Have a Wound? 3-D Bioprint Yourself a Bandage

By Christina Huynh

We've probably all had a few scrapes, scratches, and cuts that cause a wound. Some of us might have even had more serious injuries. Wounds can vary from a simple break of the skin surface to deep tissue damage of the muscles, nerves, organs, and/or bone. The largest wounds can take an entire year to heal, but infection and inflammation can make the healing process problematic. One current treatment for healing of severe wounds is called autologous split-thickness skin graft (ASSG). Using a skin graft involves removing a piece of skin from a secondary surgical site on the patient, stretching the skin, and reapplying the graft onto the primary wound. If you're thinking this process seems counterintuitive—because it creates a wound at another location on the body that could potentially scar—many in the field agree. Scientists have been hard at work, trying to come up with an alternative to ASSG. Their hard work has led to an exciting process called 3-D bioprinting! 3-D bioprinting is an emerging technology that does not require creating additional wounds, can be applied to internal wounds, and allows a natural and complete recovery within only a few months.

Bioprinting is a unique form of tissue engineering where a 3-D structured graft is created with layer-by-layer precision. Mesenchymal stem cells are used as the base of the bandage, extracellular matrix proteins as structural framework/support, and tissue-specific cells (that correspond to the tissues in the wound) as filler. Mesenchymal stem cells (MSCs) are used for this application based on their ability to differentiate into various connective tissue cell types and, importantly, for their ability to repair damaged tissues. The extracellular matrix is a meshwork of fibrous proteins, like collagen, that contribute to tissue strength and structural integrity. The MSCs and tissue-specific cells are dispensed from the bioprinter as bioink. The bioinks are printed in a cross-hatch pattern onto extracellular matrix, which provides structural support that mimics both the outer shape and the inner architecture of native tissue.

The cells used as the bioinks are collected from the patient's bone marrow and adipose tissue. The collection of these cells involves a less invasive process and does not harm or scar the body like ASSG or traditional skin grafts do. Incredibly, the stem cells are not harmed during the bioprinting process, so they can differentiate and functionally adapt to initiate the wound healing process. Furthermore, this process eliminates the concern for inflammatory immune response and/or rejection because the cells are collected from the donor. What makes 3-D bioprinting even more appealing is that the graft can be customized in both size and shape to tailor it for each individual's wound.

Three steps are all it takes to order your own customized "bandage".

① Collect the information from the wounded tissue/organ for model design

② Transfer the design to the bioprinter equipped with the collected stem cell bioinks

③ Print!

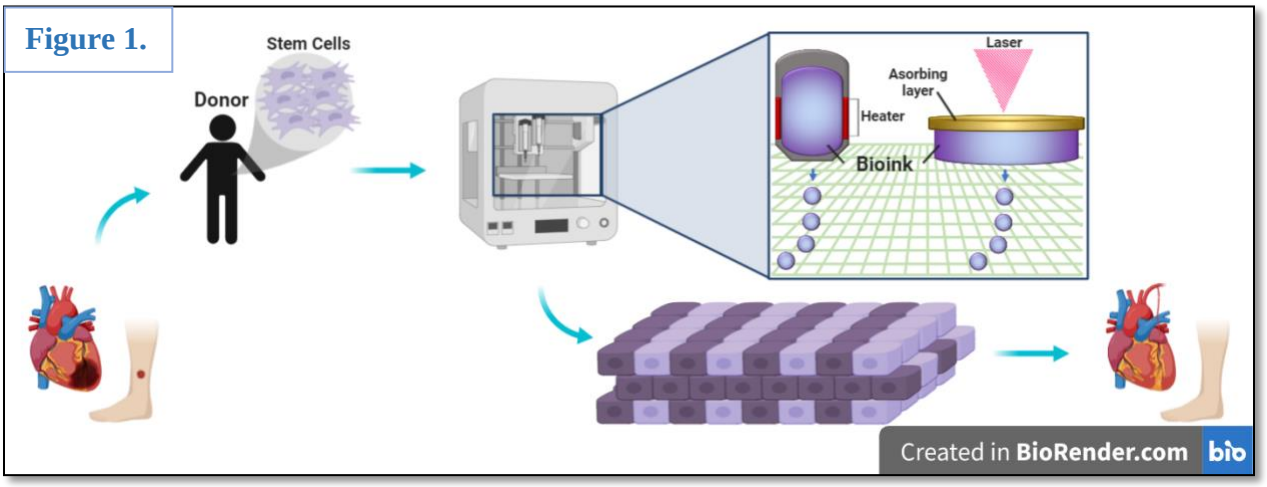

Figure 1. Process layout of fixing a a deep tissue or skin surface wound with your own stem cells and bioprinter.

Different wound types require different types of treatments. The tissue graft can be printed by two different bioprinter types. One is a thermal inkjet bioprinter and the other is a laser-assisted bioprinter as seen in **Figure 1**. The thermal inkjet heats the ink cartridge to produce bioink droplets from the nozzle. This bioprinter's set up, preparation, and printing speed are fast. The thermal inkjet bioprinter is ideal for surface wounds or cosmetic touch ups to old wounds that have left scars. On the other hand, the laser-assisted bioprinter is perfect for severe wounds that require precision and detail. As illustrated in **Figure 1**, this bioprinter uses a laser to generate pressure through a sheet, called the absorbing layer, to form the bioink into dots. It's very similar to pushing out individual ice cubes from a silicone tray mold! In exchange for slower preparation time and print speed, the laser-assisted bioprinter can print finer details. This is necessary for treating internal wounds like muscles and organs.

The field of bioprinting is constantly improving and has tremendous potential to help any individual. Sometime in the near future, this amazing technology will enable severe wounds to be efficiently treated without the need for skin grafts.

References

[1]Boland, T., Xu, T., Damon, B., & Cui, X. (2006). Application of inkjet printing to tissue engineering. *Biotechnology Journal: Healthcare Nutrition Technology*, *1*(9), 910-917.

[2]Gruene, M., Deiwick, A., Koch, L., Schlie, S., Unger, C., Hofmann, N., ... & Chichkov, B. (2011). Laser printing of stem cells for biofabrication of scaffold-free autologous grafts. *Tissue Engineering Part C: Methods*, *17*(1), 79-87.

[3]He, P., Zhao, J., Zhang, J., Li, B., Gou, Z., Gou, M., & Li, X. (2018). Bioprinting of skin constructs for wound healing. *Burns & trauma*, *6*(1).

[4]Jang, J., Park, H. J., Kim, S. W., Kim, H., Park, J. Y., Na, S. J., ... & Kim, S. W. (2017). 3D printed complex tissue construct using stem cell-laden decellularized extracellular matrix bioinks for cardiac repair. *Biomaterials*, *112*, 264-274.

[5]Murphy, S. V., & Atala, A. (2014). 3D bioprinting of tissues and organs. *Nature biotechnology*, *32*(8), 773.

[6]Velnar, T., Bailey, T., & Smrkolj, V. (2009). The wound healing process: an overview of the cellular and molecular mechanisms. *Journal of International Medical Research*, *37*(5), 1528-1542.