SJIF Impact Factor: 6.711

WORLD JOURNAL OF ADVANCE HEALTHCARE RESEARCH

ISSN: 2457-0400
Volume: 8.
Issue: 6
Page N. 249-254
Year: 2024

Review Article www.wjahr.com

TISSUE ENGINEERING IS THE ARCHITECHTURE OF SCAFFOLD

Dhrubo Jyoti Sen[1]* and Angshul Saha[2]

[1]Department of Pharmaceutical Chemistry, School of Pharmacy, Techno India University, Salt Lake City, Sector–V, EM–4, Kolkata–700091, West Bengal, India.
[2]PM SHRI Kendriya Vidyalaya No.1 Salt Lake, Kolkata–700064, West Bengal, India.

Article Received date: 17 April 2024 **Article Revised date:** 07 May 2024 **Article Accepted date:** 27 May 2024

***Corresponding Author: Dr. Dhrubo Jyoti Sen**
Department of Pharmaceutical Chemistry, School of Pharmacy, Techno India University, Salt Lake City, Sector–V, EM–4, Kolkata–700091, West Bengal, India.

ABSTRACT
The goal of tissue engineering is to assemble functional constructs that restore, maintain, or improve damaged tissues or whole organs. Artificial skin and cartilage are examples of engineered tissues that have been approved by the FDA; however, currently they have limited use in human patients. Examples of tissue engineering fall into one or more of three categories: "just cells," "cells and scaffold," or "tissue-inducing factors."

KEYWORDS: Biomaterials, Cell transplantation, Regenerative medicine, Stem cell, Tissue engineering.

History
The Tissue Engineering Society (TES), conceived of and founded by Drs. Charles A. and Joseph P. Vacanti in Boston in 1994, was officially incorporated in the state of Massachusetts on January 8, 1996. Tissue engineering is a biomedical engineering discipline that uses a combination of cells, engineering, materials methods, and suitable biochemical and physicochemical factors to restore, maintain, improve, or replace different types of biological tissues. Tissue engineering often involves the use of cells placed on tissue scaffolds in the formation of new viable tissue for a medical purpose, but is not limited to applications involving cells and tissue scaffolds. While it was once categorized as a sub-field of biomaterials, having grown in scope and importance, it can is considered as a field of its own. Thus the growing development of tissue engineering needs to solve four main problems: cells, engineering development, grafting and safety studies.[1]

Figure 1: Joseph P Vacanti [Born: 1950; researcher in tissue engineering and stem cells and the Vandam/Covino Professor of Anesthesiology, Emeritus, at Harvard Medical School] and Robert Samuel Langer (born August 29, 1948) is American biotechnologist, businessman, chemical engineer, chemist, and inventor.

Blood is considered a specialized connective tissue as it connects all systems of the body and transports oxygen, nutrients, and wastes. Skeletal muscle is the largest tissue in the body, constituting about 40% of its mass.

Epithelial: Skin, lining of hollow organs
Connective: Blood, bone, fat, cartilage, extracellular matrix
Muscle: Skeletal muscle, heart, inner layers of hollow organs
Nervous Brain, spinal cord, nerves

Eugene Bell is father of tissue engineering. Eugene Bell seeded collagen gels with fibroblasts, referring to them as contracted collagen gels. All of these examples represent seeds of the new discipline now known as Tissue Engineering. The three 'pillars' of tissue engineering and regenerative medicine are cells, scaffolds and chemical signals. Tissue engineering in wound repair: the three "R"s--repair, replace, regenerate. Tissue engineering combines the principles of materials and cell transplantation to develop substitute tissues and/or promote endogenous regeneration. Tissue engineering (TE) is a therapeutic option within regenerative medicine that allows to mimic the original cell environment and functional organization of the cell types necessary for the recovery or regeneration of damaged tissue using cell sources, scaffolds, and bioreactors.[2] As mentioned above, the cell, scaffold and growth factor are the three key materials for tissue engineering. The cell synthesizes matrices of new tissue, while the scaffold provides the appropriate environment for cells to be able to effectively accomplish their missions. Tissue Engineering is used in Dentistry. It is used in cardiovascular repair, Neural repair, Skeletal muscle repair, etc. In vitro meat – Artificial meat prepared under in vitro conditions. Stem cells are attractive for these applications due to their unique ability to self-renew and differentiate into multiple tissue-specific cells. They are demanding to manufacture and very expensive at the moment as the process is very labour-intensive. The main risks in tissue engineering are tumourigenity, graft rejection, immunogenity and cell migration.

