Session A2
8197

Disclaimer—This paper partially fulfills a writing requirement for first year (freshman) engineering students at the University of Pittsburgh Swanson School of Engineering. *This paper is a **student, not a professional***, paper. This paper is based on publicly available information and may not provide complete analyses of all relevant data. If this paper is used for any purpose other than these authors' partial fulfillment of a writing requirement for first year (freshman) engineering students at the University of Pittsburgh Swanson School of Engineering, the user does so at his or her own risk.

THE ROLE OF HYDROGEL MATRICES IN WOUND HEALING

Evan Bennis, eab149@pitt.edu, Mena 1:00, Hannah Keeney, hak98@pitt.edu, Sanchez 3:00

Abstract—*While the field of medicine has been at the epicenter of technological growth and innovation, little change has occurred in areas such as wound healing. The age-old treatment of antiseptic and gauze persists as the primary way to treat an injury, and while this method has proven to be effective, it is highly inefficient. This procedure requires medical personnel to frequently administer medication and constantly redress wounds to prevent infections. Identifying this as an area of potential improvement, Dr. Xuanhe Zhao of the Massachusetts Institute of Technology (MIT) decided to apply his previous research of hydrogels to meet this demand for greater efficiency.*

Dr. Zhao developed a 'smart' bandage, which successfully integrates the hard and dry nature of electronics with the soft elasticity of the body to heal wounds. The dual properties of the hydrogel bandage allow it to recognize, indicate, and address injury abnormalities through an advanced feedback loop between the body and the mechanical device itself. The main component of Zhao's hydrogel bandage is the water-based hydrogel matrix which gives the product the ability to stretch across nearly any body part, including joints. However, this rubbery aspect also lends itself to the insulation of conductive wires, semiconductor chips, LED lights, and temperature sensors, which all contribute to the utility of the Band-Aid of the future.

Key Words—Cross-linking, Drug delivery, Elastomer-Hydrogel hybrid, Ferrogel, Soft Active Materials Lab, Wound healing, Xuanhe Zhao

ROOM FOR IMPROVEMENT

Hospitals are chaotic. Doctors, nurses, physicians and surgeons all have places to be. Patients to assist. Wounds to dress. However, most would agree that seeing an unconscious patient being rushed to the emergency room certainly takes precedence over a patient who burned himself with boiling water two days ago. This does not mean that a patient can simply be left unattended after being admitted to a hospital just because another patient has a more serious issue. Burn victims still need extensive care. Wounds are constantly developing. Doctors must routinely check up on burn victims to ensure the wound is getting enough oxygen, to ensure it is not getting infected, and to ensure the pain from a burn isn't unbearable. After each check-up, the wound will be redressed and bandaged. The process repeats itself until the patient is deemed healthy and discharged. While the process is effective, it is inefficient. Since a doctor is essentially repeating the same process over and over, there is an opportunity for automation.

THE HISTORY OF WOUND CARE AND PROBLEMS WITH CURRENT TREATMENT

Initially, some might believe wound care is a trivial part of a healthcare professional's job. When children get cuts and scrapes, mothers simply wipe on some Neosporin and cover it with gauze and adhesive tape. If mothers with no healthcare-related education easily heal injuries, why are wounds suddenly being referred to as a 'silent epidemic?'

Further research revealed that chronic wounds have snowballed into a much more serious threat to our society and healthcare system. Chronic wounds are more serious than acute wounds, as they persist for longer periods of time and are less responsive to treatment. Although chronic wounds are becoming a major problem worldwide, the United States represents the largest market for wound care products and services, with over 1,000 outpatient wound care centers, according to the Baylor Scott & White Wound Care and Hyperbaric Medicine Clinic. Furthermore, the U.S. is home to over 6.5 million people with chronic wounds, and the cost of care exceeds $50 billion per year [1]. More efficient wound-healing procedures could potentially save the healthcare industry billions of dollars, yet minimal efforts have been made to reduce this cost. Treating cutaneous injuries is a meticulous process, as open wounds are prone to infection and must be kept dry and clean at all times. These injuries require multiple time-consuming visits in which medical personnel must remove and replace specialized dressings. In addition to this complication, outpatient wound care treatment also faces an ongoing knowledge barrier. Some physicians have a limited understanding of the basic principles of wound evaluation and management [1]. This is detrimental to the wound-healing process, as injuries could take longer to heal if certain symptoms are not immediately recognized and dealt with.

