THE USE OF COLLAGEN HYDROGELS COUPLED WITH FIBROBLASTS AS FULL THICKNESS SKIN GRAFTS

Amritha Justin, amj106@pitt.edu, Mandala 10:00, Katherine Miller, kam421@pitt.edu, Mandala 10:00

Abstract*—Nearly 500,000 burn victims each year, in the US alone, require skin grafts, which are created with skin or bioengineered skin substitutes and are used to treat non-healing wounds. This paper will examine a particular skin-grafting technique that treats non-healing burns using collagen hydrogels seeded with fibroblasts as full thickness skin grafts. For large wounds that penetrate deep, like burns, full thickness grafts (FTSGs) are the most ideal solution as they tend to be thicker, match pigmentation better, and contract much less than split thickness grafts do during healing. Unfortunately, many severe burns are not able to be covered by FTSGs that are derived from donor skin, which is why bioengineers and healthcare professionals must create novel biomaterials that act as FTSGs.*

The technology presented in this paper takes advantage of the human body's natural skin healing pathway. When the body detects any lesion in the skin, an abundance of collagen and other proteins are produced and fibroblast cells start migrating to the lesion during the wound healing process. Both fibroblasts and collagen share a similar quality: both promote the regeneration of tissues. A popular biomaterial that is frequently used to treat skin wounds is a hydrogel. A collagen hydrogel coupled with fibroblast cells helps regenerate the skin cells in an open wound faster because it is essentially a skin graft made of materials that are naturally produced during the wound healing process in vivo. This approach for a bioengineered skin graft is revolutionary since many of these skin grafts in the current market are acellular.

Key Words—Bioengineering, Burn wounds, Collagen hydrogels, Fibroblast cells, Skin grafts, Tissue Engineering.

THE OVERVIEW, PURPOSE, AND LIMITATIONS OF TRADITIONAL SKIN GRAFTS

According to the American Burn Association, there were around half a million burn victims that needed emergency medical attention in 2016 alone [1]. Such traumatic injuries may sometimes require more than standard burn care, which is where the skin grafting technology comes into play. Skin grafts are either skin derived from a donor site that is located elsewhere on the patient's body, or biological skin substitutes, and they are generally used for the restoration of non-healing wounds, such as second or third-degree burns [2]. Though there are many viable types of skin grafts that work well *in vivo* for other non-healing wounds, such as soft tissue trauma, it is more of a challenge to find suitable skin grafts for burns, as burns sometimes completely damage all three layers of skin [3]. For this reason, many medical professionals and engineers alike have attempted to create a new, "living" skin graft that is composed of active cells and proteins that are normally found *in vivo* during the natural wound healing process [4]. One such skin graft is the collagen hydrogel that is seeded with fibroblast cells. In order to fully understand how the "living" collagen hydrogel works, it is important to firstly understand the natural wound healing process *in vivo* and secondly understand how traditional skin grafts generally interact with the components of the human body.

THE NATURAL WOUND HEALING PROCESS

As seen in Figure 1, the skin includes three primary layers: the epidermis, the dermis, and the hypodermis, also known as the subcutaneous fat layer. The epidermis is the top-most layer of the skin and is a stratified thin tissue that consists primarily of the epidermal cells that secrete keratin, known as keratinocytes. There are no blood vessels present and this layer receives nutrients from the dermis. The dermis is composed of two layers: the papillary dermis and the deeper reticular dermis. The papillary dermis is thinner than the reticular dermis and has connective tissue that contains capillaries, elastic fibers, and reticular fibers. The reticular layer is made up of dense connective tissue containing blood vessels, branching collagen fibers and elastic fibers. These branching collagen fibers are arranged parallel to the surface in layers. Finally, the hypodermis layer of skin is composed of subcutaneous fats that are made up of adipocytes, which are fat cells, and form groups, which are then separated by connective tissue. The subcutaneous layer also includes collagen and

elastin fibers, blood vessels, nerves, sweat glands, and hair follicle roots [5].

