

ARTIFICIAL TISSUE FABRICATION: A REVIEW ON THE ANATOMY BEHIND TISSUE ENGINEERING

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ABSTRACT: The fabrication of artificial tissues is a process that uses bio-molecules and bio-fabrication technologies in creating functional artificial tissues that resemble or has the ability to regenerate biological tissues. The fundamental basis combines the integration of biological principles with engineering approaches.

This paper aims at showing how knowledge of human anatomy guides the design and functionality of engineered tissues.

An extensive literature review was done on tissue engineering techniques that could be used to regenerate biological tissue. Various methods and significant technologies involved in scaffolding engineering, stem cells signaling, decellularization methods were reviewed. Stem cells and scaffold materials selection depends on the native tissue being replicated. Among these, mesenchymal stem cells are the most widely used in all tissue fabrication. Advanced methods such as decellularization, scaffold-free fabrication and scaffold-based fabrication are employed to achieve structural and functional tissues.

This review reveals that a solid anatomical understanding is an essential fundamental concept in recreating a functional

artificial tissue. The integration of stem cells with various scaffold technologies that mimic the three-dimensional extracellular matrix, along with the application of growth factors, has enhanced the development of artificial tissues that mimic their natural counterparts. Despite major advances in biomaterials, growth factors, and stem cell applications, challenges remain in replicating the three-dimensional complexity of certain human tissues and translation into clinical practice.

Conclusively, artificial tissue fabrication is a revolutionary approach in regenerative medicine, and to gain the complexity and functionality of native biological tissues, integration of anatomical knowledge into tissue engineering processes is required. Interdisciplinary research is the key to future research, as artificial tissues will be a potential solution to many medical issues.

Keywords: *Scaffolds, Stem cells, Growth factors, decellularization.*

1.0. INTRODUCTION

Tissue engineering is an evolving field that seeks to create functioning artificial tissues and organs that may restore the healthy, functional, and homeostatic 3D micro-environment (Daniel *et al.*, 2018). A commonly applied definition of tissue engineering, as stated by Langer and vacancies, is "an interdisciplinary field that applies the principles of engineering and life sciences toward the development of biological substitutes that restore, maintain, or improve biological tissue function or a whole organ" (Atala, 2023).

Regenerative medicine is a vastly emerging interdisciplinary field of research and restore, repair and regenerate damaged tissues or organs (Atala, 2023, Daniel *et al.*, 2018). The fundamental concepts of artificial tissue fabrication are stem cells, scaffolds, growth factors and bio-reactors. There are several techniques and materials used in artificial tissue fabrication which have been successful clinical applications in humans thereby reducing organ shortage and improving regenerative medicine. Understanding human tissue and cellular anatomy is essential in fabricating a tissue or organ.

2.0. METHODOLOGY

Articles published 2015-2025 were selected in pub med, google scholar, science direct, research gate, and web of science, using search terms such as tissue fabrication, stem cell therapy, scaffolds, 3D bio printing, tissue regeneration, bioreactors, growth factors, mesenchymal stem cells and related keywords. We restricted the research to human original peer-reviewed studies with human and animals tissue fabrication. The inclusion criteria are: (a) Peer-reviewed journal articles and book chapters, news, educational videos both on web and official YouTube channels; (b) Articles that emphasizes on the use of stem cells in tissue regeneration and engineering; (c) Studies on biomaterials, scaffolds and bio fabrication techniques; (d) Research on the functional anatomy of engineered tissues; (e) Preferably within the last ten years was reviewed to ensure up-to-date methodologies and advancements; (f) Books and Articles with researches on new technologies and techniques in fabricating tissues were included; (g) Studies presenting experimental results and case studies related to tissue engineering were included; (h) in vitro, in vivo, and ex vivo studies on Human and animal model studies relevant to anatomical integration of engineered tissues were included. The Exclusion Criteria are; (a) Research on tissue regeneration that does not involve artificial tissue fabrication. (b) Preprints, editorials, opinion pieces, and non-scientific articles were excluded (c) Articles older than 15 years, unless they provide foundational knowledge; (d) Non-English Articles; (e) Unpublished articles; (f) Studies with lack of proper citation or poor methodology. (g) Articles on old and non- clinical approved applications. The title/abstracts were screened by two reviewers and subsequently the full text reviewed, differences resolved by discussion. Extracted data were types of study design, samples, methodology, and significant molecular outputs. Qualitative determination of risk of bias was done by assessing the size of the sample and controls, along with validating the assay used. Studies were mapped in the case of key terms and processes.