Evan Bennis
Hannah Keeney

A THEORETICAL SOLUTION

Hydrophilic polymeric networks, commonly referred to as hydrogels, entered the medical scene in the 1960s, as the first materials developed for use inside the human body, according to the Journal of Biomedical Sciences [2]. Over time, science has increasingly demanded more from hydrogels. The first wave of the technology simply focused on its ability to swell when put in contact with water, while the second wave of expectation aimed to make the hydrogel respond to specific stimuli, such as temperature, pH, or molecular concentration [2]. Doing so would theoretically give the hydrogel a biocompatible characteristic which could evolve into hundreds of new medical applications, effectively altering the new standard of several fields of medicine. For instance, researchers began to imagine applications of the material in areas such as cosmetics, immunotherapy, wound healing, optometry, drug delivery, and tissue engineering [2].

While many researchers have developed successful products that incorporate hydrogels, most of them are designed to provide one primary benefit to the user, such as contact lenses or cosmetic masks. However, Dr. Xuanhe Zhao of the Massachusetts Institute of Technology had greater ambitions for the material. He has worked to build a 'smart' bandage which combines the drug delivery, wound healing, and electronics applications into one useful tool. Zhao's hydrogel bandage operates through a feedback loop which is able to recognize, indicate, and respond to temperature changes automatically. This automation component could theoretically solve the inefficiency problem with outpatient wound care treatment.

Ideally, the hydrogel bandage would immediately respond to any temperature changes of the affected area by activating drug reservoirs that transport pharmaceuticals to the affected area. This function would achieve a sustained and targeted release of medication over time, thereby heightening the effect of the drug as well as lowering its side effects. The implementation of this technology in hospitals and care centers would effectively combat the current inefficiency of the system in place by catalyzing the recovery process. Any inflammation or sign of infection would be identified and addressed much more quickly with this product, which is constantly checking for temperature changes, than by a medical professional, who only periodically checks when the patient schedules a visit.

XUANHE ZHAO

Xuanhe Zhao is an expert in the soft materials field and the pioneer of the product discussed in this paper: the hydrogel bandage. Just a year after completing his PhD at Harvard, Dr. Zhao co-founded the Soft Active Materials (SAMs) laboratory at MIT, the eventual ground zero for his hydrogel bandage [3]. Since founding the SAMs lab, he has submitted over 60 publications related to soft materials and their various properties [4]. He is truly an expert in his field, and there is a lot to be learned from his extensive research.

LAYING THE FOUNDATION: CURRENT HYDROGELS

The applications of hydrogels are endless. They are already being used in contact lenses and home wound-care treatments, but that is just the beginning. The hydrogel's water-based nature makes it compatible with the body as well as all kinds of embeddable objects such as electronics, titanium, glass, and ceramics. However, current hydrogels have limitations that prevent them from reaching their potential. Specifically, previous hydrogels are actually not very flexible. For reference, an alginate hydrogel with very similar applications ruptures when stretched to just 1.2 times its original length [5]. The hydrogels that can stretch far are often very brittle, especially in the presence of abnormalities in the nanostructure which are rather common. In order to achieve fracture strengths which are closer to those of the skin and rubber, Zhao drew inspiration from nature and human skin in creating his flexible, robust hydrogel from the fundamentals of materials science.

ZHAO'S HYDROGEL

Hydrogels are the material of the future. The number of applications is beyond the imagination because of how versatile the material is. Zhao's hydrogel begins to explore this endless array of possibilities. Like existing hydrogels, Zhao's hydrogel is centered around the basic idea of flooding a network of polymer chains with extensive amounts of water. However, as a professor with a materials science background, Zhao wanted to create something that surpassed the capabilities of all current hydrogels—something with properties that had never been seen before. He approached his task through the fundamentals of effective hydrogels, which he outlines in his commentary, "Designing Toughness and Strength for Soft Materials."