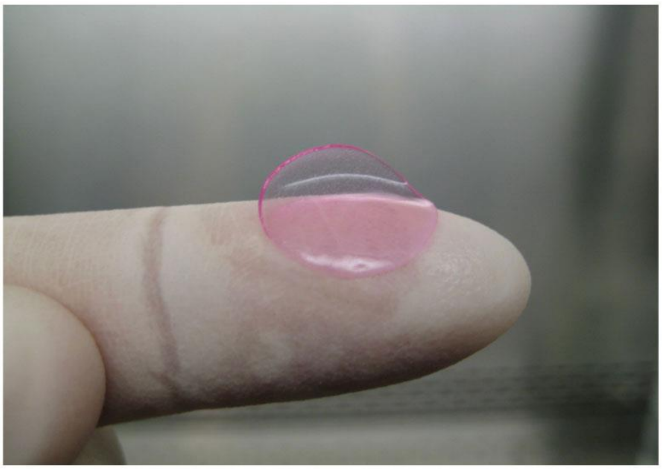


Figure-2: ***A mini bioengineered human liver that can be implanted into mice. Source: MIT website.***

Goal of tissue engineering: The goal of tissue engineering is to assemble functional constructs that restore, maintain, or improve damaged tissues or whole organs. Artificial skin and cartilage are examples of engineered tissues that have been approved by the FDA; however, currently they have limited use in human patients. While most definitions of tissue engineering cover a broad range of applications, in practice, the term is closely associated with applications that repair or replace portions of or whole tissues (i.e. organs, bone, cartilage, blood vessels, bladder, skin, muscle etc.). Often, the tissues involved require certain mechanical and structural properties for proper functioning. The term has also been applied to efforts to perform specific biochemical functions using cells within an artificially-created support system (e.g. an artificial pancreas, or a bio artificial liver). The term regenerative medicine is often used synonymously with tissue engineering, although those involved in regenerative medicine place more emphasis on the use of stem cells or progenitor cells to produce tissues.[3] Tissue engineering procedure involves several steps, which start from cell selection, cell isolation, and culturing of primary (progenitor or stem) cells; inducing their differentiation to certain phenotypes; seeding and cultivation; design of adequate scaffolds, including selection of proper materials and routes to design the biological structure. Recent progress suggests that engineered tissues may have an expanded clinical applicability in the future and may represent a viable therapeutic option for those who would benefit from the life-extending benefits of tissue replacement or repair. Overview.