The literature search (2015-2025) initially yielded 91 unique records. After removing duplicates and applying inclusion/exclusion criteria, 83 full-text articles were assessed, of which 78 met criteria. Most studies were small exploratory

investigations (N < 50 donors or samples) due to ethical and logistical constraints; few were randomized trials. Common limitations included variability in sample preparation and lack of vivo confirmation. Overall bias risk was moderate, reflecting consistent replication of key findings across independent groups.

3.0. LITERATURE REVIEW

This literature reviews how tissue engineering is an interdisciplinary field that combines the principles of anatomy, engineering, and biomaterials science to create a functional artificial tissue for clinical applications (Atala, 2023). This chapter provides a comprehensive review on how anatomy is fundamental to understanding tissue bioengineering in both in-vitro or in-vivo fabrication and integration or interaction within the human body; focusing on cellular interactions, scaffold engineering, biomaterials (growth factors), bioreactors and clinical applications (Zhang *et al.*, 2017)

3.1. CONCEPTS OF ARTIFICIAL TISSUE FABRICATION

Four fundamental principles involved in tissue fabrication are stem cells, scaffolds, growth factors and bioreactors.

3.1.1. STEM CELLS IN TISSUE ENGINEERING

In tissue fabrication, stem cells are employed because of their ability to differentiate into all cell types (Liao & Zhai., 2018). They are;

1. Embryonic stem cells are pluripotent stem cells that can differentiate into all cells types in the body excluding the extra embryonic tissues such as placenta and its derived from the inner cell mass of a blastocyst (Haitao *et al.*, 2018).
2. Adult stem cells are stem cells that can differentiate into all cell types within a specific cell range I.e. multi potent stem cells (Smith & Jones, 2023). Bone marrow-derived mesenchymal stem cells (MSc) is the most common stem cells used in cell therapy. MSCs possess pro-androgenic properties and secrete several growth factors, such as VEGF, EGF, FGF etc.; (Cheng *et al.*, 2020). MSCs can also regulate immune responses and mobilize varied kinds of immune cells.

These immunomodulatory effects are mediated by MSC-derived cytokines such as IL-10, PG-E2, TGF- β , IDO, and nitric oxide (Gao *et al.*, 2016).

3. Induced Pluripotent stem cells (iPS cells): iPS are reprogrammed adult somatic cells. iPS cells can differentiate into all cell types found in the body (Menasche *et al.*, 2023). Somatic cells (derived from skin) are cultured in vitro and reprogrammed with gene vectors encoding transcription factors associated with pluripotency (kim *et al.*, 2021; Takahashi & Yamanaka, 2016). Growth factors such as c-Myc, Oct-3/4, SOX2, and KLF4 (Takahashi & Yamanaka, 2016) are commonly used for reprogramming, although other growth factors such as Nanog, and LIN-28 have also been used successfully (Wang *et al.*, 2019).

3.1.2. CELL SOURCES

These stem cells can be sourced from.

1. Autologous cells: The donor and the recipient cells are derived from the same individual (Baltazar *et al.*, 2020)
2. Allogeneic: The Cells are obtained from a donor of the same species as the recipient (Baltazar *et al.*, 2020).
3. Xenogeneic: These cells are derived from a species that are different from the recipient; for example, porcine cells (pig) or bovine cells (cow) can be used for tissue fabrication in humans (Simon *et al.*, 2017).
4. Isogenic cells: These cells are derived from individuals with identical genetic codes, providing an immunologic benefit similar to autologous cells. Examples include cells from identical twins (Zhao *et al.*, 2021).

3.1.3. SCAFFOLDS

Scaffolds are engineered materials designed to support the formation of new functional tissues by facilitating desirable cellular interactions (Eltom *et al.*, 2019). These structures mimic the extracellular matrix (ECM) of native tissues, creating an environment that allows cells to attach, migrate, and influence their own microenvironments (Hussain *et al.*, 2023). Scaffold must be.

- Biodegradable (Niu *et al.*, 2022).
- Degrade into non-toxic substance (Niu *et al.*, 2022).
- Biocompatible (Hussain *et al.*, 2023).
- Made with controlled pore size and porosity (Li *et al.*, 2021).

