Proposal of a Bioinspired Patch for the Real-time Monitoring of Neurological Trauma

Wei Luo *

College of Arts and Sciences, The University of North Carolina at Chapel Hill, Chapel Hill, 27514, United States

* Corresponding author email: luow7@ad.unc.edu

Abstract. Neurological trauma, damage to the brain, spine, or nerves, can happen as a result of both neurosurgery and vehicle accidents. It may be risky to cause damage during surgery because of humans' ineffective capacity to repair neurons; as a result, the market may require a medical device specifically made to address this problem. The accessory limb model (ALM), one of the most typical regeneration models, has demonstrated that it has significant potential to improve regeneration outcomes and might be used for the regeneration of human brain tissues. Nowadays, many implanted medical devices interact with circuitry outside the body via cables or wireless RF telemetry. However, wires usually result in a huge chance to increase surgical difficulties such as wire breakage, infection, and electrical noise. Intrabody communication, as a result, became a preferable and safer way of communication in the design of implantable medical devices, and is used in the device introduced in this article.

Keywords: Neurosurgery; Regeneration; Medical Device.

1. Introduction

Scientists have been studying tissue regeneration for years in an effort to enhance humans' and other species' limited capacity to replace damaged or injured neurons in the brain. The development of the Accessory Limb Model, which was created as a gain-of-function examination in axolotls for the exploration of effective regeneration, marks recent advancement. Normally, vertebrates are capable of regenerating various organs, such as the tissues in the central nervous system. Among those vertebrates, urodele amphibians like the axolotl, have the special ability to repair the spinal cord and some parts of the brain after mechanical injury, showing a potential clinical use in neurosurgery [1].

Yet, surgeries are unpredictable, it is possible to damage brain tissues during surgery, therefore a method of solving such an emergent situation is needed. Neurosurgery is a precision surgery that requires a lot of concentration from the surgeons, an accident injury to brain tissues will interrupt the entire process of the surgery, so a monitoring device is also preferable in surgery. Up till now, wireless radiofrequency telemetry (RF) has been widely used in multiple implantable medical devices in order to avoid complications caused by wires during surgery. Unfortunately, wireless RF telemetry still faces a lot of obstacles due to its significant power requirement and weak transmission of signals through tissues. This low-efficiency transmission is later improved by an alternative method called galvanic intrabody communication, which has been proven to be a more effective way of communication from studies of various applications of implanted medical devices [2].

Nonetheless, there is still a lack of practical and efficient applications which utilize these two features to manufacture an integrated device that resolves the accident injury during surgery. This article introduces a potential design of a microdevice that can cope with emergent trauma in surgery and provides real-time monitoring of trauma recovery.

2. Design Proposal

2.1 Design Overview

Due to the axolotl's enormous potential to improve regenerative outcomes, its prospective application as a bioink material for the regeneration of human tissue has been widely discussed. The resurgence of the axolotl as a model regenerative system and the convergence of tissue engineering enables the creation of novel methods for engineering successful regeneration. Among these mechanisms, the ability to govern the progenitor cells is the key factor for the success of tissue regeneration [3]. Intrabody communication is a newly proposed communication technique that enables a more efficient way of wireless communication with implanted devices by utilizing the body's natural conductive qualities to transmit signals [4]. Therefore, it is theoretically possible to manufacture a 'first-aid' medical device that can achieve efficient wound dressing for physical injuries during neurosurgery and wirelessly monitor the wound's conditions over time, preventing the entire surgery process to be messed up. It is also applicable for general drug delivery and spinal cord or brain signal monitoring via microsurgery.

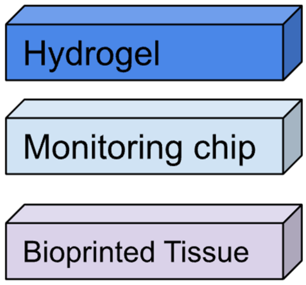

Figure 1. A schematic view of the design structure

As it is shown in Figure 1, this is a tri-layer-structured microdevice. The bottom layer, which is directly in contact with the testing spot, is made of a piece of bioprinted tissue and is designed for drug delivery and tissue regeneration. A signal-detecting device will be stacked on the tissue and is responsible for recording the fluctuations in biosignals around the testing spot and transmitting data to vitro devices. Bioimages can therefore be made from this data acquisition, further analysis of the images is required to obtain the regeneration progress in the testing area. The top layer will be an Antibacterial Hydrogel which is effective in wound healing [5]. The dehydration property of hydrogel will spontaneously resize itself, causing the margin of the wound to be closer to each other and resulting in a less time-consuming process.

