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Advancing Plastic Surgery Through Tissue Engineering

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ABSTRACT

Tissue engineering (TE), once a concept confined to the realm of imagination, is now rapidly emerging as an independent field in medicine and seamlessly integrating into various other specialties. The flexibility of the discipline allows for tissue engineering to be included in multiple medical fields. The specialty of plastic surgery is heavily affected by tissue engineering because of the many scenarios of use in the field, as well as the advantages of using TE. These reasons have led to tissue engineering gaining a reputation of being considered an ideal solution to many problems. This article gathers and compiles research from previous papers similar to this topic and highlights how TE is a large factor in plastic surgery as well as describes the discipline and procedure of tissue engineering. In order to successfully complete the process, a certain procedure must be completed. This includes harvesting and developing tissue, attaching the new graph, and rehabilitation of the injury. However, like other methods of treatment, there is a probability that complications could occur during the process. For example, the newly created graft could be rejected by the patient. An additional factor that must be addressed is accessibility, which is limited due to the experimental nature as well as the cost of the field. All of these factors show the advantages and disadvantages of the discipline. The significance of this paper is to show how tissue engineering can be performed with the appropriate cells and highlight the capabilities of tissue engineering in plastic surgery.

Introduction

Many people worldwide have experienced physical trauma, congenital deformities, cancer-related surgeries, or more causes that create the need for tissue engineering. Tissue engineering is a multistep process in which cells are harvested from the patient, grown, and placed back into the patient. In tissue engineering, cells are harvested from the patient in order to cultivate and rebuild more tissue. This new tissue can then be surgically placed back into the patient, causing their tissue loss to be resolved. According to (Rogers, 2019), researchers in the late 1980s came across the idea of tissue engineering. Now it has formed its growing medical field. A central concept in TE is the concept of cell culture, which is when microorganisms are grown in a laboratory away from the primary organism and are programmed to create multiple cells. After the process of cell culture, the newly grown cells are placed in tissue scaffolding and prepped before surgically joining back with the patient in need of new tissue.

There are multiple techniques to place the tissue back into the patient which will be mentioned in the following article. Tissue engineering is widely used in plastic surgery and can be used in people injured or complicated by car crashes, deformities, thermal injuries, and many more scenarios. This article is intended to fill the gap which is the understanding of tissue engineering and describe the process for others to learn and improve their knowledge of the topic. Some limitations in previous work that this article will address include how to incorporate and place the newly generated cells back into the patient. This will cover how to perform tissue engineering, its advantages, challenges in the process, rehabilitation, and accessibility. What is tissue engineering, and how is it performed? How does it relate to the field of plastic surgery?

Scenarios of Use for Tissue Engineering

There are multiple scenarios in which tissue engineering can be functional and effective in plastic surgery. TE allows for situations in which alternative surgical operations are limited as a result of complications or effectiveness in the scenario. Tissue Engineering finds a solution to many of these complications by creating healthy tissue from the patient's already existing cells, making it a safer and more reliable option as opposed to other methods of cell replacement such as bioprinting. Some scenarios where tissue engineering has an advantage include car accidents/physical trauma, thermal injuries, congenital deformities, and cancer-related surgeries, especially brain cancers. All of these complications give rise to the primary need for TE and are situations where the discipline is commonly applied. "These range from injury due to events such as car accidents and sports-related trauma, to neurodegenerative diseases such as Alzheimer's disease and amyotrophic lateral sclerosis…This leaves a crucial area for investigation and development into possible tissue engineering solutions" (Lynch et al., 2021). As described by Lynch, Kondiah, and Choonara (2021), there is a large area where tissue engineering can be operated when in relation to these injuries. Overall, there are multiple ways and scenarios in which to use TE, knowing that it is a suitable option. As this medical discipline grows and evolves, the number of scenarios will only increase, making it also a more accessible option as well.