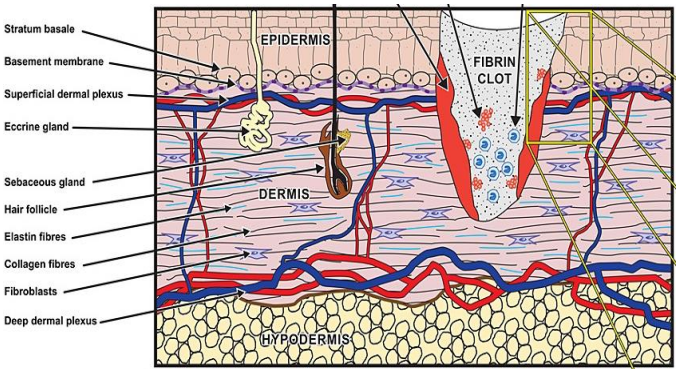

FIGURE 1 [5]
The Layers of the Skin and the Wound Healing Process

Normal wound healing consists of three phases. The inflammatory phase is the first step in the healing process. It consists of the clearance of microbial contamination and removal of devitalized tissues. This phase is initiated by the entering of platelets into the wound through damaged blood vessels and the release of a platelet-derived growth factor. The second phase, the proliferative phase, is characterized by the formation of scars and tissue regeneration. This phase includes the release of tissue factor which ends in the formation of a fibrin clot [5]. This fibrin clot is the source of the scaffold for migrating cells, which are fibroblast cells, to repair the wounds. The migrating fibroblast cells include neutrophils, keratinocytes, and macrophages that devour debris and bacteria. The last phase, a remodeling phase, optimizes the structural integrity and strength of the wound. The keratinocytes introduced in the second phase migrate over the gel like substance to provide a new epidermal layer, while fibroblastic cells proliferate to produce extracellular matrix and endothelial cells, which are both attracted by factors that were released earlier. The matrix, overtime, is gradually replaced with type III and type I collagen and covered by a layer of keratinocytes [6][7].

It is in the proliferative and remodeling phases, when fibroblast cells migrate to the wound and beds of collagen are layered to form a new epidermis, that most skin grafts are placed onto the wound site [6][7]. This is why a non-traditional skin graft, such as a collagen hydrogel seeded with fibroblast cells, that incorporates such vital biological wound healing factors has potentially revolutionary implications.

THE FUNCTION AND TYPES OF TRADITIONAL SKIN GRAFTS

Skin Grafts on a Cellular Level

Now that the process of *in vivo* wound healing has been established, the interaction of traditional skin grafts with cells and other biological components can be examined.

An autograft is a tissue graft obtained from one part of patient's body for use on another part of the same patient's body. These grafts can consist of the entire epidermis and a component of variable thickness of the dermis. If the entire thickness of the dermis is included, the graft is called a full thickness skin graft (FTSGs). Accordingly, if the graft is composed of less than the entire thickness of the dermis, the graft is referred to as a split thickness skin graft (STSGs) [8].

After transplantation, a common source of failure is a poor recipient site. This could be caused by poor vascularity or by great surface contamination. If the graft was applied by the dermis side, it produces superficial results which leads to complete graft loss. Similarly, stretching the graft too tightly, handling the graft ineptly, or applying excess pressure can also lead to partial or complete graft failure. An example of a general skin graft is shown in Figure 2.

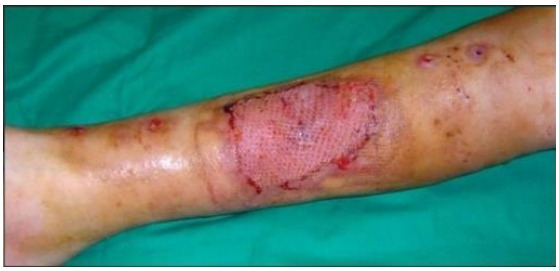

FIGURE 2 [6]
Example of a General Implanted Skin Graft

Comparison of Full Thickness Skin Grafts with Split Thickness Skin Grafts for Burn Wounds

Deciding between a full thickness graft and a split thickness skin graft depends on the wound condition, location, thickness, size, and the aesthetic concerns. Full thickness skin grafts do not have as broad of a range as split thickness skin grafts, however split thickness skin grafts do not require very ideal conditions for survival of the skin cells. Split thickness skin grafts are often used to resurface large wounds, line cavities, resurface mucosal deficits, close flap donor sites, and resurface muscle flaps. Split thickness skin grafts, however, do have significant disadvantages as compared to full thickness skin grafts. STSGs, when placed over areas with small amounts of underlying soft tissue, are more fragile. They tend to contract significantly during healing and tend to be either hypopigmented or hyperpigmented. Split thickness skin grafts, additionally, are more functional than cosmetic in their thinness, abnormal pigmentation, and frequent lack of smooth texture and hair growth. Often times when used to treat burn wounds on the face, split thickness skin grafts produce an undesirable mask-like appearance [6][8].

