Bioengineering

AIMS Bioengineering, 9(1): 22–25.
DOI: 10.3934/bioeng.2022002
Received: 27 December 2021
Revised: 27 December 2021
Accepted: 28 December 2021
Published: 28 December 2021

http://www.aimspress.com/journal/Bioengineering

Editorial

Bone tissue engineering at a glance

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The term and concept of "tissue engineering" was officially coined over 30 years ago, in 1988, at a National Science Foundation workshop as "the application of engineering principles and methods from life sciences to a fundamental understanding of the structure-function relationships of normal and pathological mammalian tissues and the development of biological substitutes to restore, maintain or improve tissue function". While the field of tissue engineering is relatively new, the idea of replacing one tissue by another dates back several centuries [1]. Thus, and for many years now, the replacement by implantation and transplantation of a tissue from a given site to another site in the same patient (an autograft) or in a different patient (a transplant or an allograft) has been innovative and beneficial, but both techniques present major problems. On the one hand, harvesting tissue for an autograft is expensive, painful, limited by anatomical limitations, and associated with donor site morbidity due to infection and injury. On the other hand, allografts and tissue grafts have serious constraints: limit of access to enough tissues or organs for all patients who need it, rejection by the immune system of the recipient patient, potential risks of introduction of infection or disease... [2]. It is in this context that the development of biofabrication strategies arouses considerable interest in order to develop methods, tools and products having the objectives of mimicking and replicating the anatomical and functional characteristics of human tissues.

Bone tissue is the second largest transplant tissue in the world. Millions of bone grafts (autografts and allografts) are performed each year around the world, while there is currently no satisfactory alternative to bone grafting. Traditional surgical treatments for fractures and bone defects, mainly comprising bone grafts and implantation of metal prostheses, achieve good clinical results, but these treatments also have serious drawbacks, such as infection, pain, cost. high, and the need for additional surgery. In some cases, such as bone defects, osteoporotic fractures, or bone defects/fractures in oncologic patients after radiation therapy, regeneration of bone tissue is hampered, and then requires modern strategies such as bone tissue engineering [3].

Tissue-engineering technologies involve the intimate interaction between three different components: (1) the scaffolding material that holds and cohesions cells together and forms the physical structure of tissue, i.e. acts as a model for the formation of new tissues, (2) the cells synthesizing the final tissue and (3) the signaling mechanisms (mechanical and/or chemical) that direct cells to express the desired tissue phenotype. Particular attention must be paid to the specific properties of each of these three components, in order to ensure the quality of the modified and neo-synthetized tissue and therefore the potential for clinical success when the engineered tissue is subsequently implanted into an injured site in vivo [4].

Biological and clinical evaluation of medical devices, including biomaterials, has also been implemented by ISO's ad hoc technical committee since 1988. Since then, sets of standards have been produced and are kept up to date. technological innovation in this highly biomedical field. If it is absorbable, its degradation products must also be biocompatible and not harmful. For application in a living organism, such as humans, all scaffolding materials must have very specific characteristics. First of all, to be defined as a biomaterial, the material must be biocompatible so that it can exist in harmony with the biological fluids, tissues, and cells of the host, without causing harmful effects locally or systemically. In the case of bone tissue, the scaffolding material must exhibit three fundamental bioactivities and properties: osteoinduction, osteoconduction, and osteointegration. Osteoinduction belongs to the ability to induce osteogenic differentiation of a cell that is not yet engaged [5]. In that context, an osteoinductive biomaterial can directly induce osteogenesis through the recruitment, proliferation, and differentiation of bone related stem cells such as mesenchymal stem cells. Osteoconduction refers to the ability to provide the microenvironment allowing the occurrence of in-place bone formation (osteogenesis) and bone growth [6]. Osseointegration refers to the ability of a biomaterial to elaborate direct contacts and anchoring between the exogenic material it-self and the host bone tissue, without growth of fibrous tissue at the bone-implant interface [7]. These 3 fundamental bioactivities and properties can be supported by different physical characteristics related to this specific mineralized hard material, such as stiffness and mechanical strength, viscosity, shear stress, geometry, hydrophilicity, surface charge, wettability, surface roughness and topography, porosity and pore size, permeability, mechanical stability, as well as controlled degradation rate [8]. All these parameters are crucial to encourage cell migration, adhesion, proliferation, and differentiation, but also for nutrients and oxygen transport throughout the scaffolds [9]. Another key consideration for designing a scaffold is its delivery capability through the releasing biological active agents that can induce important properties such as faster healing, antimicrobial, and antitumoral activity.