3.1.4. TECHNIQUES USED IN SCAFFOLD SYNTHESIS

Material selection is based on target organ or tissue. Material selection is essential aspect of producing a scaffold. These are natural or synthetic scaffolds (Hussain *et al.*, 2023). Natural material used in tissue fabrication are mostly from protein sources such as collagen, fibrin, gelatin, elastin etc.; because of the presence of strong binding sites on their surface for these stem cells to seed onto. (Hussain *et al.*, 2023), others natural occurring materials used are polysaccharidic materials such as chitosan, hyaluronic acid (Bian *et al.*, 2016), and decellularized extracellular matrix tissues (Fujimoto *et al.*, 2020). Commonly used synthetic materials are PLA, PLGA, PGA, and PCL (Dorati *et al.*, 2017; Magazzini *et al.*, 2021). This synthetic material has no binding sites, so they are usually seeded with adhesive protein on their surface to create a binding site for cell attachment (Reddy *et al.*, 2021). Usually, this synthetic material is combined with bioactive proteins such as gelatin (Reddy *et al.*, 2021), to make a hydrophilic ECM-like structure called an “hydrogel” (Liu *et al.*, 2017) which a stronger component used in bone and cartilage fabrication (Hashemi-Afzal *et al.*, 2025).

The following are techniques used in scaffolding. These are.

1. Nano fibers self-assembly (Moore & Hartgernik, 2017).
2. Solvent casting and particulate leaching (Prasad *et al.*, 2017).
1. 3. Textile technologies for scaffolding (Akbari *et al.*, 2016; Doersam *et al.*, 2022)
3. CAD/CAM technologies (Marrelli *et al.*, 2016; Pardal-Peláez *et al.*, 2024)
4. Electrospinning method (Zulkifli *et al.*, 2023)

2. 6. Self-assembled recombinant spider silk nano membranes (Gustafsson *et al.*, 2020)
3. 7. Emulsification freeze-drying (Fereshteh, 2018)
4. 8. Thermally induced phase separation (Zeinali *et al.*, 2021)
5. 9. Gas-foaming method (Costantini & Barbetta, 2018; Januariyasa & Yusuf, 2020)

3.1.5. GROWTH AND REGULATORY FACTORS

TABLE 2.1. The table below are list of growth factors used in tissue engineering.

Growth factors	Action	Use in tissue fabrication
Platelet-derived growth factor (PDGF)	Endothelial cells proliferation	1. Angiogenesis 2. Wound healig (Wu <i>et al.</i> , 2019)
Fibroblast growth factor (FGF)	Cell proliferation	1. Bone and cartilage regeneration 2. Endothelial cell proliferation 1. Angiogenesis (Farooq <i>et al.</i> , 2021)
Epidermis growth factor (EGF)	Cell proliferation	1. Migration and differentiation of stem cells 2. Wound healing (Kim <i>et al.</i> , 2016)
Transforming growth factor (TGF-beta)	Cell proliferation and ECM formation	ECM production (Alsawalha <i>et al.</i> , 2021)
Vascular endothelial growth factor (VEGF)	Endothelial cell proliferation	Angiogenesis (Gnavi <i>et al.</i> , 2017)
Bone morphogenetic protein-2 (BMP-2)	Bone Cells proferation	Bone and cartilage regeneration (Agrawal & Sinha, 2017)

3.1.6. BIOREACTORS

A bioreactor is a device used in tissue engineering that provides a controlled environment for growing cells or tissues, and cell culture. It maintains the ideal conditions for the cells to proliferate, differentiate, or carry out specific biological functions, such as oxygen and nutrient supply, temperature control, and waste removal (Naveen *et al.*, 2018). Examples are big glass bioreactor (TurboSquid, 2015), tissell biaxial bioreactor (Quinxell technologies, 2025), a Rotating wall vessel bioreactor (Naveen *et al.*, 2018)

3.2. PROCESS OF TISSUE FABRICATION

There are different methods used in tissue fabrication or tissue engineering. These are

1. Cell-based tissue engineering
2. Cell and scaffold-based tissue engineering.
3. Decellularization method

3.2.1. CELL-BASED TISSUE ENGINEERING

This is an innovative approach in the field of regenerative medicine and tissue engineering that aims to create functional tissues or organs without the use of exogenous scaffolding materials. It's make uses of cell culturing technology and 3D imaging construct (Bishop *et al.*, 2017). Stem cells are harvested and cultured to form a confluent sheet, when the temperature is lowered, the cell sheet detaches intact, preserving the ECM and cell-cell connections. Multiple sheets can be stacked to create thicker tissues (Kobayashi *et al.*, 2019). This method is commonly used in cardiac, dental and corneal tissue engineering; (Pati *et al.*, 2015). Another technique is the spheroid Culture method. Here, Cells are aggregated into 3D spheroids, which can be used to model tissues or as building blocks for larger constructs (Białkowska *et al.*, 2020). 3D MSC spheroids promote the secretion of HGF, VEGF, FGF2, MMP-2, and MMP-14, compared to 2D cultures. They are often used in drug testing (Irina *et al.*, 2023).