While both full thickness skin grafts and split thickness skin grafts leave second wounds, the split thickness skin graft donor site must reepithelialize, or restore the epithelium, which is a membranous tissue over a denuded area, such as a burn site by natural growth or plastic surgery. This reepithelialization often causes significant discomfort and requires ongoing wound care until the wound site is healed. Additionally, when thick split thickness skin grafts or full thickness skin grafts are harvested, more characteristics of the normal donor skin are maintained because of more collagen content, dermal vascular plexuses, and epithelial appendages are contained within thicker grafts. Therefore, because of these characteristics, these thicker grafts require more optimal conditions for survival of the skin cells, and have a higher incidence of graft failure than split thickness skin grafts. Full thickness skin grafts have a better color match due to their thicker nature and inclusion of additional dermal structures. They contract to a much a lesser degree than the split thickness skin grafts, which, in turn, allows them to provide a much better cosmetic appearance as well as functional results. The wound site requires a much less intensive care regimen than split thickness skin grafts [5][8].

Autografts that only consist of an epidermal layer, often referred to as cultured epidermal autografts, such as Epicel and Laserskin, use a graft of skin from the patient; this is later expanded in the lab to produce autogenous keratinocytes for grafting. Cultured epidermal autografts are unfortunately attributed with high rates of infection and graft loss, which further indicates the importance of a dermal layer.

While it is significantly more challenging to produce an effective material to replace the dermis, there are major advantages, as discussed above, to having a dermal component of a skin graft. Acellular dermal allografts, like AlloDerm, are composed of cadaveric dermis that acts as a scaffold for the growth of tissue. Another dermal allograft, Integra, is a bilaminate membrane that consists of a collagen layer that is bonded to a thin silicone layer [6]. The collagen layer serves as the dermal analogue while the silicone layer acts as a temporary epidermis. Cells from the patient's underlying tissue occupy the dermal layer once it is revascularized, meaning that the blood circulation of the area is restored. A very thin split thickness skin graft is placed over the new dermis after the removal of the silicone layer from the new dermal layer after the aforementioned process is completed. The treatment of full thickness skin grafts with this dermal component has been shown to produce skin elasticity and transepidermal water loss matching those of the surrounding skin [5][6].

As discussed in the aforementioned paragraphs, full thickness skin grafts have more of a functionality that is similar to that of normal skin. Thus, it is apparent that for deep penetrating wounds, such as traumatic burns, autograft FTSGs are the most ideal as they tend to be thicker, match pigmentation better, and contract much less than split thickness grafts do during the healing process. However, there are still many challenges with FTSGs, as, though they have a generally higher cell survival rate, many of these allografts are acellular, meaning that there is potential for an even higher cell survival rate if these grafts incorporated cells. This is why engineers have created a novel type of "living" skin graft: the collagen hydrogel coupled with fibroblast cells.

A NOVEL TYPE OF FULL THICKNESS SKIN GRAFT: THE COLLAGEN HYDROGEL COUPLED WITH FIBROBLASTS

An Overview of Hydrogels

A hydrogel is a material like no other. Hydrogels are three dimensional networks of hydrophilic polymer chains. These chains are then crosslinked to form matrices with high water content. Hydrogels are extremely flexible in that their properties are primarily determined by the fabrication material. Many engineers find them appealing for skin graft use because some fabrication materials include naturally occurring proteins *in vivo*, including collagen, chitosan, hyaluronic acid, and elastin. These specific examples are applicable in biological settings because of their cell signaling abilities and general biocompatibility [9].

Hydrogels can also be crosslinked in a number of different ways, both chemically and physically. Chemically crosslinked hydrogels are obtained by chemical reactions, enzymatic crosslinking, radical polymerization and energy irradiation. As compared to physically crosslinked gels, chemically crosslinked gels have higher mechanical properties, such as tensile and compressive properties, that allow the gel to be manipulated without compromise *in vivo*. However, their residual chemical crosslinkers may cause cytotoxicity. On the other hand, physically crosslinked gels consist of physical interactions between polymer chains, which creates a hydrogel more favorable for *in vivo* application since they are biocompatible as they are formed through hydrogen bonds, protein interactions, and changes in environmental conditions. Many of these physically crosslinked hydrogels are based on agarose, alginate, and collagen, and are favored for tissue regeneration as the gels exist in aqueous solutions without chemical crosslinkers [9].

