated and relieved. While there are synthetic as well as natural polymers for printing, the choice of the material is made according to the location and type of fracture.
Keywords: 3D Printing, Biodegradable Polymers, Grafting, Scaffold.

I. INTRODUCTION

Bones have number of functions in a human body; the main amongst all is to give proper structure and to protect organs in the body. Bone also has the ability to repair itself in the proper structure making it a unique composite of the body [1]. From the childhood, the structure of bones changes and the bones align themselves according to the necessity in the human body [2]. However, the function of the bones can be affected by sudden heavy impact on it, making it weak and/or fracture [3]. Sometimes, if the impact is high enough, it takes months to repair the bone and yet there is no assurance that the structure of the bone will remain the same [18]. In such cases, Doctors/Surgeons do their best to get the patient relieved and recovered at a faster pace. Open fractures [7] due to accidents are considered most complex injuries as there is an involvement of bones, soft tissues and skin getting torn. In such cases, the risk of infection increases as the wound remains open to surrounding environment and a small contaminant can worsen the case. In such cases, it becomes equally important for the doctors to classify the injury, clean it and do the initial splicing of the bone. Later on, the bone is mostly adjusted using screws and bolts which are either removed or gets dissolved in the body.

Bones may also fracture due to minor household accidents of the senior citizens [4], which, not being open fracture, can lead to dangerous ill effects if neglected. In such cases, doctors apply traction for correction and adhesion of the bone. Under all circumstances, the real challenge faced by patients and Doctors is the recovery.

India, being a densely populated state, is equally exposed to road accidents. The fatalities in road accidents have increased to 1145590 in 2007 from 77000 in 1997 with the rate of 101 fatalities per million persons from 81 fatalities per million persons [8][9][10]. The data can be taken as a rough indicator for the risk faced by the people in India. With the increasing accidents, it has become quiet challenging to get organs to every needy patient for replacement in the body. Due to the reason, artificial bones are being designed to replace the broken ones.

Human bone is a porous structural element which is mainly made up of hydrogen phosphate, carbonate, and traces of pyrophosphate, sodium, magnesium, potassium, strontium, fluorine, and chlorine. All the elements make the external structure of the bone and help to provide strength to it. The bone is made up of two different structures namely Cancellous and Cortical. Cancellous is the inner spongy part of bone which is 50-90% porous by volume while Cortical is the outer dense part of bone which is less than 10% porous by volume [5].

In the cases where grafting [5][18] is necessary, the process may at later stages bring in complications related to the binding of the bone. Fresh allografts from another person may get rejected by the patient’s body. Due to this, the bone’s cortisol may not repair completely, leaving the bone weakened at the point of fracture.

Another problem with grafting is the arrangement of grafts and the cost associated with it. Though the graft may be taken from the patient's own body, additional costs for incision, removal, stitching, medicine, etc. will get accounted. If autografting is to be performed, the process may increase complexities like weaker donor muscles, long term potential infection increased morbidity, etc [5]. Most of the times, in case of open fracture, plates and screws are also used to keep the graft/bone in position. Such materials are mostly susceptible to rejection by the body and might cause irreparable damage to the bone structure.

To avoid such consequences, Doctors and engineers are collaboratively working on designs and materials for bone scaffolds which can be used in place of bulky plates and screws and also as a replacement to grafts. While the materials are being selected so as to get dissolved in the body or become a part of the bone keeping the weight minimum, the designs are made in accordance to the fracture anatomy and rigidity. The scaffolds [11][12][20][21][24] are generally made using additive manufacturing technique wherein the cells or the material is manufactured layer by layer [16].

II. ADDITIVE MANUFACTURING PROCESS

Though Additive Manufacturing is a comparatively new technique of manufacturing, but due to its vast applications, it has gained its recognition in every major sector in the world. Additive manufacturing is the process of layer by layer addition of material till the product is made. The process is also termed as Rapid Manufacturing or 3D Printing. As there is negligible loss of material, the process is preferred for intricate parts manufacturing. There are mainly 2 types of additive manufacturing processes namely Direct Printing and Indirect Printing. Direct Printing includes Inkjet, Pressure and Laser printing while Indirect Printing includes Binding, Extrusion and Laser printing. While in direct printing, cells can be prepared and are 'ready to use', indirect printing gives us parts that are to be processed before using. Bioprinting can be done in any of the mentioned additive manufacturing methods, selected according to the needs [13][14][15][20].