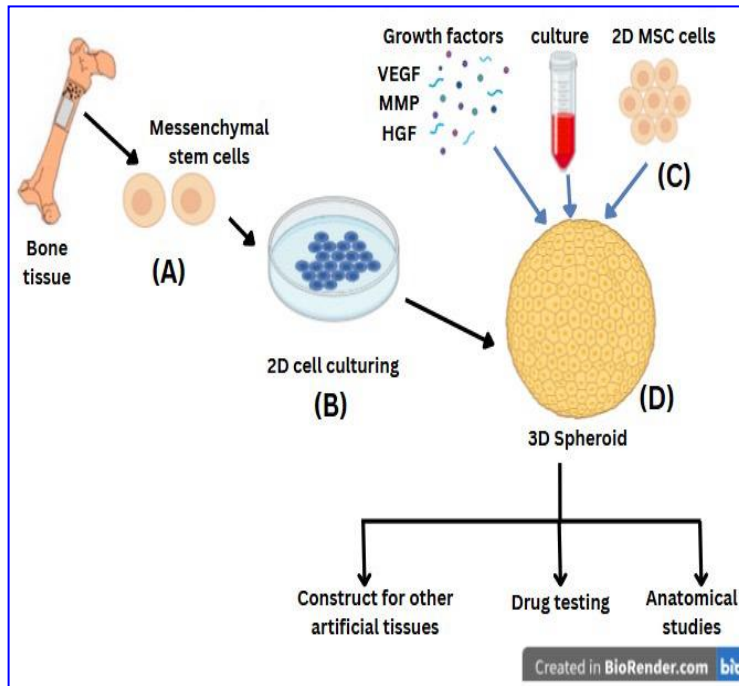


Figure 2.1: MSC stem cells spheroid fabrication. A- harvest of MSC from the human bone marrow. B- expansion and multiplication of the MSC stem cells in the laboratory. C – incorporation of 2D MSC stem cells with growth factors in a culture media. D- formation of three-dimensional MSC spheroid. *Image created with biorender*

3.2.2. CELL AND SCAFFOLD-BASED TISSUE ENGINEERING

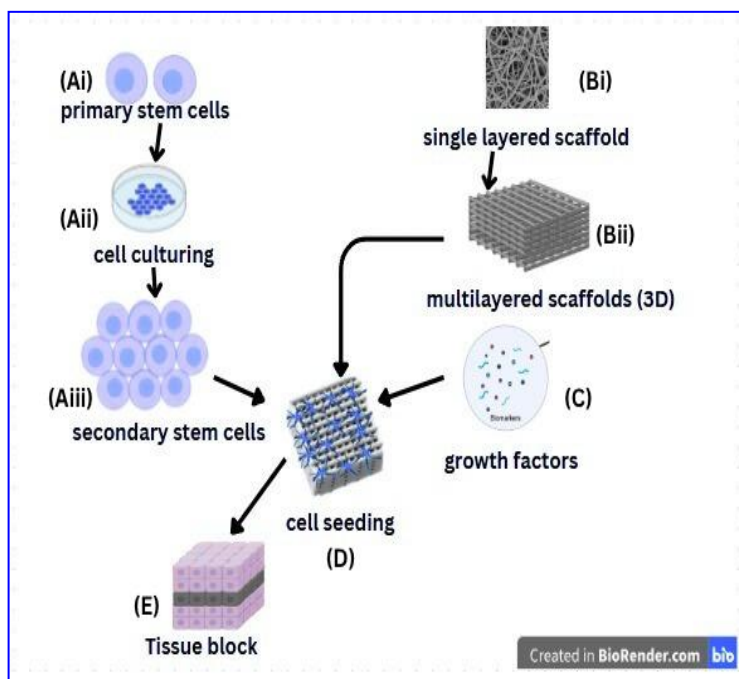


Figure 2.2: Cell-based and scaffold-based tissue engineering. Ai-Aiii involves the expansion of stem cells from the donor to multiply the number of cells available for fabrication. Bi-Bii is the fabrication of a scaffold into three-dimensional matrix that mimics the ECM; usually made with controlled pore size. C are the growth factors that helps to regulate the differentiation of the stem cells into desired cells. D is the seeding of the stem cells and growth factors onto the 3D- scaffold. E is the formation of an artificial tissue block. *Image created from biorender,*

A. Skin tissue engineering

1. Skin cells spray: The cellular spray is designed to treat severe second-degree burns. Cultured epithelial autografts are harvested from the recipient's unaffected skin, cultured in lab to form secondary stem cells which are suspended into a solution of silicon (scaffold). These suspensions can be sprayed onto burn wounds using special spray devices and spray nozzles that facilitate even distribution of CEA over wounds (Stewart *et al.*, 2017).