Collagen hydrogels have been found to be the most effective means of creating a full thickness skin graft so far, as collagen is a naturally occurring material *in vivo*. In addition, collagen also happens to play an integral role in the wound healing process, especially in the proliferative and remodeling phases, which, as stated earlier, are the phases in which skin grafts are generally applied [7][9].

Efficacy of Collagen Hydrogels Coupled with Fibroblasts in a Laboratory Setting

As noted in the previous section, collagen hydrogels are already highly suitable for applications of skin regeneration *in vivo*. However, since deep penetrating burns, such as third-degree burns, oftentimes burn through the epidermis, dermis

and subcutaneous fat layers, leaving them damaged beyond normal repair, additional resources may be needed to aid the restoration of skin for these types of traumatic wounds. This is where the seeding of fibroblasts cells, which is another biological component that plays an integral role in the wound healing process, specifically the proliferative phase, comes into play. With the coupling of "living" components that naturally promote the regeneration of skin, the fibroblast cells and collagen protein dual hydrogel should be able to effectively overcome the obstacles of traditional FTSGs and treat burn wounds effectively, as seen in Figure 3.

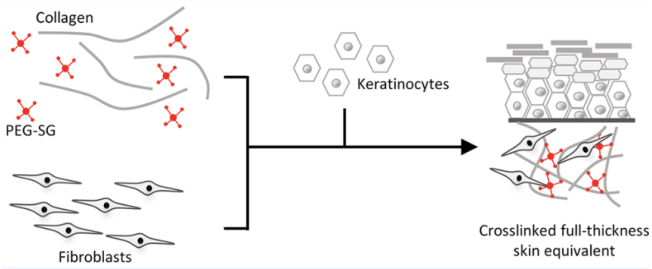

FIGURE 3 [10]
Interaction of Collagen and Fibroblasts to Form Skin Grafts

This hydrogel combo was tested in a laboratory setting in 2017 by Christian Lotz, Freia Schmid, Eva Oechsle, et al. in the Department of Tissue Engineering and Regenerative Medicine (TERM) at the University of Würzburg. This group found that coupling fibroblast cells and a collagen hydrogel together did in fact increase the cell survivability and proliferation rate, which is a stellar marker for this skin graft's capabilities in aiding the regeneration of skin. This group went further than just testing the dual hydrogel; they also explored the effects of a variant of polyethylene glycol (PEG-SG) as a crosslinker, a chemical process that is shown in Figure 4 [10].

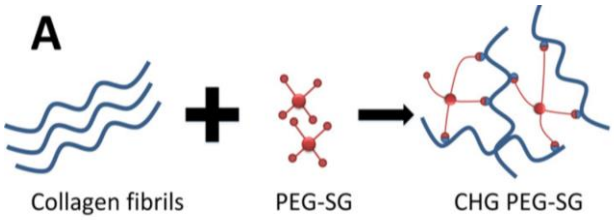

FIGURE 4 [10]
Interaction of Collagen and the PEG-SG Chemical Crosslinker

Interestingly, they found that small doses of PEG-SG to crosslink the collagen gel actually improve the hydrogel's cell-proliferation and viability properties. This discovery is rather revolutionary, as chemical crosslinkers have previously been thought to be a hindrance in the biocompatibility properties of a hydrogel [10].

Another group, Fabienne Hartmann-Fritsch, Thomas Biedermann, Erik Braziulis, et al., from the Department of Surgery of the University of Zurich has also researched on collagen hydrogels coupled with fibroblasts. On top of confirming that collagen hydrogels with fibroblast cells significantly aided skin tissue regeneration, this group aimed to strengthen the hydrogel *in vivo* by creating biodegradable meshes as shown in the scanning electron microscope image in Figure 5 [11]. An *in vitro* cell viability assay was performed and it was found that these meshes were able to increase the regenerative properties of the collagen and fibroblast hydrogel. The graft applications for this hydrogel are more clearly shown in the macroscopic analysis in Figure 6 [11]. Though the graft has a slight pink undertone, it is apparent that gross hyperpigmentation or hypopigmentation, which is a common fault with split thickness skin grafts, does not seem to be an issue that concerns full thickness skin grafts from collagen hydrogels seeded with fibroblasts, as the seeded fibroblast cells integrate with the patients' own [8].