2.2 Fabrications and Methods

2.2.1. Bottom Layer

The bottom layer of the patch will be manufactured via 3D Bioprinting, which integrates biomaterial scaffolds and cells to produce alternatives for damaged tissues. Bioprinting manufactures substitutes for diseased tissues by placing cells enclosed in specific bioinks at precise positions within the final constructions [6]. The majority of 3D bioprinting methods fall into two categories: nozzle-based, such as droplet- and extrusion-based bioprinting; and light-enabled, such as stereolithography apparatus-based, two-photon polymerization-based, laser-assisted, and computed axial lithography bioprinting [7, 8]. Extrusion-based bioprinting, which works with a variety of biocompatible materials, is now the most popular bioprinting technique.

The bio ink is often inserted in a syringe-like tool used in extrusion-based 3D bioprinting as shown in Figure 2, which uses pistons to control the pneumatic pressure and mechanical force so that the bioink can be driven through the nozzle [8]. This method of bioprinting allows for the rapid deposition of bio inks with high viscosity and cell concentrations, which would be suitable for axolotl stem cells. As a crucial component of 3D bioprinting, bio inks must satisfy a number of requirements, such as sufficient biocompatibility, biological qualities, providing growth support for cells, etc [9–10]. For 3D bioprinting, modifiable materials are frequently employed, such as ion-cross-linkable hydrogels, temperature-sensitive polymers, and photopolymer bio inks. 3D bioprinting allows for the rapid creation of human tissues, which can be used to assess potential drug targets. The axolotl will be used in the creation of this bioinspired healing patch as a specialized bio ink that produces reproducible and effective human tissues derived from the axolotl's stem cells, thus forming the healing patch's base layer.

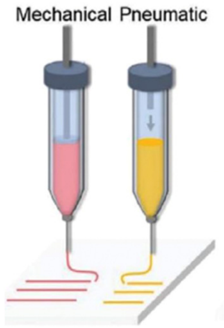

Figure 2. Schematic of extrusion-based bioprinting

The axolotl can regenerate a variety of organs, but whether the tissue it creates is appropriate for the brain injury is a crucial consideration in this design because it directly affects how well the brain functions again.

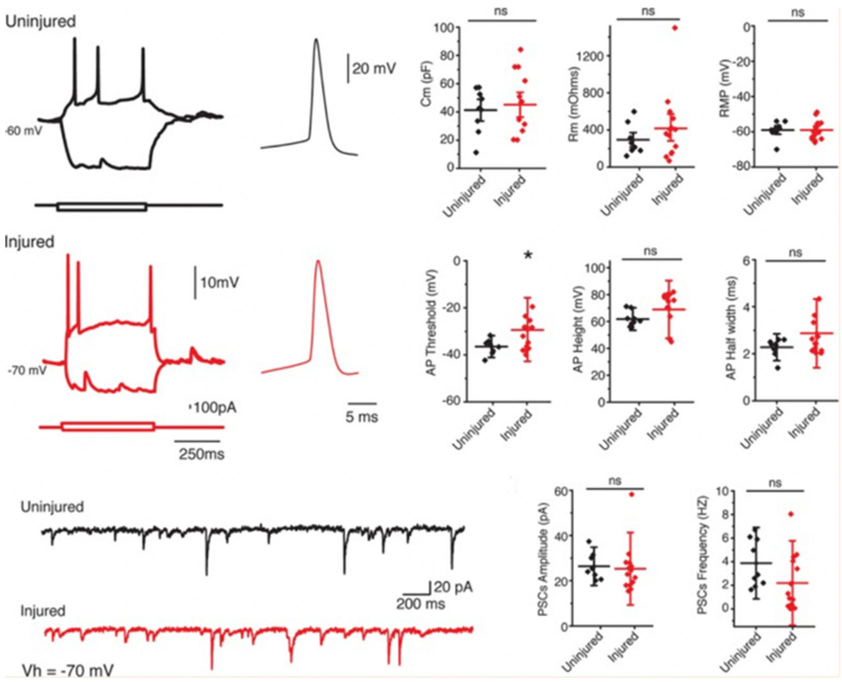

Figure 3. Experimental data in Amamoto, et al.'s research

Amamoto, et al. have revealed the solution to this mystery in their research. They have examined whether the functional features such as the tissue structure and connectivity can recover after mechanical injury in a wide range of neuronal subtypes via the model system of adult axolotl pallium. The data shown in Figure 3 provide proof for the similarity in electrophysiological features between regenerated neurons and uninjured neurons, proving a feasibility of using axolotls as the bioink to produce the brain tissue for accident injuries [11].

2.2.2. Signal Detecting and Monitoring

The signal-detecting sensor will use implant-to-implant communication. The electrical and biological signals will be collected in the implanted device and sent through this transmission to receiver electrodes, which can be wirelessly RF telemetered to equipment outside the body. By using this communication, there will be less power required to tranmit signals to the implanted reception electrodes compared to the circumstances when electrodes are placed on the skin. One successful approach was done by Al-Ashmouny et al., who created a two-electrode device and put it to the test on a rat under anesthesia, and it turned out to work [4].