Mechanical Dissipation

The first key property of a robust, yet flexible hydrogel is a high mechanical dissipation and stretchability. While having a high-fracture strength is ideal, materials with this characteristic are typically not flexible. To compensate, hydrogels must have the ability to dissipate stress away from a potential fracture point in order to minimize fractures. Effectively dissipating stress allows the hydrogel to be used in applications that require them to carry a load. Additionally, by possessing the ability to stretch without breaking, Zhao's hydrogel can stretch around joints and move with the body making it a viable candidate for biomedical use.

Below Flaw-Insensitive Length Scale

The second property that sets Zhao's hydrogel apart is its below flaw-insensitive length scale. To effectively describe what this means, it is important to understand that hydrogels are not always created perfectly. The process of cross-linking can sometimes leave the hydrogel with flaws and impurities that can significantly lower the fracture strength of the hydrogel. However, by using a length scale of polymer chains that is on the order of a few nanometers, the effect of tears can be kept to a minimum [6]. To explain this, we will first look to nature. Materials found in nature and in the human body were a major source of inspiration Zhao, so by highlighting them it will be made more apparent why the nanostructure of the hydrogel is of utmost importance. In a paper published by the Proceedings of the National Academy of the Sciences (PNAS), the nanostructures of enamel, dentin bone, and nacre are evaluated because a 'brick and mortar' nanostructure is visible in all of them. What all of these structures have in common is a large aspect ratio of the embedded mineral platelets [7].

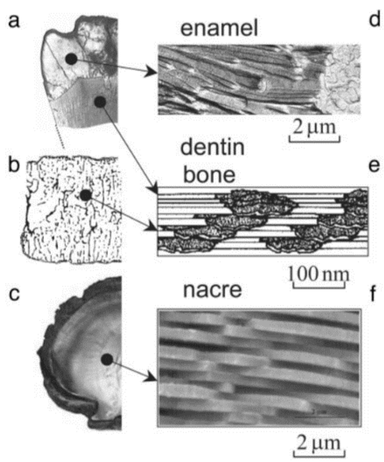

FIGURE 1 [7]
The ratio of the length to the thickness of mineral platelets in natural materials.

As seen in Figure 1, the lengths are much larger than their diameters. This is what compensates for the low shear modulus of the protein phase. The design of Zhao's hydrogel can be traced back to the structure of these organic materials. The polymer networks that make up the hydrogel consist of polymers with a diameter that is below the critical length scale. That is, fractures in the single polymer chain do not have a significant effect on the fracture strength of the material because of how small the polymers themselves are. By integrating this idea into the creation of his hydrogel, Zhao can ensure that existing flaws do not have an adverse effect on the integrity of the hydrogel.

Simultaneous Fracture

The third fundamental that Zhao used in the creation of his hydrogel is the simultaneous stiffening and fracturing of polymer chains. What typically makes soft materials weaker than hard materials is that the whole material does not fracture in unison. Imagine bending a soft eraser until it breaks. The eraser does not break all at once. Instead, some of the polymer fractures immediately after being stressed, making it much easier for others to follow. The same principle applies to hydrogels. If any polymer chains snap, the fracture strength of the remaining chains will decrease significantly. The reason this happens is because of non-uniform chain lengths. If one polymer is longer than another, then it can be stretched further than a short chain [4]. The way that Zhao approached this problem in his hydrogel was through cross-linking.

