## **Future Trends in Bone Grafting**

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Since, Urist, M.R and Strates, B.S., in 1971, first published their work on BMP (bone morphogenic protein), in the Journal of dental Research (1) their research has propelled and expand the field of tissue regeneration (TE).

TE is centered on the concepts of tissue formation, regeneration and sustained functional remodeling. This is in contrast to the classic, "spare part" replacement therapy of the past with its associated harvest site morbidities (2). TE is especially an enticing application since bone, is a dynamic, highly vascular tissue that has the unique ability to remodel without scar. There are over one million major skeletal defects requiring major bone grafts reconstructions every year. This does not account for the vast numbers of small alveolar grafts that are performed by dentists yearly in their clinics. To grow new bone, demands the contemporary surgeon not only have a thorough knowledge of its biology but also a different perspective.

This understanding includes how to incorporate a milieu of cells, extracellular matrixes, promotion of intercellular communications, and growth factors. Unfortunately, bone does not grow in a 3 dimensional form (3-D). Therefore, a TE requirement for bone grafting is the need to provide a three dimensional construct. A bio-compatible 3-D scaffold must have several special unique properties to recapitulate the missing defect. The construct must have a specific architecture that allows the incorporated cells to easily access the required nutrients, vascularity and growth factors to survive and replicate. Furthermore, the scaffold must also allow for its induction and conduction it must eventual be replaced with native bone, mimicking the original defect. The small size of defects can be successfully repair using progenitor cells mesenchymal stem cells (MSCs) in combination with small biocompatible scaffolds (3). However, large defects that integrate with the surrounding bone still remains a challenge. Novel biotechnologies are now being developed that can provide

a highly complex construct representative of the native tissue's organization called tissue printing. Printing bone scaffolds is a proto-typing based technology that utilizes printed porous constructs with drops or fibers of cell-laden hydrogelsb (4) Hydrogels are the current prevalent substances used in bioprinting due to their high water content, biocompatibility, cytocompatibility and biodegradability.

The field of bone printing in combination with osteogenic cells and hydrogel on a printed scaffold is only just emerging These hydrogels can be deposited on a platform consisting of other multiple cell types in a 3-D structure containing a collagenous strong yet flexible matrix (5). Introduction of relevant growth factors, such as, BMPs or vascular endothelial growth factors (VEGF) can be easily added to the printed construct without losing their bioactivity.

An alternative future method to encapsulating the growth factors is to replace the scaffold with plasmid DNA encoding the growth factors, which could lead to a more prolong and sustained effect. As aside from printed bones for clinical application; printed bone equivalents could also be used to study pharmacokinetics and a possible model system to look a bonerelated disease (5). Finally, bone engineering on a major scale remains a challenging endeavor. A living bone implant is multidependent on, vascularization, osteogenic differentiation of stem cells and an architecture that promotes these functions within a strong construct. Bio-active tissue printing approach addresses these complex tissue designs. Bone implants can be placed in combination with internal fixation and interim stabilization until sufficiently incorporated. Bio-printed bone implants may well start a revolutionary change in musculoskeletal reconstruction if it can live up to its expectations and potential of neo-vascularization and bone formation in an ortho-topic environment.

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