Advantages of Using Tissue Engineering

As previously stated, the multiple advantages in the discipline of tissue engineering outweigh the advantages of other methods for tissue transportation and replacement. Other methods to replace tissue, including transplants, decellularized organs, or 3D printing have a higher risk for hazard when compared to tissue engineering. These examples of alternative methods have solutions that commonly make the newly formed cells being transported into the patient much more difficult to bind to the already existing cells in order to heal the injury that was sustained. This leads to a higher risk of the patient rejecting the new cells with further possible complications including infections and the possible transmission of other diseases from transplanted tissue. In tissue engineering, however, there is more localized toxicity near the area of injury, creating less of a risk for any further complications. This is also the reason why TE is more commonly used during cancer-related surgeries."A distinctive feature of tissue engineering is to regenerate a patient's own tissues and organs that are entirely free of poor biocompatibility and low biofunctionality as well as severe immune rejection. Owing to the outstanding advantages, tissue engineering is often considered as an ultimately ideal medical treatment" (Ikada, 2006). As stated by Ikada (2006), rejection of tissue is a much more declined risk when using TE since the cells that have been developed are already familiar with the patient's existing cells and vice versa. In short, TE is a much more reliable solution when compared to other methods of tissue replacement.

Harvesting and Developing Cells

There are certain steps and methods that need to be followed in order to successfully perform the discipline of tissue engineering. In order to begin the process, a medical professional must harvest cells from the patient in need of cells. "Harvesting is performed by separating the cell culture from the growing medium and several techniques are used to perform this delicate operation; centrifugation, microfiltration, depth filtration and filtration through absolute pore size membranes" (Cell Harvesting - Getting Cultural, 2009). According to Cell Harvesting - Getting Cultural (2009), centrifugation is the more frequently used method in order to harvest cells due to the fact that it can be done at levels of factory production. Centrifugation is the process in which an instrument called a centrifuge is used in order to separate liquids as a way of harvesting cells. An alternative common technique used to harvest cells is biopsies. This is when tissue is extracted from the patient in order to use the cells during the process of tissue engineering. Cells that can be used during TE include tissues from adult stem cells, morula, fetal cells, and somatic cells.