Figure 2.3: Image A shows a patient with first degree burn. Image B shows when the damaged skin is sprayed with mesenchymal stem cells and wrapped with a protective nylon. Image (C/D) shows the healing process. Image E shows the formation of a functional skin (Badiavas & Falanga, 2003).

2. Manufactured synthetic skins: Also known as bioengineered skin substitutes are manufactured skin layers that mimics the biological layers of skin and are used for wound healing, burn treatment, and tissue engineering applications (Hussein *et al.*, 2023). They can be categorized as acellular e.g Integra® (Shale, 2019), AlloDerm® Biobrane® (Kavita *et al.*, 2019) or cellular skin substitutes such as Dermagraft® (Shawa *et al.*, 2025). Integra® is the most commonly us synthetic skin. It contains two layers mimicking the first two layers of skin I.e the epidermal and dermal layer. The upper layer made up of silicon, an inner layer consisting of glycosaminoglycan from shark's cartilage and cow's tendon (Shale *et al.* 2019).



Figure 2.4: A case study of a man with third degree burn seen in image and b. Image c shows the implantation of Integra®. Image D is progression in skin growth; recipient cells start migrating into the second layer of the Integra®. Image E shows the removal of the upper layer of the Integra®, replaced with skin grafts. Image f shows the healing and regeneration of a like-life skin (Demiri *et al.*, 2013).

B. Bone tissue engineering

Hydrogels are mostly used in bone regeneration made through different techniques such as 3D bio printing or electron nano fibres to create a hollow-like structure of the bone (Liu *et al.*, 2017). The bone marrow mesenchymal stem cells are seeds onto this

hydrogel, implanted into the defected bone site for bone regeneration. The integration of the patient's own cells starts migrating onto this implanted hydrogel, then the bone cells start to differentiate, proliferate, and mature thereby making their own extra cellular matrix as the hydrogel (scaffold) starts to degenerate and absorbed by the body as a non-toxic material and a whole bone structure is formed (Noah *et al.*, 2021). Another innovation is the Gene- and RNAi-activated scaffolds loaded with nucleic acids aimed at promoting bone tissue repair (Bin *et al.*, 2021).

C. Cartilage engineering

Due to its limited ability to self-repair, cartilage is an ideal candidate for tissue engineering. This approach involves harvesting small biopsies of cartilage from the patient in a minimally invasive manner, isolating chondrocytes from the donor tissue, and expanding the cells *in vitro* (Agrawal & Sinha, 2017; Makris *et al.* 2015). New techniques involve the use of chondrocytes cells (Coates & Fisher, 2018), fibroblast (because of the high density of glycosaminoglycans and collagen type ii) (Irawan *et al.*, 2018), bone marrow derived; adipose derived; and synovial derived stem cells, has the ability in regeneration of cartilage (Fellows *et al.*, 2016). Natural polymers have been explored as bioactive scaffolds for cartilage engineering such as alginate, agarose, fibrin, collagen, gelatin, chitosan, chondroitin sulfates, and cellulose (Strauß *et al.*, 2024). Synthetic polymers currently explored for cartilage repair include poly (α -hydroxy esters), poly (NiPAAm), poly (propylene fumarates), polyurethanes and hydrogels (Ansari *et al.*, 2019; Fahmy *et al.*, 2020). Growth factors like TGF- β , FGF, BMP, and IGF, along with other soluble factors like hyaluronic acid, chondroitin sulfates, and insulin, were also seeded together to aid cell growth, differentiation and maturation in cartilage engineering (Shen & Wu, 2024).

D. Artificial trachea

A South Korean team was first to successfully transplant 3D bioprinted artificial trachea (Park *et al.*, 2019). Synthetic polymers such as polycaprolactone (PLCA) or poly lactic acid (PLA) that can withstand mechanical stress and mimic trachea's flexibility are selected for fabrication (Khalid *et al.*, 2023; Park *et al.*, 2019). A 3D bio printing techniques is used to create a scaffold tissue that mimic the structure and

dimension of trachea cells (Park *et al.*, 2021). Epithelial cells are seeded evenly onto the 3D scaffold surface using techniques such as static seeding or dynamic cell culture in a bioreactor (Lee *et al.*, 2019; Rahmani *et al.*, 2023).