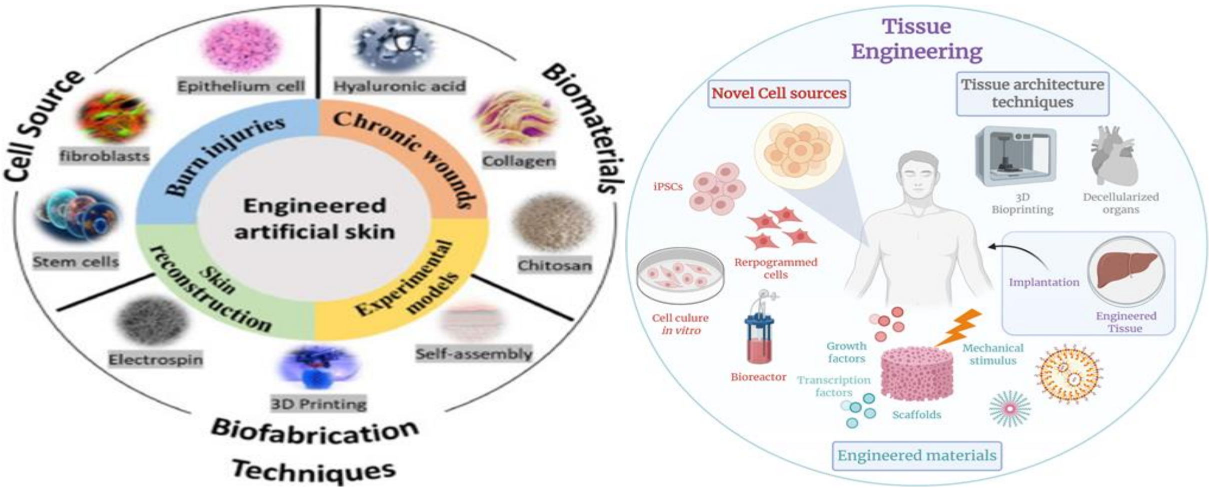


Figure 3: Tissue engineering.

There are 4 basic types of tissue: connective tissue, epithelial tissue, muscle tissue, and nervous tissue. Connective tissue supports other tissues and binds them together (bone, blood, and lymph tissues). Epithelial tissue provides a covering (skin, the linings of the various passages inside the body). Tissue engineering is based on three essential components that are cells of variable sources, guiding tissue formation scaffolds, and microenvironment and its inductive factors. Cells, scaffolds and growth-stimulating signals are generally referred to as the tissue engineering triad, the key components of engineered tissues.[4] Scaffolds, typically made of polymeric biomaterials, provide the structural support for cell attachment and subsequent tissue development. As cellulose fibers resemble the collagen fibers of bone tissue, cellulose has been implicated in bone tissue engineering applications. In particular, bacterial cellulose can serve as a localized delivery system to increase the local concentration of cytokines. Basic strategy for cell-based vascular tissue engineering is de- scribed in Figure 1 and consists of 3 fundamental steps: cell isola- tion, in vitro amplification and implantation. Generally, there are four main challenges in tissue engineering which need optimization. These include biomaterials, cell sources, vascularization of engineered tissues, and design of drug delivery systems. Biomaterials and cell sources should be specific for the engineering of each tissue or organ.[5]

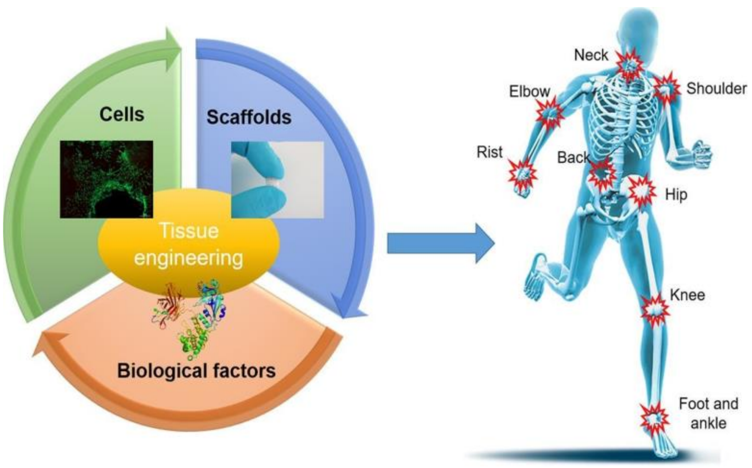


Figure 4: Scaffold of tissue engineering.

