Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/12643
DOI URL: http://dx.doi.org/10.21474/IJAR01/12643

RESEARCH ARTICLE

BONE SUBSTITUTES IN 3D PRINTING OF BONE SCAFFOLDS FOR GUIDED BONE REGENERATION

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Manuscript Info

Manuscript History
Received: 25 January 2021
Final Accepted: 28 February 2021
Published: March 2021

Key words:-
Bone, 3D Regeneration, Scaffolds, 3D Impression

Abstract

Purpose: The purpose of this study is to:Highlight the difficulty of using a bone (autologous, allograft) in tissue engineering.Present the different bone substitutes (of natural or synthetic origin used in guided bone regeneration alone or in combination.Describe the different materials and 3D printing techniques of bone scaffolds for bone regeneration.

Material And Methods: Research to the Scaffolds and its use in dentistry between January 2012 and December 2020 in Medline via PubMed, Google Translate, Google Library.

Results:38 articles were found in the database with the following keywords: bone, 3D regeneration, scaffolds, 3D impression.

Conclusion: It is generally accepted that the problems and challenges in the development and application of 3D printing can be solved by printing 3D scaffolds.

Introduction:-

The management of bone and joint pathologies of infectious, tumor or inflammatory origin often requires, in addition to therapeutic treatment, surgical intervention and the use of permanent or temporary medical devices.

Because of its osteo-inductive, osteo-conductive and osteogenic capacities, autologous tissue represents the “golden standard”, unfortunately it is only available in limited quantities and the donor site can be weakened during sampling. Tissues taken from cadavers present an infectious risk, while heterografts and xenografts pose problems of HLA compatibility and do not make it possible to provide the cellular component and the growth factors necessary for tissue regeneration.

Biomaterials have been developed to replace transplants with a longer term organ replacement vision. Over the past 60 years, three generations of biomaterials for orthopedic use have followed one another:

- bio-inert materials (first generation): the main requirement was to achieve an appropriate combination of their physical and mechanical properties with those of the tissue to be replaced, while minimizing their toxicity as well as the recipient's immune response.

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- bioactive materials (second generation) which appeared at the beginning of the 1980s, it was marked by the development of bioactive materials which are intimately integrated into the biological environment, thus improving the tissue response.

-materials designed to stimulate cellular responses and having a therapeutic function (third generation). Combines the bone substitute with an organic component in order to give the system a therapeutic function additional to that of supporting bone regrowth (Drug Delivery System) or to stimulate cellular and molecular activity in the environment of the implant (Tissue Engineering).

Materials And Methods:-

The bibliographic search was carried out using the scientific search engines Pub Med, Google scholar and science direct. Regarding the selection criteria, the articles included were articles meeting the objectives of the journal, whose publication date is beyond 2012 and only publications in English and French were retained.

The excluded articles were articles not meeting the objectives of the review, prior to 2012, with titles and abstracts that do not appear relevant and in languages other than French and English.

Relevant articles were identified after reading their titles, abstracts or reading the entire document.

Results:-

38 articles were selected using the three search engines, these articles were read and analysed.

Definitions:

Scaffold or matrices, these supports form a three-dimensional network that will serve as a guide for the differentiation, growth and organization of the cells that adhere to them. This artificial extracellular matrice will serve as a basis for the regeneration of tissue damage, and can in some cases constitute a reservoir of nutrients, growth factors and oxygen necessary for the growth of cells engaged in the process of tissue regeneration.

Scaffold specifications:

The use of scaffolds requires compliance with specifications:

1. **Biocompatibility**: It must not cause any inflammatory reaction which could cause immune rejection.
2. **Biodegradability**: The products resulting from its degradation must be neither cytotoxic or pro-inflammatory. Their elimination must be done without interference with other organs.
3. **Porosity** : The pore diameter must be compatible with colonization, adhesion and cell migration at the graft site.
4. **Resistance** : The scaffold must have high mechanical properties to withstand the loads at the implantation site
5. **Absorbability**: Its resorption must be concomitant with the formation of the tissue. Slowly enough to serve as a framework for the cells, but not too much at the risk of occupying a large volume of the lesion and thus hampering tissue formation
6. **Treatment** : They must be sterilizable without losing their physical and mechanical properties

The origin of bone substitutes:

The origin of bone substitutes can be natural or synthetic.

Bone substitutes of natural origin:

Allografts:

Are taken directly from the corpses within 24 hours of death and will undergo sterilization to avoid any risk of contamination.

Xenografts

The origin of xenografts are diverse: coral, mammals (sheep, horse) but the bovine origin is the most frequent.

Biological Hydroxyapatite:

Are xenografts ceramized at very high temperature and transformed into hydroxyapatites.

Calcium Carbonates:
It has high compressive strength, but brittle and has low tensile strength. It is used as a growth factor.