E. Artificial ligaments

These are primarily used in anterior cruciate ligament (ACL) reconstruction (Boulos *et al.*, 2016). Types of artificial ligament commonly used are:

- i. Ligament advance reinforcement system made from polyethylene terephthalate (Li & Chen, 2015). It is made up of an intraosseous section knitted to prevent deformation and abrasion and an intra-articular portion (longitudinal) to promote cell growth (Li & Chen, 2015).
- ii. Leeds Keio ligaments, comprised of polyester mesh, the porous nature of the Leeds Keio ligaments allows new tissue to grow into the mesh, helping the ligament integrate with the body over time (Iliadis *et al.*, 2016);
- iii. PGA Dacron artificial grafts: these are made from 75% biodegradable polyglycolic acid and 25% Dacron, offering a balance between strength and degradation. PGA degrades overtime allowing the body to replace it with natural tissue, while Dacron provides permanent support (Jia *et al.*, 2017).
- iv. Kennedy LAD ligaments- made of polypropylene ribbons and was designed to provide protection to a weak portion of quadriceps patellar tendon graft during anterior cruciate ligaments reconstruction (Dauner & Planck, 2015).

F. Artificial brain tissue

Artificial brains have been successfully grown as brain organoids made by self-arrangement of induced pluripotent stem cells and embryonic stem cells (Chen *et al.*, 2019; Qian *et al.*, 2019). Recent studies revealed the creation of 3D printed neural tissue (Zhu *et al.*, 2023). This artificial brain tissues are used mainly for drug testing, studying brain diseases and pathologies (Lovett *et al.*, 2020).

G. Artificial tendons

These are used for tendon repair or replacement. The most suitable scaffold use is a medium-chain length polyhydroxyalkanoate, a biodegradable, biocompatible material with hyper-elasticity and tensile strength like that of human tendon

flexibility (Tawonsawatruk *et al.*, 2023). First the MCL-PHA is dissolved in a solvent such as chloroform to create solution, this solution is then poured into a mold designed in a cylindrical shape with holes. A portion of human tendon are threaded into the holes as a suture; this design allows the integration and proliferation of the fibroblast cells and tenocytes cells on the surface of MCL-PHA scaffold (Pereira, 2016; Reddy *et al.*, 2022). Another scaffold used is Ortho-tape; a polyethylene terephthalate that is non-absorbable, woven with longitudinal and transverse fiber crossing at right angle. This is mostly used in Achilles tendon repair (Abdullah, 2015).

H. Synthetic vascular grafts

They are used to bypass damaged blood vessels, where autologous grafts are unavailable. Common materials used are Teflon® and Dacron® (Durán-Rey *et al.*, 2021). These materials have been used in medium to large-caliber vessels construction but not in grafts with diameters less than 6 mm due to thrombosis and intimal hyperplasia, leading to poor latency rates. (Durán-Rey *et al.*, 2021)

3.2.3. DECELLULARIZATION

Decellularization involves the removal of the cells and antigens from a biological tissue while preserving only the extracellular cell matrix. The cell removal is done by washing the tissues with chemicals detergent like SDS and triton-100 (Mendibil *et al.*, 2020), enzymatic digestion using trypsin (Gadre *et al.*, 2024) or freeze-thaw cycles (Ding *et al.*, 2022). Types are.

A. Decellularized heart valves: Artificial heart valve has been in use and successful for children with valve defects as they grow with the child. Bio prosthetic valves are usually made from animal tissue (heterograft/xenograft) preserved with glutaraldehyde to cross-link collagen fiber and reduce enzymatic degradation; porcine aortic valves are the most commonly use (Nguyen *et al.*, 2022); alternative to animal tissue valves are sometimes used, where valves are used from human donors, as in aortic homograft and pulmonary autografts (Nguyen *et al.*, 2022).