Regenerative medicine: It is a broad field that includes tissue engineering but also incorporates research on self-healing – where the body uses its own systems, sometimes with help foreign biological material to recreate cells and rebuild tissues and organs. The terms "tissue engineering" and "regenerative medicine" have become largely interchangeable, as the field hopes to focus on cures instead of treatments for complex, often chronic, diseases. This field continues to evolve. In addition to medical applications, non-therapeutic applications include using tissues as biosensors to detect biological or chemical threat agents, and tissue chips that can be used to test the toxicity of an experimental medication. The goal of tissue engineering is to assemble functional constructs that restore, maintain, or improve damaged tissues or whole organs. Artificial skin and cartilage are examples of engineered tissues that have been approved by the FDA; however, currently they have limited use in human patients. Among the most important recent developments in tissue engineering are the use of three-dimensional bioprinting, organ-on-a-chip, and induced pluripotent stem cell technologies.

There are three main components in TE including cells, biomaterials, and signals. Choosing the best combination of these components is a vital decision in a TE process.[6]

Tissue engineering and regenerative medicine in current medical practices: Currently, it plays a relatively small role in patient treatment. Supplemental bladders, small arteries, skin grafts, cartilage, and even a full trachea have been implanted in patients, but the procedures are still experimental and very costly. While more complex organ tissues like heart, lung, and liver tissue have been successfully recreated in the lab, they are a long way from being fully reproducible and ready to implant into a patient. These tissues, however, can be quite useful in research, especially in drug development. Using functioning human tissue to help screen medication candidates could speed up development and provide key tools for facilitating personalized medicine while saving money and reducing the number of animals used for research. Tissue engineering involves the combination and synergy of cells, bioactive factors and scaffold biomaterials to further promote bone healing and regeneration based on improving the microenvironment at the site of locally infected bone defects.

Some examples of research in this area are described below

Controlling stem cells through their environment: For many years, scientists have searched for ways to control how stems cells develop into other cell types, in the hopes of creating new therapies. Tissue engineering combines medical technology with the native regenerative properties of living organisms. Through well-integrated processes, tissue engineering allows for greater regenerative potential than can be found in nature alone. Biomaterials are an integral component of tissue engineering.[7]

Implanting human livers in mice: Researchers have engineered human liver tissue that can be implanted in a mouse. The mouse retains its own liver as well, and therefore its normal function-but the added piece of engineered human liver can metabolize drugs in the same way humans do. This allows researchers to test susceptibility to toxicity and to demonstrate species-specific responses that typically do not show up until clinical trials. Successful tissue engineering relies on four specific criteria: cells, growth factors, scaffolds, and the mechanical environment. The qualifications you need to work in tissue engineering vary, but typically include at least a bachelor's degree in biology, math, engineering, or a related field. Many employers prefer candidates who have earned a master's degree and have experience in lab work.

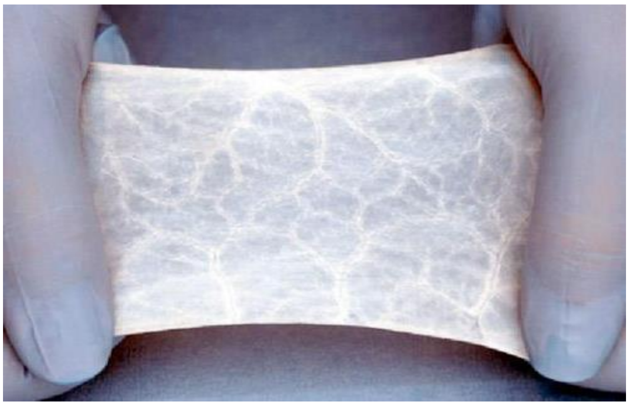


Figure 5: ***A Biomaterial made from pigs' intestines which can be used to heal wounds in humans.***

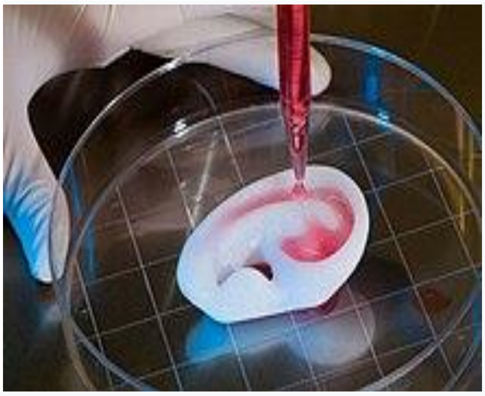
Engineering mature bone stem cells: Researchers completed the first published study that has been able to take stem cells all the way from their pluripotent state to mature bone grafts that could potentially be transplanted into a patient.[8]