Synthetic bone substitutes:
Calcium Phosphates:
Calcium phosphates are derived from orthophosphoric acid used in medicine, pharmacy, agriculture and analytical chemistry
We distinguish:
-the monocalcium phosphates which are the most acidic and water-soluble which makes them non-biocompatible so they are never found in biological tissues.
-dicalcium phosphates subdivided into anhydrous dicalcium phosphate and dihydrate.
-tricalcium phosphates which have a porous form of calcium phosphate encapsulated by connective tissue. it is subdivided into apatic tricalcium phosphate whose chemical formula is close to that of hydroxyapatite as well as crystallized tricalcium phosphate which is obtained by direct synthesis (it is a constituent element of orthopedic cements).
-tetracalcium phosphates is an equimolar mixture of calcium carbonate with calcium prophosphate.
- octacalcic phosphates depending on the conditions of synthesis they can exist either in crystalline form or in amorphous state.

Hydroxyapatite:
It is considered to be the most stable and less soluble substitute among calcium phosphates. Its synthesis can be carried out either by reaction in the solid state or by the wet process.

Polymers:
These are mainly acrylic cements or aliphatic polyesters.

Bioglass:
Very osteo-conductive. They induce rapid bone formation and create a barrier delaying epithelial migration. They have a much greater mechanical resistance than calcium hydroxide.

Composite:
The combination of calcium-based bioactive ceramics with polymers improves the mechanical properties and the osteoconductive power of scaffold.

Calcium Sulphates:
It is the oldest of the bone substitutes, it is non-porous. It is characterized by good resorbability and has the possibility of including antibiotics.

3D Scaffold printing Processes:
The "OPTOFORM" Process
It is based on stereo-lithography, the ceramic material added in powder form to form a viscous paste.
The ceramic powder does not sinter during shaping, only the resins react at this time, they are intermediate components in the manufacture of prostheses acting as a binder which will subsequently harden. The paste contains dispersants, in order to ensure homogeneity of the suspension of the filler in the resin. A temperature of 1120 ° is sufficient for good sintering.

The "FCP DE 3D Céram" Process
Fast Ceramic production technology makes it possible to produce tailor-made or small series of bone substitutes and cranial implants.

It allows ceramic components to be produced in successive layers using a laser which polymerizes a paste composed of photosensitive resin and ceramic.

The parts are then subjected to a heat treatment which eliminates the resin and densifies the ceramics to 100%.

3D dimensional printing
The principle is to spread a layer of powdery material (ceramics, metals or polymers) on the support, then a binder glue (often binder dilute phosphoric acid is used) is printed on the powder to define a 2D shape.

Then, a second layer of powder is deposited, then the glue is sprayed again and binds the two layers together. The cycles are repeated until the 3D structure is obtained, then the excess powder is removed by brushing at the end of the procedure.

The FDM process "Fused Deposition Modeling"
The principle of FDM is to deposit by hot extrusion a viscous material in the form of parallel lines on each plane. The orientation of the lines is changed between each plane to create three-dimensional structures whose pore size, porosity and interconnectivity are controlled. The modification of the orientation of the gun and the adjustment of the extrusion parameters (movement speed, material flow) make it possible to adapt the diameter of the fibers. The layers merge together before the material is completely dry.

Discussion:-

1. The porosity and pore size of scaffolds play an essential role in bone formation in vitro and in vivo. Kaplan D et al found that in vitro lower porosity stimulates ontogenesis by suppressing cell proliferation and forcing cell aggregation while in vivo higher porosity and larger pore size ensure better bone growth.
2. WARNKE.PH et al studied the behaviour of human osteoblasts on HA and TCP scaffolds. Commonly used bone replacement material BioOss (R) served as a control. Biocompatibility was assessed by scanning electron microscopy (SEM), fluorescence microscopy after staining. As a result, both versions were colonized by human osteoblasts, but the number of cells present on the HAP scaffolds exceeded that of TCP while the number of cells present on the BioOss (R) scaffolds exceeded that of TCP.
3. In cases of osteoporosis the rate of failure of scaffold implantation is high due to the reduced capacity for bone regeneration compared to normal bone. A study by Tripathi G et al whereby calcium-deficient hydroxyapatite (CDHA) bone scaffolds with phytoestrogens were made for the regeneration of osteoporotic bone tissue by a combination of 3D printing and chemistry cementitious, as a process at room temperature. This study based on quercetin as the main phytoestrogen has revealed that it plays an important role in both improving bone formation and suppressing bone resorption and promises great potential in the regeneration of osteoporotic tissue.

Conclusion:-

We have focused on the effect of composition and hierarchical structure on the physical and chemical and biological properties of scaffolds.

It is generally accepted that the problems and challenges in the development and application of 3D printing:
1. precision (need for clinical individualization)
2. difference between bioactive scaffold printing and others under various materials
3. the high production cost of a 3D printer

In the future, 3D printed scaffolds will be a perfect replacement for bone defects with optimal clinical individualization. Due to the interdisciplinary cooperation and technological innovation, 3D printers will be more precise and lower cost.

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