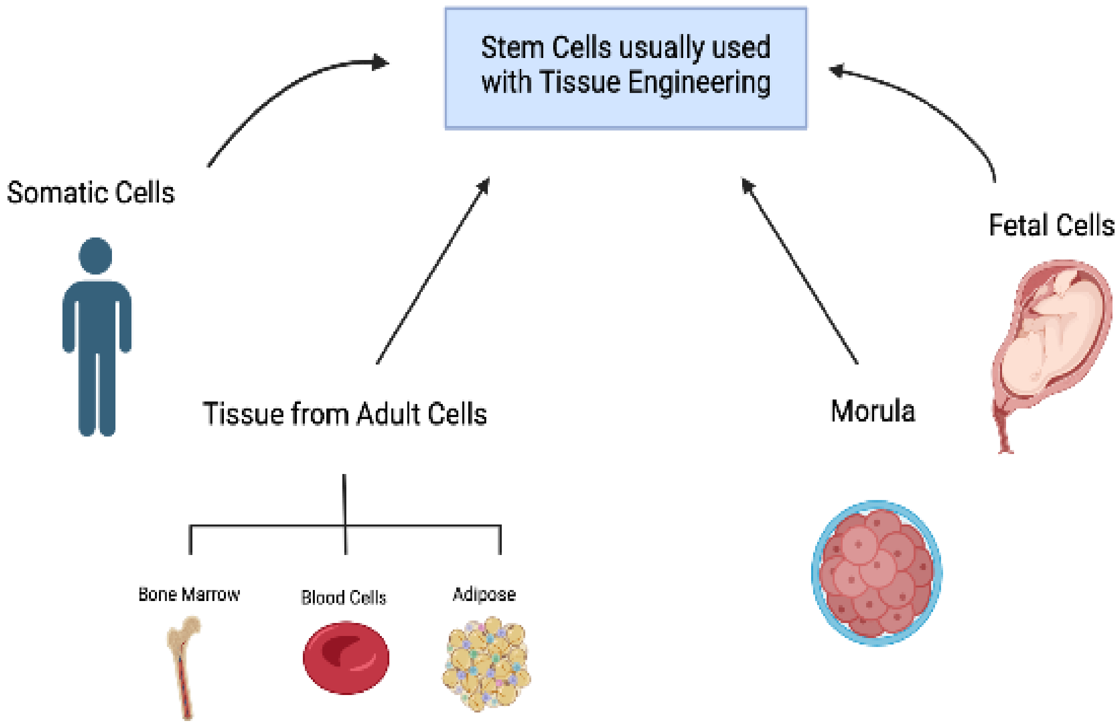

Figure 1. The diagram above describes the stem cells in which tissue engineering can be and is commonly used in order to successfully complete the discipline. This diagram was created by the author using BioRender.

These cells are also the most commonly used since they are the easiest to heal and develop with scaffolding. In order to maintain these cells in a laboratory, a proper environment is needed. This means the cells need to have a cell scaffold, which allows the cells to continue to proliferate and grow. These scaffolds can be created with various different polymeric biomaterials (Chan, Leong, 2008). “The very first criterion of any scaffold for tissue engineering is that it must be biocompatible; cells must adhere, function normally, and migrate onto the surface and eventually through the scaffold and begin to proliferate” (O’Brien, 2011). These scaffolds must have strength and size which cannot be reached without proper vascularization. If not, these scaffolds will not keep shape during the implementation of the cells (O’Brien, 2011). Another factor that cells depend on during the process of cell culture includes growth factors. Growth factors are used in order to ensure the health of the tissue, assist the cells during the process of proliferation, as well as give the cells the nutrients in order to survive the process. There are specific growth factors for different scenarios and cells. For example, epidermal growth factor (EGF receptor) for developing and cultivating epidermal cells. Growth factor receptors (GFR) are crucial for the health of the cells going through cell culture in order to survive. The last factor that is needed to ensure the cells stay healthy is mechanical stimuli. “Mechanical stimulation during tissue culture can be an effective strategy to enhance the mechanical, structural, and cellular properties of tissue-engineered constructs” (Salinas, et al., 2018). As stated with the quote by Salinas, Hu, Athanasiou (2018), these stimuli allow for the tissue to become much more effective as well as strengthen its architecture and structure. Without this factor, the cells will most likely not keep their shape and will break apart during the reinstallation of the tissue. Overall, there is a process that needs to be followed in order to successfully and safely complete the growth and harvesting of stem cells.