Artificial Pancreas: Research involves using islet cells to regulate the body's blood sugar, particularly in cases of diabetes. Biochemical factors may be used to cause human pluripotent stem cells to differentiate (turn into) cells that function similarly to beta cells, which are in an islet cells in charge of producing insulin.[9]

Tissue-engineered blood vessels: Blood vessels that have been grown in a lab and can be used to repair damaged blood vessels without eliciting an immune response. Tissue engineered blood vessels have been developed by many different approaches.[10]

Regenerating a new kidney: The ability to regenerate a new kidney from a patient’s own cells would provide major relief for the hundreds of thousands of patients suffering from kidney disease. Experimenting on rat, pig and human kidney cells, researchers broke new ground on this front by first stripping cells from a donor organ and using the remaining collagen scaffold to help guide the growth of new tissue. To regenerate viable kidney tissue, researchers seeded the kidney scaffolds with epithelial and endothelial cells. The resulting organ tissue was able to clear metabolites, reabsorb nutrients, and produce urine both *in-vitro* and *in-vivo* in rats. This process was previously used to bioengineer heart, liver, and lung tissue. The creation of transplantable tissue to permanently replace kidney function is a leap forward in overcoming the problems of Donor organ shortages and the morbidity associated with immunosuppression in organ transplants.

Steps to prepare artificial tissue: Tissue engineering procedure involves several steps, which starts from cell selection, cell isolation, and culturing of primary (stem) cells; inducing their differentiation to certain phenotypes; seeding and cultivation; design of adequate scaffolds, including selection of proper materials.[11]


A Regenerated human ear using a scaffold.

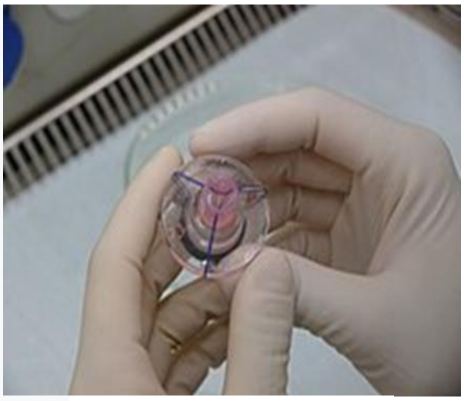

Tissue engineered heart valve.

Figure-6: Tissue in scaffold.

Regulation: There were problems getting products approved by the FDA and if they got approved there were often difficulties in getting insurance providers to pay for the products and getting it accepted by health care providers. For example, organogenesis ran into problems marketing its product and integrating its product in the health system. This partially due to the difficulties of handling living cells and the increased difficulties faced by physicians in using these products over conventional methods. Regulation is further complicated by the ethical controversies associated with this and related fields of research (e.g. stem cells controversy, ethics of organ transplantation). The fundamentals of tissue engineering involve cell sources, scaffolds for cell expansion and differentiation, as well as carriers for growth factors. Animal and human trials are a major part of the applications. Artificial skin constructed from human skin cells embedded in a hydrogel, such as in the case of bio-printed constructs for battlefield burn repairs. Artificial bone marrow: Bone marrow cultured in vitro to be transplanted serves as a "just cells" approach to tissue engineering.[12] Tissue engineering is a rapidly expanding field, combining knowledge in biological sciences, engineering, and medicine. It aims at the development of strategies to produce a variety of tissues, both in vitro and in vivo to restore, maintain, or enhance tissue function. Tissue engineering aims to fabricate functional tissue for applications in regenerative medicine and drug testing. More recently, 3D printing has shown great promise in tissue fabrication with a structural control from micro- to macro-scale by using a layer-by-layer approach. The brain is an organ composed of nervous tissue that commands task-evoked responses, movement, senses, emotions, language, communication, thinking, and memory. The three main parts of the human brain are the cerebrum, cerebellum, and brainstem.[13-15]