A 3D Printer takes .stl file format as an input, which basically is a 3D image of the object which is to be manufactured. The object is designed with the help of a Computer Aided Design Software, which is then saved in STL format. The printer processes the STL file and converts it into GCODEs, which are the instructions required for the process of manufacturing [13].

3D Printing Technologies:

SLA-Uses laser with photocurable polymer as the main raw material

SLS- Sintering of layers with thermoplastics/metal/ceramic powder as the main raw material

SLM- Uses laser with metal/ceramic powder as the main raw material

FDM- Extruder dispenses adhesive tracing the 2D cross section, with thermoplastics as main raw material

Inkjet- Head dispenses bio-material in drops, controlled by piezoelectric devices

Extrusion- Pressure is used to force the bio-material out of the nozzle.

BioLP- Hydrogels or viscous biomaterials are incident with pulse laser.

III. PRODUCT DEVELOPMENT USING 3D PRINTING IN BIO-MEDICAL AREA

Developing a product or generating an organ has been way too easy with the aid of CAD/CAM technology and 3D printing. 3D scanners have opened another dimension in the product development process. Now a days, anyone with knowledge of the required software and 3D printing machine can print an exact replica of any body part of the human body. There are number of steps involved in the product development in the biomedical stream with the use of 3D printer [13][17].

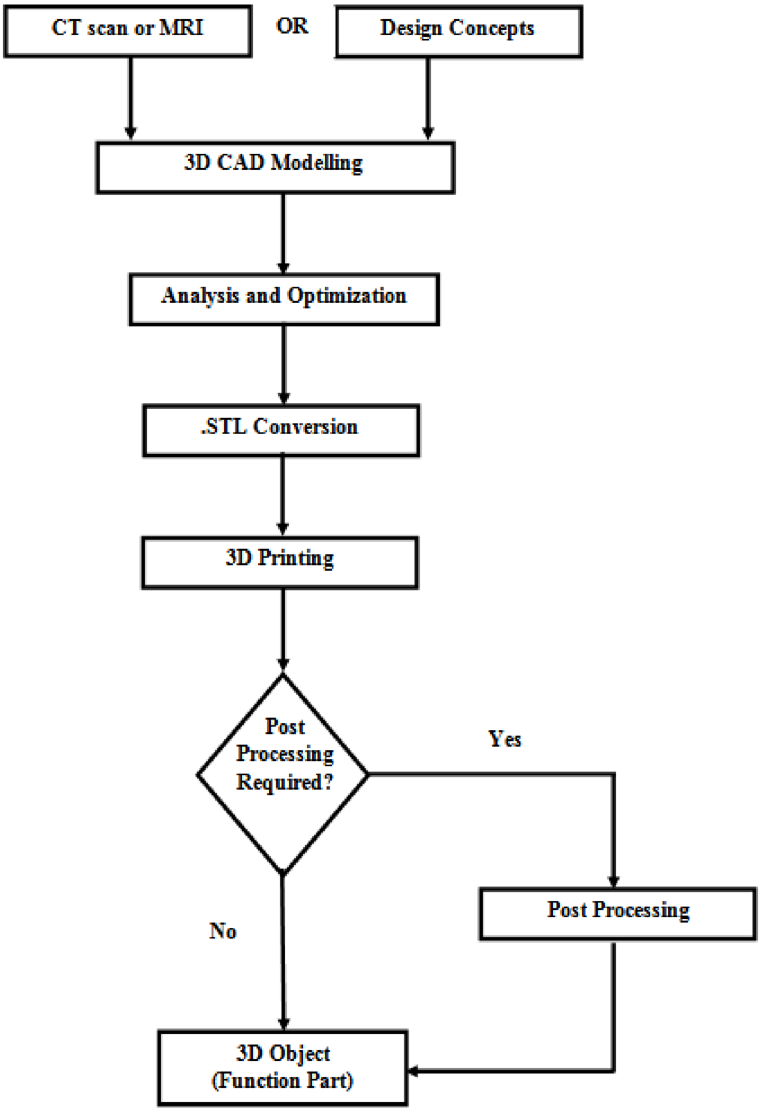

Fig.1 Schematic diagram representing the steps involved in 3D product development

Step 1. Collection of CBCT Scan data:

The first step in the process of development of a 3D Printed part is collection of Cone Beam Computer Tomography scans of the particular part in DICOM file format.