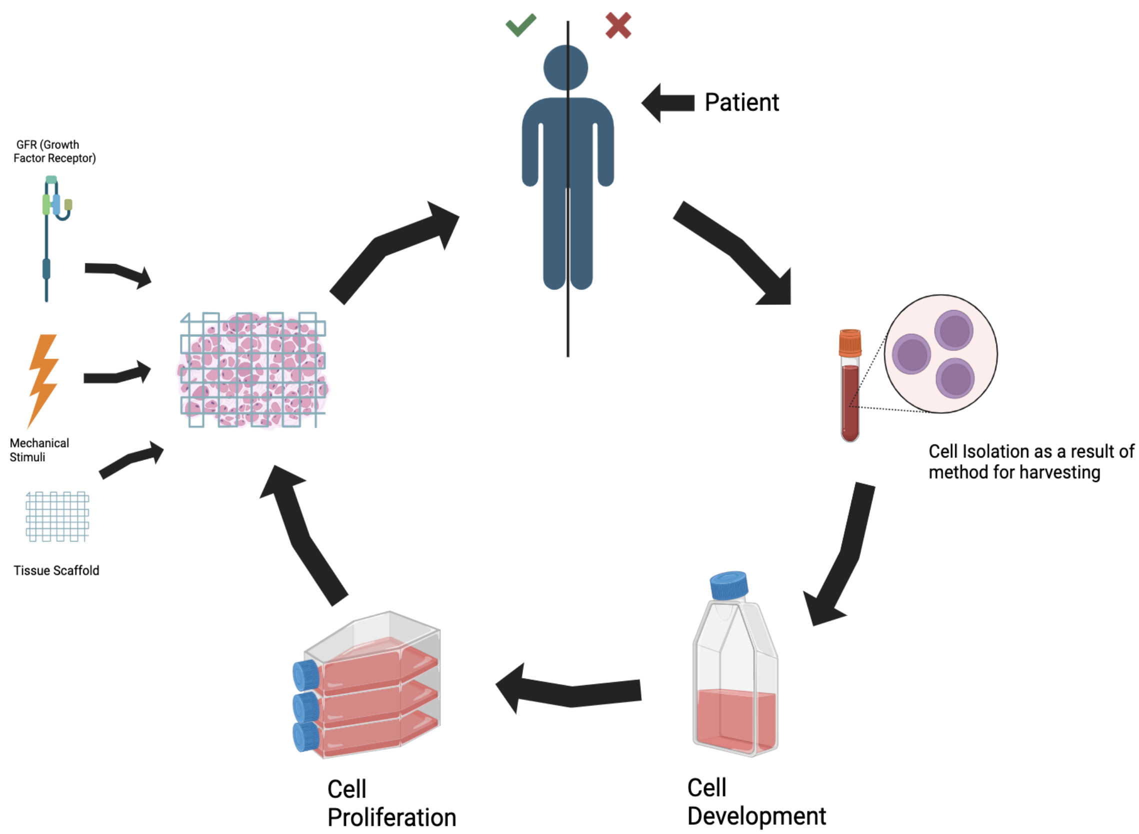

Figure 2. The diagram above describes the cycle that the isolated cells from the patient must undergo in order to be prepared for transportation and reinstallation back into the patient's body. In addition, the diagram also describes the essential factors which are required in the process. This diagram was created by the author using BioRender.

Reattaching Newly Grown Cells to Patient

To reattach cells that have undergone the process of cell culture and are ready to be reunited with the patient, there is a process that must be followed in order to successfully accomplish cell transportation. In order to accomplish the process, you first have to cultivate and finish allowing for the cell to grow and develop in its given scaffold. This is usually after the time it has used almost all of the nutrients it was given (GFR, mechanical stimuli, environment, etc.) and finished the process of proliferation. Proliferation is the process when the cell starts to divide into multiple cells and keeps multiplying until it has nearly filled the scaffold and used the nutrients. "This is a fertile and important area for tissue-engineering research – too little cell proliferation and the construct cells will die before native cells can take over; too much cell proliferation and we descend into areas of potential neoplasia as a result of engineered graft introduction" (Sarraf et al., 2005). Then the scaffold with the cells still attached is carefully removed from wherever it was placed to allow it to grow. A petri dish is usually used to house the scaffold in order for the cells to grow. When the scaffold is removed, it is then placed back into the area of injury in the patient. This is the beginning of the process of healing where the injured area starts to reform and go back to its original state with the help of the new cells and scaffold. The length of the process depends on the severity of the injury and the type of injury that the patient sustained. For example, if a scaffold is placed into a fractured bone, it could take up to twenty days to a month, depending on how serious the injury is.