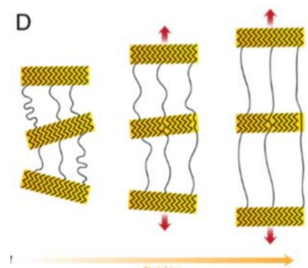

FIGURE 2 [6]
Use of hidden polymer chains to create even chain lengths

Cross-linking is a way of combining chains so that they are all the same length in an attempt to make them fracture at the same time. As shown above in Figure 2, hidden polymer chains are cross linked with the functional polymer chains. When the material is stretched, shorter chains can use the hidden chains to stretch to the length of longer chains so that they do not break as easily. Of course, the hydrogel can still break if all of the extended polymer chains reach their fracture point. The idea is that the fracture strength is much higher when all of the polymers have to be brought to failure simultaneously, so there is a lower chance of ever reaching the failure point.

Bringing the Properties Together

By being aware of all these essential properties, Zhao was able to create a hydrogel with characteristics that had never been seen before. His hydrogel could bend around joints without failure. Patients could walk, jump, and flex affected areas without the bandage breaking off. It is important to note that while each individual property that Zhao discusses is important, they are nothing without each other. A hydrogel can have an incredible ability to dissipate mechanical energy, but if the polymers are not below the flaw-insensitive length scale then even a small internal fracture will cause the hydrogel to fail [6]. Similarly, even if a hydrogel has both of these properties—a high mechanical dissipation and an appropriate length scale—it will still fracture quite easily if its polymers are not all the same length, since shorter polymers will make it easier for longer ones to fracture in the long run. Zhao's ability to combine all three fundamentals into a single hydrogel makes for a product that can change the field of medicine.

Dehydration of the Hydrogel

While Zhao's hydrogel did possess groundbreaking material properties, it soon became apparent that dehydration was a major concern, as the hydrogel dried out and lost its elasticity after just a few hours [8]. Adding salt was a viable solution, but it made the gel incompatible with the body. After testing several materials, Zhao's team ultimately settled on applying a rubbery material, known as an elastomer, to one side of the hydrogel. Although it did keep the gel hydrated, it was a particularly uncooperative adhesive, since it is naturally hydrophobic. To remedy this, benzophenone, a compound commonly used in adhesives, was applied to the elastomer and activated with UV light [8].

MATRIX MECHANISMS

The hydrogel bandage mainly serves to advance the recovery process of an injury through the collaboration of several mechanisms. Because the system is a continuous feedback loop, there is no beginning or end of the cycle.

In the past, the porous scaffolds used in popular drug delivery methods have been passive, relying largely on molecular diffusion, material decomposition, and cell migration to transport and deliver biological agents. Recognizing that this method would not provide the desired automation factor, Dr. Zhao and a team of researchers worked to revamp existing biomaterials to form an active scaffold specifically designed to respond to external stimuli.

Altering the Ferrogel

In previous studies mentioned in a PNAS publication, ferrogels—polymeric gels interlaced with magnetic particles—have been successfully manipulated with the application of magnetic fields to perform controlled drug release. Capitalizing on this unique ability, Zhao assembled his own ferrogel, covalently binding peptides consisting of the arginine-glycine-aspartic acid (RGD) amino acid sequence to alginate, a commonly-used polysaccharide [9]. Ferrogels typically have very small pores and do not readily support cell adhesion, creating difficulties when transporting larger molecules, a process that is essential to drug delivery. To address these complications, the gel was frozen at various temperatures to enlarge the interconnecting pores and covalently coupled with the peptides to ensure cell adhesion. This gel was embedded with iron oxide particles, thus completing the formation of the superparamagnetic gel [9].

The effects of the drug and cell release would be optimized in a gel that could withstand maximum deformation. Therefore, Zhao and his team curated a ferrogel with enlarged pores to maximize interconnectivity, a high concentration of iron oxide particles to allow for a large magnetic force, and a low modulus which corresponds to increased deformation. When the magnetic field is applied, the pores in the ferrogel collapse, causing a drastic volume change and forcing the water inside the pores to flow out of the gel. When the magnetic field is turned off, the water is reabsorbed into the gel, and the gel returns to its original size in less than one second [9]. This deformation paired with the efflux of water is what activates and releases pharmaceuticals enclosed within the scaffolding.