CONCLUSION

Regenerative medicine efforts are currently underway experimentally for virtually every type of tissue and organ within the human body. As regenerative medicine incorporates the fields of tissue engineering, cell biology, nuclear transfer, and materials science, personnel who have mastered the techniques of cell harvest, culture, expansion, transplantation, and polymer design are essential for the successful application of these technologies to extend human life. Various tissues are at different stages of development, with some already being used clinically, a few in preclinical trials, and some in the discovery stage. Recent progress suggests that engineered tissues may have an expanded clinical applicability in the future and may represent a viable therapeutic option for those who would benefit from the life-extending benefits of tissue replacement or repair.

REFERENCE

1. Whitney GA, Jayaraman K, Dennis JE, Mansour JM. "Scaffold-free cartilage subjected to frictional shear stress demonstrates damage by cracking and surface peeling". Journal of Tissue Engineering and Regenerative Medicine, 2017; 11(2): 412–24.
2. Langer R, Vacanti JP "Tissue engineering". Science, 1993; 260 (5110): 920–26.
3. MacArthur BD, Oreffo RO "Bridging the gap". Nature, 2005; 433(7021): 19.
4. Thomas D, Singh D "Novel techniques of engineering 3D vasculature tissue for surgical procedures". American Journal of Surgery, 2019; 218(1): 235–236.

5. Bara JJ, Richards RG, Alini M, Stoddart MJ "Concise review: Bone marrow-derived mesenchymal stem cells change phenotype following in vitro culture: implications for basic research and the clinic". Stem Cells, 2014; 32(7): 1713–23.
6. Minteer D, Marra KG, Rubin JP "Adipose-derived mesenchymal stem cells: biology and potential applications". Advances in Biochemical Engineering/Biotechnology, 2013; 129: 59–71.
7. Farahany NA, Greely HT, Hyman S, Koch C, Grady C, Pașca SP, et al. "The ethics of experimenting with human brain tissue". Nature, 2018; 556(7702): 429–32.
8. Bourret R, Martinez E, Vialla F, Giquel C, Thonnat-Marin A, De Vos J "Human-animal chimeras: ethical issues about farming chimeric animals bearing human organs". Stem Cell Research & Therapy, 2016; 7(1): 87.
9. Grobarczyk B, Franco B, Hanon K, Malgrange B "Generation of Isogenic Human iPS Cell Line Precisely Corrected by Genome Editing Using the CRISPR/Cas9 System". Stem Cell Reviews and Reports, 2015; 11(5): 774–87.
10. Mertsching H, Schanz J, Steger V, Schandar M, Schenk M, Hansmann J, et al. "Generation and transplantation of an autologous vascularized bioartificial human tissue". Transplantation, 2009; 88(2): 203–210.
11. Newman P, Minett A, Ellis-Behnke R, Zreiqat H "Carbon nanotubes: their potential and pitfalls for bone tissue regeneration and engineering". Nanomedicine, 2013; 9(8): 1139–1158.
12. Zahir-Jouzdani F, Mahbod M, Soleimani M, Vakhshiteh F, Arefian E, Shahosseini S, et al. "Chitosan and thiolated chitosan: Novel therapeutic approach for preventing corneal haze after chemical injuries". Carbohydrate Polymers, 2018; 179: 42–49.
13. Pomeroy JE, Helfer A, Bursac N "Biomaterializing the promise of cardiac tissue engineering". Biotechnology Advances, 2020; 42: 107353.
14. Cassidy JW "Nanotechnology in the Regeneration of Complex Tissues" (PDF). Bone and Tissue Regeneration Insights, 2014; 5: 25–35.
15. Nam YS, Park TG "Biodegradable polymeric microcellular foams by modified thermally induced phase separation method". Biomaterials, 1999; 20(19): 1783–90.