Challenges and Potential Complications in Tissue Reattachment

If the process of tissue engineering is not performed correctly, there could potentially be complications and other challenges. An example of one of these complications could be the rejection of the newly engineered graft. Though tissue engineering has a much lower risk of rejection when compared to other methods of tissue transportation, there is still a possibility that the already existing cells reject the new tissue. According to Janeway (2001), There are multiple reasons for possible graft rejection of the new tissue, including reactions to alloantigens, endothelial rejection, and more. This most likely would destroy and kill the new tissue, eventually causing the possibility of further complications throughout the patient's entire body. "One of the major goals of regenerative medicine is repair or replacement of diseased and damaged tissues by transfer of differentiated stem cells or stem cell-derived tissues. The possibility that these tissues will be destroyed by immunological rejection remains a challenge" (Bolton, Bradley, 2015). As described by Bolton, Bradley (2015), in order for the success of the process to be guaranteed, the chance of rejection must be first resolved. A second complication that could take place is infection in the area of injury. If the area of injury and new tissue do not properly heal, it could result in foreign microbes entering through the site of injury. Tumorigenicity is also a possibility when it comes to tissue engineering. This is described as the area becoming prone to producing tumors. "Tumorigenesis destabilises normal tissue architecture and thus throws forces in the affected tissue out of balance" (Papalazarou, et al., 2018). When the new tissue is attached, there is also a possibility of the new tissue not being supplied with enough blood, eventually leading to the tissue becoming unhealthy or dying. This is the reason the blood flow must be monitored after the operation in order to ensure the health of the tissue. Overall, there are possibilities for complications in tissue engineering as well as challenges that need to be faced during the process.

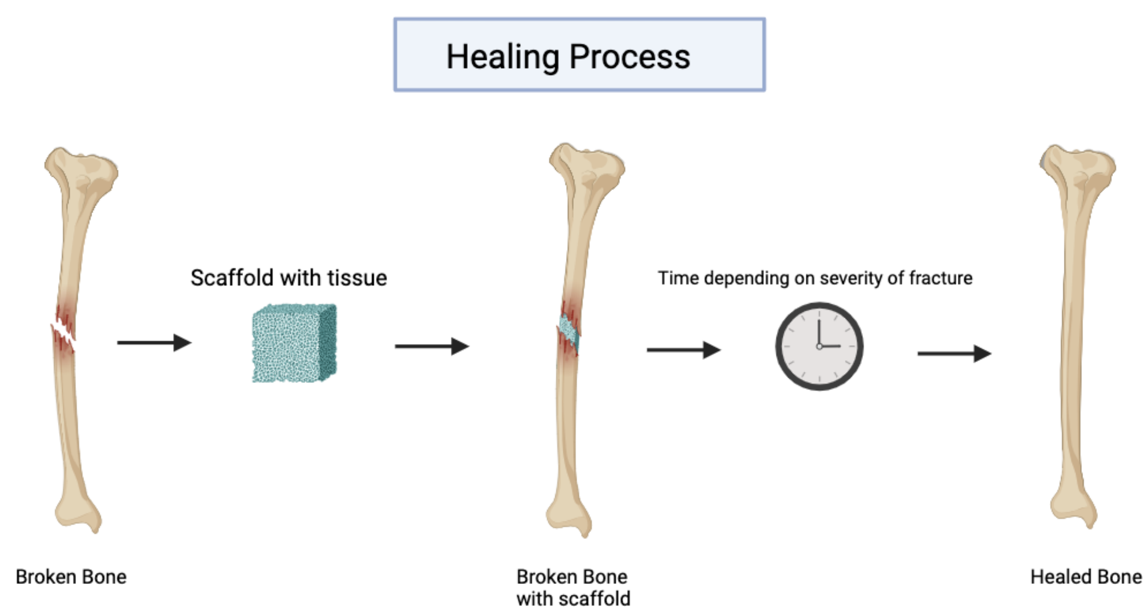

Figure 3. The diagram above describes the process of healing within tissue engineering as well as the factors included within the process. This diagram was created by the author using BioRender.