Biomaterials can be classified depending on their composition in metals (such as Fe, Mg, Zn and their alloys), ceramics (calcium phosphate ceramics such as hydroxyapatite, biphasic calcium phosphate [BCP] and tricalcium phosphate [TCP], bioactive glasses, zirconia), natural polymers (collagen, silk, chitosan, alginate, elastin, hyaluronic acid and cellulose) or synthetic polymers (such as polylactid acid [PLA], polyglycolic acid [PGA], polylactic co-glycolic acid [PLGA], poly e-caprolactone [PCL], polyethylene glycol [PEG], polybutylene terephthalate [PBT], polyethylene terephthalate [PET], polypropylene fumarate [PPF] or polyacrylic acid [PAA]), composites (defined as made of two or more substrates belonging to the same or different class of materials) and recently nanomaterials including nanoparticles [10]. All these materials can also be functionalized to improve their properties (including the three fundamental properties described above, but also to induce angiogenesis for example) [11].

The second component for bone tissue engineering belongs to the cell component where several cell types can be used to develop a bone construct, including osteoblast, embryonic stem cells (ESC), mesenchymal stem cells (MSC) and induced pluripotent stem cells (iPSC). All these cell types have largely demonstrated their ability to induce and promote and bone formation, remodeling, and healing [12].

A finally, the third part of bone tissue engineering is dedicated to signaling mechanisms that can be conveyed by the material itself, depending on its intrinsic properties and characteristics, or provided secondarily exogenously by enriching the final product with growth factors or cytokines (including TGFbeta and BMP, among others), as well as drugs [13].

At last, the recent advent and democratization of 3D printing processes, allowing the development of complex 3D structures using various biomaterials, opens up new opportunities and great flexibility in the design and production of scaffolds of different structural complexity combining adapted mechanical properties, vascularization and multicellular component [14]. In parallel, computational approaches can be carried out in order to optimize and predict the expected performances of the bone substitute produced by integrated bone tissue engineering. Finally, advances in artificial intelligence (AI), and deep learning in particular, offer the potential to improve both scientific understanding and clinical outcomes in regenerative medicine [15]. With an improved perception of how to integrate artificial intelligence into current research and clinical practice, AI offers an invaluable tool for improving patient outcomes in bone tissue engineering.

References

1. Bakhshandeh B, Zarrintaj P, Oftadeh MO, et al. (2017) Tissue engineering; strategies, tissues, and biomaterials. *Biotechnol Genet Eng Rev* 33: 144–172. https://doi.org/10.1080/02648725.2018.1430464
2. Sharma P, Kumar P, Sharma R, et al. (2019) Tissue engineering; current status & futuristic scope. *J Med Life* 12: 225–229. https://doi.org/10.25122/jml-2019-0032
3. Yue S, He H, Li B, et al. (2020) Hydrogel as a biomaterial for bone tissue engineering: a review. *Nanomaterials* 10: 1511. https://doi.org/10.3390/nano10081511
4. O'Brien FJ and Harley AB (2019) Editorial. *J Mech Behav Biomed Mater* 11: 1–2. https://doi.org/10.1016/j.jmbbm.2012.04.020
5. Friedenstein AY (1968) Induction of bone tissue by transitional epithelium. *Clin Orthop Relat Res* 59: 21–37. https://doi.org/10.1097/00003086-196807000-00003
6. Cornell CN and Lane JM (1998) Current understanding of osteoconduction in bone regeneration. *Clin Orthop Relat Res* 355: S267–S273. https://doi.org/10.1097/00003086-199810001-00027
7. Branemark PI, Hansson BO, Adell R, et al. (1977) Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10-year period. *Scand J Plast Reconstr Surg Suppl* 16: 1–132.
8. Battafarano G, Rossi M, De Martino V, et al. (2021) Strategies for bone regeneration: from graft to tissue engineering. *Int J Mol Sci* 22: 1128 https://doi.org/10.3390/ijms22031128
9. Codrea CI, Croitoru AM, Baciu CC, et al. (2021) Advances in osteoporotic bone tissue engineering. *J Clin Med* 10: 253. https://doi.org/10.3390/jcm10020253
10. Domingos M and Moxon S (2021) Advances in biofabrication for tissue engineering and regenerative medicine applications. *Polymers* 13: 1522. https://doi.org/10.3390/polym13091522

11. Simunovic F and Finkenzeller G (2021) Vascularization strategies in bone tissue engineering. *Cells* 10: 1749. https://doi.org/10.3390/cells10071749
12. Qi J, Yu T, Hu B, et al. (2021) Current biomaterial-based bone tissue engineering and translational medicine. *Int J Mol Sci* 22: 10233. https://doi.org/10.3390/ijms221910233
13. Pedrero SG, Llamas-Sillero P, Serrano-López J (2021) A multidisciplinary journey towards bone tissue engineering. *Materials* 14: 4896. https://doi.org/10.3390/ma14174896
14. Perić Kačarević Ž, Rider P, Alkildani S, et al. (2020) An introduction to bone tissue engineering. *Int J Artif Organs* 43: 69–86. https://doi.org/10.1177/0391398819876286
15. Mackay BS, Marshall K, Grant-Jacob JA, et al. (2021) The future of bone regeneration: integrating AI into tissue engineering. *Biomed Phys Eng Express* 7: 052002. https://doi.org/10.1088/2057-1976/ac154f