Recent Advances in Tissue Bioengineering

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There is a considerable demand for tissue bioengineering to eliminate the need for the associated autogenous grafts which are still considered the gold standard for maxillofacial reconstruction following trauma and cancer treatment. Contemporary advances in the bioengineering of the jawbone depend on the production of three-dimensional scaffolds that facilitate the vascularisation and encourage targeted cellular adhesion for the reconstruction of the critical-size defect. In this respect, three-dimensional (3D) printing technology is promising in that it can create complex composite tissues. Various technologies have been utilized to achieve this target. The shape of the printed scaffold can be obtained from the 3D radiographic image of the patient where the defect is digitally reconstructed using mirror imaging techniques. Using Computer Aided Design (CAD) Computer Aided Manufacturing (CAM) technology, the digital model is then converted into a printed scaffold. This is usually followed by dispensing cells into discrete locations within the scaffold. Therefore, the structure of the 3D-printed bio-scaffold should fulfil the following criteria; the incorporation of microchannels to facilitate diffusion of nutrients, and the microporosity of 100–200 μm for cell survival.

3D printing, also known as additive manufacturing, is revolutionizing the practice in the tissue engineering (TE) field. Various types of 3D printing methods are available, the main types will be discussed in the following section.

Stereolithography (STL)

STL, one of the first types of 3D printing, is a popular printing technique. A laser beam is used to polymerize liquid UV curable photopolymer resin layer-by layer starting from the bottom to the top. The UV laser beam is applied to solidified resin in a specific part of the layer. Although this can produce scaffolds very quickly with controlled texture and resolution, a limited number of materials can be used due to the associated cost. The high viscosity of the liquid resin results in variable layer thickness and surface inaccuracies.

Micro-stereolithography is a newer version of the technique that has been introduced with higher resolution which produces a layer thickness of less than 10 μm. Nano-stereolithography (NSTL) has also been developed to incorporate nanoparticles onto scaffolds and investigate the cell response.

Fused Deposition Modelling (FDM)

This technology allows the deposition of a molten layer of thermoplastic material uniformly from a heated nozzle onto the platform with a typical thickness of 0.25 mm. No chemical or physical post-manufacture cure is required. The technique has been used for the preparation of synthetic scaffolds from polycarbonate (PC) and polyphenylsulfone (PPSF). The main limitation is the low resolution and accuracy when compared to the other additive manufacturing techniques. The incorporation of biomolecules, cells and hydrogel is not possible due to the high temperatures generated during manufacture.

Selective Laser Sintering (SLS)

The technique allows the fusion of the powder of synthetic materials, which include plastics, ceramics and polymers, and combinations of these materials, in layers which are heated to the melting point using a carbon dioxide laser beam. Therefore, the method provides the opportunity to reinforce the polymers with either fiberglass, polyamide or metals. The method can produce bioactive and composite scaffolds that mimic the mechanical properties of trabecular bone. The microstructure of the scaffold is limited to the size of the particles of the used material. It is not possible to incorporate cells or cytokines during the manufacture process.

Binder-based 3D printing (3DP)

The scaffold is produced as a result of the powder particles of a wide range of polymers being glued together by a binder using electron laser beams created by a high voltage of 30 to 60KV. The process uses high vacuum chambers to obviate the oxidation usually seen in the metal parts. The method is similar to the inject printing process which is used in 2D printing on paper.

Laminated Object Manufacturing (LOM)

The scaffold is fabricated using heat and thermal adhesive coating to bond layers of sheet-based materials. Layer by layer, the details of the scaffold are cut using carbon dioxide laser. The method is cost effective but the achieved surface details are limited.

Poly-Jet

Using an injectable head, a photosensitive polymer is deposited which is then cured by ultra-violet light. It allows the creation of fine details of up to 16 µm to be printed. The main limitation is the poor mechanical properties of the printed scaffold and, in most cases, gel-type polymers are required to provide extra support.

Extrusion Bioprinting

The process involves the deposition of cells and cytokines which are encapsulated in a hydrogel matrix during the printing of the bio-scaffold. The printing, therefore, is sensitive to speed, temperature, pressure of injection of the bioink as well as the concentration of the encapsulated cells. The mechanical properties of the bio-ink is crucial to the shear properties during the extrusion of the cellular component. Therefore, optimization of the bio-ink flow, the mechanical properties of the biomaterial as well as biodegradability and bioactivity are essential.

Researchers have endeavoured to mimic the mechanical properties of natural extracellular matrix (ECM) which is crucial for guiding the fate of the differentiation of mesenchymal stem cells. Several factors contribute to the optimum environment for cell differentiation and proliferation. The nano-topography of the printed scaffolds has a direct impact on cell adhesion and proliferation. This includes the type of grooved surface, nano-pits and nano-pillars. The number of voids in the printed scaffold known as macro and micro porosity play a pivotal role in facilitating the perfusion of oxygen and nutrients as well as the creation of microvascular networks for the microenvironment of the cells. On the other hand, the biocompatibility and biodegradability are crucial for bone bioengineering. The biocompatibility of the material is dictated by its ability to interact with the surrounding tissue without stimulating cytotoxic effects. The biodegradability is the gradual fading away of the bio-scaffold, without leaving toxic residues, once the cellular network within it has integrated with the surrounding environment. Biochemical functionalization is a crucial technology to render the surface of bio-inert scaffolds bioactive to stimulate the adhesion and proliferation of a particular cell line. This applies to a wide range of polymers including methyl methacrylate, polyethylene glycol, and poly ethyl ethyl keton (PEEK). Functionalization is achieved by the application of components of the ECM on the surface of the printed bio scaffold including laminin, fibronectin, or growth factors.

Future challenges

A challenge that all the 3D-printed bio-scaffolds need to overcome is the development of an effective way of securing the scaffolds in place in the surgical site so as to allow for effective integration of the material and for ingress of cells and growth of the regenerated tissues.