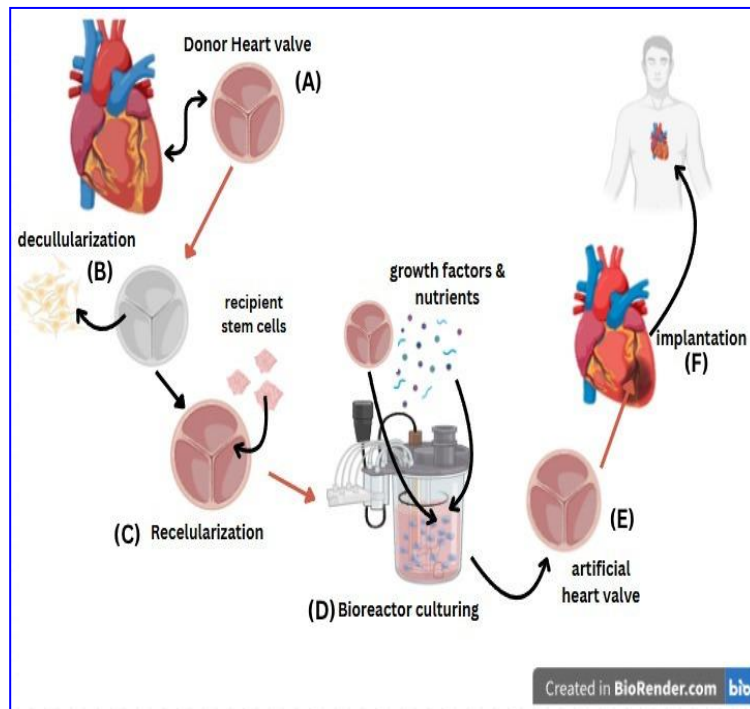


Figure 2.5: A decellularized heart valve. A is the biopsy of the donor heart valve. B is the removal of all the donor stem cells from the heart valve leaving behind only the ECM. C is the seeding of the recipient's stem cells onto the decellularized heart valve. D is placing the recellularized heart valve into the bioreactor with growth factors and nutrients to aid cell seeding and differentiation. E is the formation of an artificial health valve. F is the transplantation of the artificial heart valve onto the defected part of the heart. *Image created with biorender*

B. Decellularized whole heart tissues: The decellularized heart scaffold is injected with stems cells from the patient own cells to prevent rejection and better integration of stem cells i.e recellularization (Fujimoto *et al.*, 2020). The heart is then cultured in a bioreactor, providing it with essential nutrients and controlled environment to allows the cells to grow and mature in the decellularized heart scaffold thereby forming a functional artificial whole heart tissue. A successful clinical trial is the ghost heart done by Doris Dorcas, where the decellularized heart tissue is gotten from a pig (Duan, 2023).

C. Decellularized blood vessels: This decellularized vessels acts as a scaffold that can be implanted into the patient, own cells can populate this scaffold, making it a living part off their circulatory system (Kural *et al.*, 2022).

D. Decellularized trachea tissue: Tracheas from human cadavers or animal sources (e.g., pigs.) are commonly decellularized; then seeded with the recipient cells and cultured in a bioreactor. After fully grown trachea is achieved, it's then implanted into the recipient's body (Smith *et al.*, 2022; Brown & william, 2024)

E. Lab grown bladder: the decellularized bladder extracellular matrix is derived from porcine (pig source) bladder tissue to serve as scaffold; mesenchymal stem cells from human source are then seeded on this decellularized tissue; then cultured in a bioreactor to aid growth and maturation (Read *et al.*, 2024).

3.3. FUTURE RESEARCH AND INNOVATIONS

Researchers have developed new technology in order to overcome the challenges of engineering tissues. This is called microfluidics-organoid on chip. An organoid is a 3D cellular structure aimed at mimicking a specific organ (Silva-Pedrosa *et al.*, 2023). Organoids are stem-cell-derived replicas of organs that are capable of self-organizing and recapitulating the structural and functional characteristics of their derived organs (Azar *et al.*, 2021; Brassard & Lutolf, 2019). Microfluidic technology is also well-known for its capacity for controlling the cell culture using a network of micro-channels and micro chambers as well as controlled pressure/flow sensors (Mateusz *et al.*, 2023). The cells and the cell clusters are introduced to these microfluidics chips inside an extensive list of hydrogels to mimic the ECM. These microfluidics chips provide a dynamic environment for the cell culture as opposed to conventional methods where the cell culture is static (Mateusz *et al.*, 2023). 3D bio printing has gone a long way in replicating the 3D format of the human tissue influencing better cell integration into the scaffolds and less immunological rejection (Ventola, 2024).

4.0 DISCUSSION

Artificial tissue fabrication represents a remarkable intersection of biology, engineering, and material science, offering innovative solutions for regenerative medicine. Throughout this review, several key terms emerges, highlighting on the concept, the progress and challenges of this field.