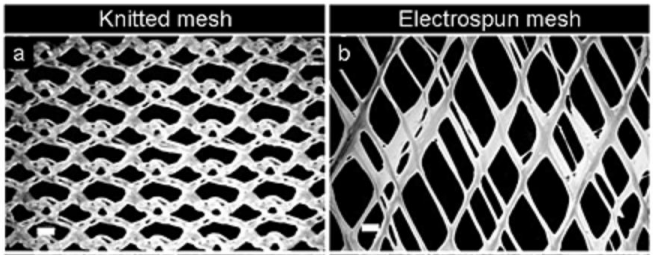

FIGURE 5 [11]
Biodegradable Meshes Used to Strengthen Collagen Hydrogels

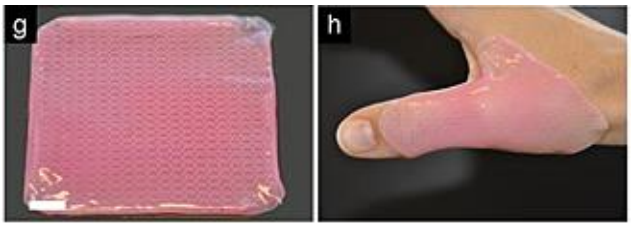

FIGURE 6 [11]
Macroscopic View of a Collagen Hydrogel Seeded with Fibroblast Cells as a of FTSG

As mentioned earlier, hydrogels are highly tunable, and the two aforementioned research groups embraced this property in order to overcome the challenges of traditional full thickness skin grafts and further amplify the advantages of a collagen hydrogel seeded with fibroblast cells as a full thickness skin graft. Such promising laboratory data concerning this novel form of full thickness skin graft paves the way for a hope for similar results in the clinical setting.

Amritha Justin
Katherine Miller

Efficacy of Collagen Hydrogels Coupled with Fibroblasts in a Clinical Setting

Many of the skin grafts on the market for commercial use, such as AlloDerm, are acellular. A unique type of commercial skin graft for patient use that is "living" and not acellular is Apligraf, which is made by Organogensesis Inc. [12]. Most importantly, Apligraf highlights the role of collagen and fibroblasts, so, as per the *in vitro* studies, it is able to increase the regenerative properties of skin by using components that are naturally occurring in the wound healing process as seen in Figure 7 [5][12].

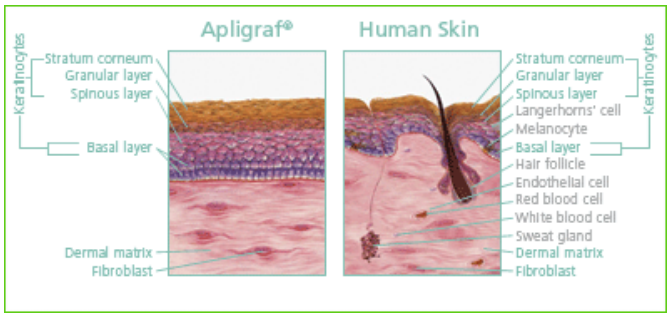

FIGURE 7 [12]
Comparison of the Active Components in Apligraf to the Natural Components in Human Skin

Though the current market for Apligraf is for veneous leg ulcer and diabetic foot ulcer patients, by looking at Figures 8 and 9, which are images of before the application of Apligraf and healing after the application of Apligraf, it is apparent that for other deep penetrating wounds, such as burns, a more durable version of Apligraf may also be appropriate [12]. This is where the combination of the clinical product, Apligraf, and the laboratory research on strengthening collagen hydrogels by means of a PEG-SG chemical crosslinker or a biodegradable meshing can be beneficial to improve this innovation for slightly more traumatic wounds [10][11][12].