Tests to Determine the Effectiveness of Macroporous Ferrogels

Figure 3, below, details a few of the tests which determined the ideal conditions of the macroporous ferrogel.

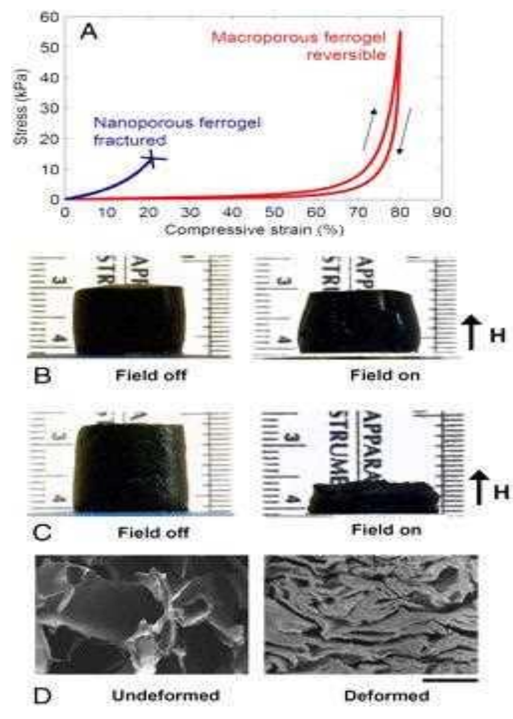

FIGURE 3 [9]
Various deformation tests between nanoporous ferrogel and macroporous ferrogel

When subjected to a compressive strain of about 20%, the nanoporous ferrogel fractured, and permanently deformed. However, the macroporous ferrogel demonstrated a significantly smaller Young's modulus (a difference of ~27.5 kPa) and withstood a reversible compressive strain of about 80% before fracture [9]. Parts B and C of Figure 3 display the results of deformation when a cylinder of nanoporous gel and a cylinder of macroporous gel were subjected to identical magnetic field gradients. The height of the nanoporous gel was reduced by ~5%, while that of the macroporous gel was reduced by ~70% of its original height [9]. Lastly, Part D clearly demonstrates the full extent of the macroporous gel's deformation.

Drugs such as mitoxantrone were tested for viability upon release from the scaffolding by seeding the gel as well as human dermal fibroblasts at various RGD densities. Lower RGD densities provided for weaker cell adhesion and therefore a greater release and more effective distribution of the drugs. The results of these tests, pictured in Figure 4, found the viability of the drug to be around 95%.

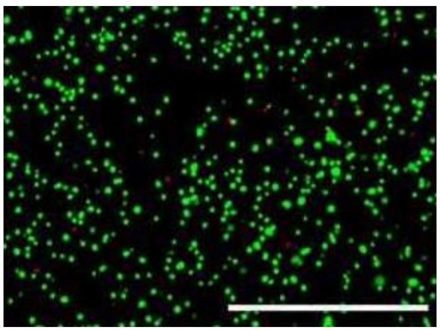

FIGURE 4 [9]
Cells released from macroporous ferrogels were stained to test their viability after their release

Additionally, the amount of drug released from the macroporous ferrogel was ~7 times greater than that of the control gel, which is displayed in Figure 5 below.

FIGURE 5 [9]
Applied magnetic stimulation to the macroporous ferrogel on the left accelerates the release of mitoxantrone, demonstrated by the increasing blue color

Lastly, to test this mechanism in vivo, the ferrogel was embedded with stem cells of mice and injected into the space directly under the skin. Below, Figure 6 demonstrates what happened when two mice—one injected with a control gel and the other with the macroporous ferrogel—were subjected to 120 rounds of an external magnetic field. The control mouse shows little to no distribution of the cells coated with membrane dye, while the mouse injected with the ferrogel shows a burst of stem cells released throughout the body.