Step 2. Modelling using CAD Software:

The CBCT scans are uploaded in software that can convert the DICOM images into 3D Model. Numbers of software are available for the same and Materialise Mimics® is among the most preferred software. The images are imported into the software and are converted to a 3D Image which can be edited to remove errors, if any.

Step 3. Analysis and Optimization:

The model created in Materialize Mimics is then transferred to Materialise 3-matic to remove any voids or abnormality due to any condition. The purpose of the software is to exactly mirror the original human body part so that the 3D Printed part will be free from defects.

Step 4. Conversion to .STL:

The model, after analysis and optimization is then saved into .STL file format, which is the input requirement for any 3D Printer's software. The STL file is then converted into GCODE which is read by the 3D Printer for its tool/extruder to reach and print.

Step 5. 3D Printing and Post-Processing:

Once the GCODEs are generated, the machine initiates its printing. It is very important to select the appropriate material for the printing as the structure and strength of final product completely depends on the material used. Post Processing is applied to give proper strength and aesthetics to the printed part. Support material, sharp edges, unnecessary protrusions are to be removed from the 3D Printed parts before it is used for any work.

IV. BIOMATERIALS

Numbers of materials are available in the market which are bio-degradable and are accepted as implants in a human body [22]. Materials are also accepted by the human body and thus replacement of bone has become a less tedious process. Polymer materials are widely used for the manufacturing of scaffolds because of their durability, bio degradability and ease of processing. The polymer materials are classified into Natural and Synthetic materials, which is not different for biodegradable polymers. The synthetic polymer that are mostly used are Poly lactic Acid (PLA) [20], Polyglycolic Acid (PGA), Polycaprolactone (PCL) [20], Polypropylene fumarate (PPF), Polyhydoxyalkanotes(PHA), Polyorthoesters, etc. The synthetic polymers can be ring chained or linear polymers. Each polymer has a different characteristic pertaining to its crystallization, melting point, acidity, mechanical properties, etc. The polymers are specifically used for a specific purpose [23][24].

Natural polymers are extracted from natural proteins like collagen, fibrin, albumin, etc. The natural polymers are highly structured and help in accelerated cell growth in the body. The polymers made from collagen are mostly used for soft tissue regeneration. Enzymatic degradation can be observed in Collagen. Albumin is the blood plasma protein and hence is used in drug delivery. Fibrin is used in blood clotting. Chondrotin sulphate is mostly used in cartilage. Chitosan is used as a scaffold material in cartilage and bones [23].

All the above mentioned polymers can be used to manufacture scaffolds and be used in the body because of their high reabsorption characteristics and biodegradability.

V. DRUG DELIVERY AND GROWTH

3D printed scaffolds have been used for bone growth as drug delivery system and growth factors. Drug absorption by the scaffolds is directly related to the exposed surface area of the scaffold. It has been found that the scaffold made up of different material/polymer releases different chemicals, required for the optimal drug delivery and proper growth of the bone [6]. The polymers which are made using water based binder shows possibility to carry drugs and thus help in the growth of the bone. It was also found that the porosity also plays an important role in biodegradability of the scaffold [25]. The voids containing the air are more liable to swell when the scaffold gets wet. This in turn starts dissolving the scaffold and helps in deposition of growth enhancing polymer chains on the broken structure of bone. It was also found experimentally that the scaffold’s compressive stiffness and porosity are inversely related to each other in a linear form. The drug delivery system is of vital importance as it decides the proper recovery of the bone. As the scaffold starts to bio degrade, it releases the drugs, which are then absorbed by the bone tissues for repairs [19]. If the process becomes fast, the structure of the fractured bone will adapt deformity and thus is not acceptable, but if the scaffold takes a lot amount of time, the recovery will not be fast enough and the bone might not get corrected in time [26].

VI. CONCLUSION AND FUTURE SCOPE

Additive Manufacturing technology will bring number of accomplishments in the field of Medical Science. With the introduction of new technological aspects in 3D Printing, researchers, doctors and engineers will be able to generate new scaffolds with various polymers integrated within the same layer. The 3D printed scaffolds made from metals can also be deliberately used in bone recovery as the designers will very precisely make the parts according to patients. As the grafting process will be no longer needed, the patients will not have to bear a huge sum of money for bone replacement/surgery.

As the process of 3D printing is getting more accurate day by day, scaffolds with pores of <100µm would be generated, which will thereby slow down the scaffold degradation process and help the bone to grow all around. With the introduction of Nano-technology in the rapid manufacturing process, researchers will discover new horizons in the field of Biomedical Engineering.

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