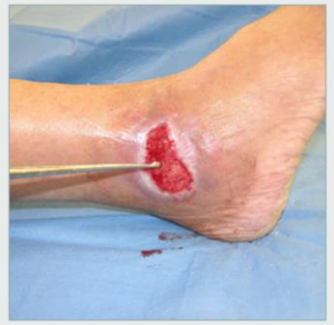

FIGURE 8 [12]
Wound Bed Before the Application of Apligraf

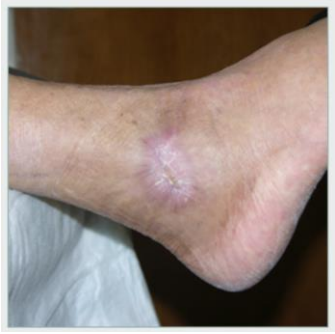

FIGURE 9 [12]
Wound Bed After Healing with the Application of Apligraf

THE IMPLICATIONS OF SUSTAINABILITY

Deep burn wound victims can spend up to a month or more healing. The patients may have to spend one to two weeks healing in the hospital after incorporating a traditional skin graft to the wound site, and an additional three to four weeks protecting their new skin grafts from infection or trauma [13]. In the United States, one day in a hospital can cost the patient an upwards of $1,986; this means that, by spending one to two weeks in a US hospital recovering from a skin graft application procedure, a patient can spend from $13,902 to $27,804 [14]. Likewise, a US hospital can also create around 0.5 kilograms of waste per patient per day; meaning that over the course of one to two weeks, a hospital can accumulate over 3.5 to 7.5 kilograms of waste per patient [15].

When looking at sustainability, it is important to consider the monetary aspect as well as the waste aspect. Sustainable development is concerned with societal development where the costs of development are not transferred to future generations, meaning an attempt is made to compensate for these costs [16]. Essentially, the main goal of monetary sustainability is to make the product affordable to the general public while also limiting the costs of production. Additionally, waste disposal issues are often exacerbated by changing patterns of consumption, urbanization, and industrial development, which means that the traditional methods for waste disposal are no longer effective [17] [18]. The majority of the materials produced by a hospital ultimately become waste, so by instituting a waste management program or changes in consumption patterns, a hospital may reduce the amount of waste it produces, and become more sustainable in this aspect.

Luckily, the novel "living" skin graft, collagen hydrogels seeded with fibroblast cells, can curb some of the sustainability issues seen with traditional skin grafts. Apligraf, the collagen hydrogel seeded with fibroblast cells that is readily available for consumers, has been shown in clinical trials that it heals wounds in a third less of the time it takes traditional skin grafts to do the same [19]. This implies that Apligraf could

potentially shorten the time skin graft patients have to stay in the hospital from one to two weeks to four to eleven days. This grossly reduces the cost of staying in the hospital to $7,944 to $21,846 [14]. Additionally, this also reduces the hospital waste generated for that patient to around 2 to 5.5 kilograms [15]. From these figures, it is evident that "living" skin grafts, like collagen hydrogels seeded with fibroblasts, especially Apligraf, prove to be a sustainable addition to the healthcare field and society as a whole. Not only will it reduce the enormous cost patients must pay hospitals to receive this type of care, it will also reduce the amount of waste produced per patient, which in turn makes this product viable for many years to come.

FUTURE DIRECTION OF FULL THICKNESS SKIN GRAFTS

As formerly mentioned, Apligraf, the novel skin graft that is commercial and also cellular as it is made from fibroblast cells and a collagen matrix, does not currently apply to the treatment of deep penetrating burns, although it does treat deep penetrating soft tissue wounds [12]. However, as shown in the laboratory *in vitro* research, collagen hydrogels are highly tunable, which allows them to be strengthened via a PEG-SG chemical crosslinker or by using a biodegradable meshing [10][11]. These two techniques to strengthen the polymer network chain of a collagen hydrogel can be useful to create an Apligraf-like commercial skin graft to be used for the treatment of burn wounds. The commercialization of Apligraf began in around 2000, after it became FDA approved, so the technology is still quite new [12]. Because of this, there is a strong inclination for the technology to change, and hopefully provide the benefits of combining both the regenerative properties of collagen and fibroblasts and the strength of the PEG-SG crosslinker or biodegradable meshing in order to put skin grafts specifically for burn wound restoration on the commercial market in the near future.