Rehabilitation and Recovery Process

Even if the process of tissue engineering is properly performed, it must be monitored after surgery. A major priority for post-operative care would be scar management and reducing the chance of infection reduced. If not, this could end up being detrimental to the health of the patient as well as the new graft. "Wound healing is a natural physiological reaction to tissue injury. However, wound healing is not a simple phenomenon but involves a complex interplay between numerous cell types, cytokines, mediators, and the vascular system" (Wallace, 2023). As the quote by Wallace (2023) stated, wound healing requires multiple factors in order to be carried out successfully. In order for wounds to heal correctly, they must be treated and evaluated by medical professionals with appropriate instruments. Most wounds generally can heal in 4 to 6 weeks, though this number is based on the severity of the wound as well as how serious the injury could be. Depending on the type of injury, a further concern in post-operative care for TE would be physical therapy and rehabilitation exercises in order to gain back functional mobility and strength. Knee injuries, muscle injuries, etc. are all examples of injuries that can be healed with TE and are also healed with physical therapy. This is an essential factor in order for the patient to become healthy. In all, there are multiple steps that need to be followed in order to keep the new tissue healthy and alive.

Cost and Accessibility

Since tissue engineering is still a growing field in its earlier stages, the cost and accessibility are non-optimal. "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" (Tissue Engineering and Regenerative Medicine, n.d.). Since the process is deemed experimental, insurance will probably not be able to cover the surgery. "Even when they are in the market, the treatments are usually labeled 'investigational' or 'experimental', which means that the treatments may not be reimbursable under most insurance schemes. The question arises as to whether tissue engineering will ever be deemed cost-effective" (Williams, 2004). As a result, tissue engineering will not be available to most families until the cost of surgery becomes more effective. Overall, tissue engineering is not very cost-effective and is limited to a certain number of people.

Conclusion

In all, tissue engineering is a reliable way to cultivate tissue and implement it back into the patient. It is a solution to many problems and is considered by some an ideal treatment. Tissue engineering is frequently used in multiple scenarios and is very commonly used in the field of plastic surgery. Some examples of scenarios include thermal injuries, cancer-related surgeries, congenital deformities, and more. To perform tissue engineering, there is a process and steps that must be followed in order to carry out the procedure successfully. The advantages of tissue engineering include less of a risk for graft rejection, minimized toxicity, and more. Some possible complications of tissue engineering can be tumorigenesis, inflection, and more. Rehabilitation, cost, and accessibility depend on the severity and seriousness of the injury. All in all, tissue engineering is a growing medical field that keeps constantly evolving due to technological advancements. As time passes, this semi-experimental will become polished and be more accessible to people around the globe in order to become a solution to problems involving plastic surgery and others.

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References

Rogers, K. (2018). Tissue Engineering. Encyclopedia Britannica. https://www.britannica.com/science/tissue-engineering

Lynch, C. R., Kondiah, P. P. D., & Choonara, Y. E. (2021). Advanced Strategies for Tissue Engineering in Regenerative Medicine: A Biofabrication and Biopolymer Perspective. *Molecules (Basel, Switzerland)*, *26*(9), 2518. https://doi.org/10.3390/molecules26092518

Ikada Y. (2006). Challenges in tissue engineering. Journal of the Royal Society, Interface, 3(10), 589–601. https://doi.org/10.1098/rsif.2006.0124

Cell harvesting — getting cultural. (2009e, March 18). Filtration and Separation. https://www.filtsep.com/content/features/cell-harvesting-getting-cultural/#:~:text=Harvesting%20is%20performed%20by%20separating,through%20absolute%20pore%20size%20membranes.

Chan, B. P., & Leong, K. W. (2008). Scaffolding in tissue engineering: general approaches and tissue-specific considerations. *European spine journal : official publication of the European Spine Society, the European Spinal Deformity Society, and the European Section of the Cervical Spine Research Society*, *17 Suppl 4*(Suppl 4), 467–479. https://doi.org/10.1007/s00586-008-0745-3

O'Brien, F. J. (2011). Biomaterials & scaffolds for tissue engineering. *Materials Today*, *14*(3), 88–95. https://doi.org/10.1016/s1369-7021(11)70058-x

Salinas, E. Y., Hu, J. C., & Athanasiou, K. (2018). A Guide for Using Mechanical Stimulation to Enhance Tissue-Engineered Articular Cartilage Properties. Tissue engineering. Part B, Reviews, 24(5), 345–358. https://doi.org/10.1089/ten.TEB.2018.0006