Liao & Zhai (2018) reported that stem cells have the ability to differentiate into all cell types. Different types of stem cells including embryonic stem cells, induced pluripotent stem cells, and mesenchymal stem cells are the most commonly used because of their unique potentials. ESCs provide high differentiation capacity but pose ethical concerns but iPSCs offer a promising alternative with patient-specific applications, minimizing immune rejection and providing large scale of stem cells in vivo when needed. Although the availability of reliable cell sources remains a challenge, particularly in scaling up production for clinical applications and also vascularization of these stem cells during growth and development. Additionally, ensuring controlled differentiation and avoiding unwanted mutations are critical concerns in stem cell-based tissue engineering.

Scaffolds is the most essential concept as it's served as temporary extracellular matrices (Hussain *et al.*, 2023) guiding cell attachment, proliferation, and differentiation. The selection of biomaterials is crucial, with synthetic polymers (e.g., PLGA, PCL) and natural materials (e.g., collagen, chitosan) each presenting distinct advantages and benefits. Synthetic materials offer durable properties but usually have no binding site, so are using coated with adhesive proteins to create a binding site on its surface for cell attachments whereas natural materials support cell adhesion but may lack mechanical stability. The choice of fabrication techniques such as electrospinning, solvent casting, or 3D bio printing significantly influences scaffold properties. Despite technological advancements, achieving optimal pore structure, biodegradability, and bioactivity remains a persistent challenge in order to mimic the 3D structures of the human body (Hussain *et al.*, 2023)

Growth factors play a role in regulating cellular activities in the developing engineered tissues (Goonoo & Bhaw-Luximon, 2019). Key growth factors such as VEGF and TGF-beta into scaffolds or bioreactors due to their ability in angiogenesis and cell differentiation respectively. However, maintaining controlled release of growth factors is a challenge as excessive or insufficient exposure can lead to undesired cellular responses. Strategies such as encapsulation in nanoparticles and tethering growth factors into scaffold matrices have improved growth factors delivery. Bioreactors provide dynamic environments that enhance tissue maturation

by replicating physiological conditions such as mechanical stimulation, nutrient flow, and oxygenation. Systems like perfusion bioreactors and rotating wall vessels have demonstrated improved tissue functionality compared to static cultures. Also, maintaining sterility and preventing contamination remains a critical aspect tissue engineering (Naveen *et al.*, 2018).

Stem cell-only based Tissue fabrication relies solely on cell self-organization to recreate biological issues without the use scaffolds (De Pieri *et al.*, 2021). While it eliminates concerns regarding biocompatibility, it often results in mechanically weak tissues.

Cell and Scaffold-Based Tissue fabrication is most widely used strategy but mimicking the 3D structure of native tissues remains a challenge, particularly in complex organs with specialized cell functions such as liver and kidney (Pati *et al.*, 2016). Additionally, repopulating decellularized scaffolds with patient-specific cells remains a key component scientist are trying to provide although induced stem cells show a promising potential (He *et al.*, 2024)

Advances in artificial tissue fabrication are the use of 3D bioprinting and organ-on-a-chip models in improving bio fabrication, enhanced vascularization and immune responses.

CONCLUSION

Artificial tissue fabrication represents a transformative approach in regenerative medicine, with anatomy serving as its foundational component. The integration of anatomical knowledge into tissue engineering processes is essential for replicating the complexity and functionality of native tissues. Continued interdisciplinary research will drive future innovations, making artificial tissues a viable solution for medical challenges, reduction of organ donor and a more conventional surgical practice.

RECOMMENDATIONS

1. Enhancing Vascularization and Functional Maturity: Integrating advanced fabricate pre-vascularized scaffolds

2. Improving Scaffold Design and Material Selection: Developing 3D mimicked and biocompatible scaffolds that can better replicate the natural ECM.
3. Addressing Immune Reaction and Biocompatibility: Utilizes patient-specific cells to minimize immune response. Usage of engineered immune-tolerant biomaterials that reduce inflammatory reactions after implantation. Also, the Implementation of immunomodulatory strategies, such as coating scaffolds with anti-inflammatory agents.
4. Acceptance in the clinical world: most people believe artificial tissues are not as functional as a human donor tissue thereby inhibiting the utilizations in the medical world. If these tissues are being used more, the lesser the stereotypes would be.
5. As an anatomy course: if this topic is being introduced as a new course, this will open new mindset to this topic, thereby creating more innovative minds and ideas to concur some of these limitations.

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