SOURCES

[1] "Burn Incidence and Treatment in the United States: 2016." American Burn Association. 2016. Accessed 1.28.2018. http://ameriburn.org/who-we-are/media/burn-incidence-fact-sheet/

[2] L. Christenson and C. Kaczkowski. "Skin Grafting." Encyclopedia of Surgery. Accessed 1.10.2018. http://www.surgeryencyclopedia.com/Pa-St/Skin-Grafting.html

[3] "Alternatives to Skin Grafts." Advanced Tissue. 7.16.2014. Accessed 1.10.2018. https://www.advancedtissue.com/alternatives-skin-grafts/

[4] M. Khosh. "Full-Thickness Skin Grafts." Medscape. 4.8.2017. Accessed 1.28.2018. https://emedicine.medscape.com/article/876379-overview

[5] D. Markeson, J. Pleat, J. Sharpe, et al. "Scarring, stem cells, scaffolds and skin repair." Journal of Tissue Engineering and Regenerative Medicine. 10.29.2013. Accessed 1.28.2018. http://onlinelibrary.wiley.com/doi/10.1002/term.1841/full

[6] B. Wood. "Biologic Skin Substitutes." Medscape. 3.27.2015. Accessed 1.10.2018. https://emedicine.medscape.com/article/1295109-overview#a5

[7] A. Nuschke. "Activity of mesenchymal stem cells in therapies for chronic skin wound healing." Organogensis. 12.10.2013. Accessed 2.10.2018. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4049892/

[8] M. Wax, A. Pittman, T. Ghanem. "Split-Thickness Skin Grafts: Overview, Graft Selection, Donor Site Selection." Medscape. 6.27.2017. Accessed 1.28.2018. https://emedicine.medscape.com/article/876290-overview#a2.

[9] N. Annabi, A. Tamayol, J. Uquillas, M. Akbari, L. Bertassoni, C. Cha, G. Camci-Unal, M. Dokmeci, N. Peppas, and A. Khademhosseini. "25th Anniversary Article: Rational Design and Applications of Hydrogels in Regenerative Medicine". Advanced Materials. 11.4.2013. Accessed 1.10.2018. http://onlinelibrary.wiley.com/doi/10.1002/adma.201303233/full.

[10] C. Lotz, F. Schmid, E. Oechsle, et al. "Cross-linked Collagen Hydrogel Matrix Resisting Contraction to Facilitate Full-Thickness Skin Equivalents" ACS Applied Materials and Interfaces. 5.20.2017. Accessed 1.28.2018. http://pubs.acs.org/doi/10.1021/acsami.7b04017

[11] F. Hartmann-Fritsch, T. Biedermann, E. Braziulis, et al. "Collagen hydrogels strengthened by biodegradable meshes are a basis for dermo-epidermal skin grafts intended to reconstitute human skin in a one-step surgical intervention." Journal of Tissue Engineering and Regenerative Medicine. 12.10.2012. Accessed 1.28.2018. http://onlinelibrary.wiley.com/doi/10.1002/term.1665/full

[12] "What is Apligraf?" Apligraf: Add Life to Healing. 2010. Accessed 1.28.2018. http://www.apligraf.com/professional/what_is_apligraf/index.html

[13] "Skin Graft." Icahn School of Medicine at Mount Sinai. Accessed 3.20.2018. http://www.mountsinai.org/health-library/surgery/skin-graft

[14] E. Rappleye. "Average cost per inpatient day across 50 states." Becker's Hospital Review. 5.19.2015. Accessed 3.20.2018. https://www.beckershospitalreview.com/finance/average-cost-per-inpatient-day-across-50-states.html

[15] "Health-care waste." World Health Organization. 2.2018. Accessed 3.20.2018. http://www.who.int/mediacentre/factsheets/fs253/en/

[15] "Health-care waste." World Health Organization. 2.2018. Accessed 3.20.2018. http://www.who.int/mediacentre/factsheets/fs253/en/

[16]"Definitions of Sustainability." 4.3.2015 Accessed 3.20.2018. http://www.ecifm.rdg.ac.uk/definitions.htm
[17] "Sustainability Roadmap for Hospitals." 2.2016. Accessed 3.20.2018. http://www.sustainabilityroadmap.org/topics/waste.shtml#.Wr7MaCPMzy9
[18]"Concepts for Sustainable Waste Management." 3.9.2018. Accessed 3.20.2018. https://www.giz.de/en/worldwide/15109.html
[19] "How does Apligraf compare?" Apligraf: Add Life to Healing. 2010. Accessed 3.20.2018. http://www.apligraf.com/patient/what_is_apligraf/how_does_apligraf_compare.html

ACKNOWLEDGMENTS

We would like to thank Dr. Mandala, our Engineering 0012 Professor, Ms. Ferda, our Engineering Writing Instructor, Jake Meadows, our Conference Co-Chair, and Dr. Schaub, our Conference Chair, for helping us throughout the writing process.

Amritha Justin
Katherine Miller