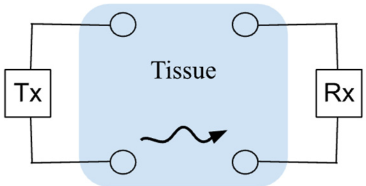

Figure 4. A schematic view of the implant-to-implant communication

As illustrated in Figure 4, the technique employed two electrodes interface with the tissue, one is for transmitting signals and the other is for signal receiving. Both electrodes will be made of platinum-iridium wire with a diameter of 50 m. The signal transmitting electrode is an insulated complementary metal–oxide–semiconductor chip with a volume less than 1 mm^3, and is responsible for the transmission of alternating current signals to the signal receiving site. In the experiment, both electrodes were embedded in rat's brain, and it turned out that the channel from the current to the transmitter had a greater resistance compared to the channel which went through the brain to the receiving site because of the isolation of circuit ground of the transmitting electrode from the tissue. As a result, the signal was sent to the recording location with great efficiency, demonstrating that signals may be successfully incorporated into a real-time monitoring system.

2.2.3. Top Layer

Wound dressings can be used to cover the injury and offer a momentary shield to external infections. Acting like an induction template, the wound dressings can also help direct the reorganization of epidermal cells, subsequent infiltration as well as the integration of host tissues. To promote wound healing, a variety of wound dressings have been manufactured, including hydrocolloids, semipermeable membranes, and semipermeable foams. Hydrogels, as one of the most popular wound dressing materials, are the most competitive choices nowadays because of their superior hydrophilicity, biocompatibility, and extracellular matrix with a three-dimensional (3D) porous structure [12]. Accordingly, the device will be fused with a hydrogel layer on top to enhance the wound-healing process.

3. Conclusion

The combination of ALM and galvanic intrabody communication provides a feasible solution of how a biomaterial can be best interfaced with a monitoring device for constructing a novel form of a bioinspired wound healing patch for neurosurgery. This proposal highlights the extraordinary regenerative ability of adult axolotls and the use of implant-to-implant communication by referring to data evidence from former successful research. However, this proposal is lack of vitro and vivo experiments to prove the feasibility of its structure, further investigation is still required to study this design.

References

[1] Seyedhassantehrani, N., Otsuka, T., Singh, S., & Gardiner, D. M. (2017). The Axolotl Limb Regeneration Model as a Discovery Tool for Engineering the Stem Cell Niche. Current stem cell reports, 3(3), 156–163.

[2] Benabid, A. L., Chabardes, S., Mitrofanis, J., & Pollak, P. (2009). Deep brain stimulation of the subthalamic nucleus for the treatment of Parkinson's disease. The Lancet. Neurology, 8(1), 67–81.

[3] Bryant, S. V., Endo, T., & Gardiner, D. M. (2002). Vertebrate limb regeneration and the origin of limb stem cells. The International journal of developmental biology, 46(7), 887–896.

[4] Ferguson, J. E., & Redish, A. D. (2011). Wireless communication with implanted medical devices using the conductive properties of the body. Expert review of medical devices, 8(4), 427–433.

[5] Martino, M. M., Briquez, P. S., Ranga, A., Lutolf, M. P., & Hubbell, J. A. (2013). Heparin-binding domain of fibrin(ogen) binds growth factors and promotes tissue repair when incorporated within a synthetic matrix. Proceedings of the National Academy of Sciences of the United States of America, 110(12), 4563–4568.

[6] Tasnim, N., De la Vega, L., Anil Kumar, S., Abelseth, L., Alonzo, M., Amereh, M., Joddar, B., & Willerth, S. M. (2018). 3D Bioprinting Stem Cell Derived Tissues. Cellular and molecular bioengineering, 11(4), 219–240.

[7] Tang, M., Rich, J. N., & Chen, S. (2021). Biomaterials and 3D Bioprinting Strategies to Model Glioblastoma and the Blood-Brain Barrier. Advanced materials (Deerfield Beach, Fla.), 33(5), e2004776.

[8] Rahmani Dabbagh, S., Rezapour Sarabi, M., Birtek, M. T., Mustafaoglu, N., Zhang, Y. S., & Tasoglu, S. (2022). 3D bioprinted organ-on-chips. Aggregate, e197.

[9] Gopinathan, J., & Noh, I. (2018). Recent trends in bioinks for 3D printing. Biomaterials research, 22, 11.

[10] Gungor-Ozkerim, P. S., Inci, I., Zhang, Y. S., Khademhosseini, A., & Dokmeci, M. R., (2018). Bioinks for 3D bioprinting: an overview. Biomaterials science, 6(5), 915–946.

[11] Amamoto, R., Huerta, V. G., Takahashi, E., Dai, G., Grant, A. K., Fu, Z., & Arlotta, P. (2016). Adult axolotls can regenerate original neuronal diversity in response to brain injury. eLife, 5, e13998.

[12] Liang, Y., He, J., & Guo, B. (2021). Functional Hydrogels as Wound Dressing to Enhance Wound Healing. ACS nano, 10.1021/acsnano.1c04206. Advance online publication.