Sarraf, C. E., Harris, A. B., McCulloch, A. D., & Eastwood, M. (2005). Cell proliferation rates in an artificial tissue-engineered environment. Cell proliferation, 38(4), 215–221. https://doi.org/10.1111/j.1365-2184.2005.00347.x

Janeway, C. A., Jr. (2001). *Responses to alloantigens and transplant rejection*. Immunobiology - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK27163/#:~:text=Rejection%20is%20caused%20by%20immune,as%20foreign%20by%20the%20recipient

Bolton, E. M., & Bradley, J. A. (2015). Avoiding immunological rejection in regenerative medicine. Regenerative medicine, 10(3), 287–304. https://doi.org/10.2217/rme.15.11

Papalazarou, V., Salmeron-Sanchez, M., & Machesky, L. M. (2018). Tissue engineering the cancer microenvironment-challenges and opportunities. Biophysical reviews, 10(6), 1695–1711. https://doi.org/10.1007/s12551-018-0466-8

Wallace, H. A. (2023, March 7). Wound healing phases. StatPearls - NCBI Bookshelf. https://www.ncbi.nlm.nih.gov/books/NBK470443/

Tissue engineering and regenerative medicine. (n.d.-b). National Institute of Biomedical Imaging and Bioengineering. https://www.nibib.nih.gov/science-education/science-topics/tissue-engineering-and-regenerative-medicine

Williams, D. (2004). Benefit and risk in tissue engineering. Materials Today, 7(5), 24–29. https://doi.org/10.1016/s1369-7021(04)00232-9

Su, X., Wang, T., & Guo, S. (2021). Applications of 3D printed bone tissue engineering scaffolds in the stem cell field. Regenerative therapy, 16, 63–72. https://doi.org/10.1016/j.reth.2021.01.007

Tavelli, L., McGuire, M. K., Zucchelli, G., Rasperini, G., Feinberg, S. E., Wang, H. L., & Giannobile, W. V. (2020). Biologics-based regenerative technologies for periodontal soft tissue engineering. Journal of periodontology, 91(2), 147–154. https://doi.org/10.1002/JPER.19-0352

Simunovic, F., & Finkenzeller, G. (2021). Vascularization Strategies in Bone Tissue Engineering. Cells, 10(7), 1749. https://doi.org/10.3390/cells10071749

Walgenbach, K. J., Voigt, M., Riabikhin, A. W., Andree, C., Schaefer, D. J., Galla, T. J., & Björn, G. (2001). Tissue engineering in plastic reconstructive surgery. The Anatomical record, 263(4), 372–378. https://doi.org/10.1002/ar.1117

Heinrich, M. A., Liu, W., Jimenez, A., Yang, J., Akpek, A., Liu, X., Pi, Q., Mu, X., Hu, N., Schiffelers, R. M., Prakash, J., Xie, J., & Zhang, Y. S. (2019). 3D Bioprinting: from Benches to Translational Applications. Small (Weinheim an der Bergstrasse, Germany), 15(23), e1805510. https://doi.org/10.1002/smll.201805510

Ambekar, R. S., & Kandasubramanian, B. (2019). Progress in the advancement of Porous Biopolymer Scaffold: Tissue Engineering application. Industrial & Engineering Chemistry Research, 58(16), 6163–6194. https://doi.org/10.1021/acs.iecr.8b05334

Al-Himdani, S., Jessop, Z. M., Al-Sabah, A., Combellack, E., Ibrahim, A., Doak, S. H., Hart, A. M., Archer, C. W., Thornton, C. A., & Whitaker, I. S. (2017). Tissue-Engineered Solutions in Plastic and Reconstructive Surgery: Principles and Practice. Frontiers in surgery, 4, 4. https://doi.org/10.3389/fsurg.2017.00004

Bio science. (2020, March 18). Tissue engineering | Technique | Procedure | Bio science [Video]. YouTube. https://www.youtube.com/watch?v=Mktxmj41cR8