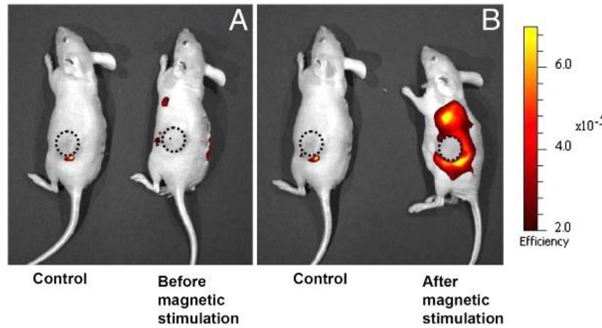

FIGURE 6 [9]
Mesenchymal stem cells released from a macroporous ferrogel by magnetic stimulation

Additional Matrix Elements

Inspired by blood and lymphatic vessels in skin, researchers decided to simulate these in the hydrogel by printing tiny microfluidic channels onto the surface of the elastomer [10]. Red, blue, and green food coloring easily flowed through these circuits, and maintained their shape and robustness even under deformation.

In order to integrate the electronics, such as the LED indicator lights and the temperature sensors into the biocompatible hydrogel, researchers mimicked neurons in the body which send stimulus signals back and forth in ionic circuits [8]. Fortunately, hydrogels are mainly composed of water and are therefore excellent ionic conductors. To promote the conductivity of the ions through the gel, the material was dipped in saltwater and connected to an LED light. Electrodes were strategically placed at either end and an ionic current flowed through the hybrid material, illuminating the light [8]. Even with the addition of this hardware, the product still maintained its original robustness and elasticity. These ionic currents made it possible to incorporate temperature sensors that stimulate a drug release response as well as indicator lights to alert patients when medication levels are low.

PRODUCT COMPARISON

To determine whether the hydrogel bandage would be successful as a commercial product, it is important to weigh its costs with its benefits, as compared to the current methods of wound treatment.

Characteristics of the Ideal Wound Care Treatment

As outlined by Baylor Scott & White Health medical professionals, "chronic wounds require dedicated nursing care that represents a significant cost for national health systems" [11]. It is extremely difficult to heal these wounds, as the healing process often relies heavily on unique characteristics of the patient and individual wound conditions, which can make wound care highly inefficient, as each case must be closely examined. Factors such as extreme dryness, infection or unnatural bacterial presence, prolonged exposure to moisture, cell death, pressure, trauma, and abnormal fluid accumulation can all extend the recovery timeline, thus draining monetary resources from the healthcare system [11].

The optimal treatment for a chronic wound should be able to keep the affected area hydrated, permeable to gases, protected from external infectors and heat, as well as completely sterile with easy removability [11]. Although these characteristics would provide an effective environment for efficient healing, the product should also have marketability components. These would include patient benefits such as comfort and wearability, practical benefits such as infrequent need for redressing and cost effectiveness, and technical benefits such as a long shelf life or reusability.

Current Methods of Wound Care

One of the most widely-used wound management tools in hospitals is gauze. This material is readily available, very cheap, and versatile so that it can be used to treat many different kinds of wounds. Additionally, gauze has been soaked in various active ingredients like iodine and zinc oxide to enhance its performance, which has shown positive results [11]. However, one of the largest drawbacks to the widespread employment of gauze in hospitals is the damage it causes when removed. Often, gauze removal results in the stripping of newly-formed epithelial tissue and trauma to the patient, setting the recovery timeline back every time the wound needs to be redressed. Furthermore, according to the World Health Organization (WHO), over 180,000 deaths a year occur due to burns and scalds [12]. However, more meaningful is that strictly fire-related burns "account for 10 million Disability Adjusted Life Years (DALYs) lost globally each year" [13]. A DALY is a measure of the impact a disease has on an effected person, measured in years taken off a lifetime. While hydrogels may not able to prevent deaths caused by extremely severe burns, they could potentially extend an injured patient's life by giving the affected area the care it needs [13].

Additionally, traditional methods of wound care are time-consuming because gauze needs to be changed each time that wound drainage soaks it, which could be as often as multiple times in a single day. Furthermore, gauze is known to dry out wounds because it does not allow for adequate air flow to the affected area, giving doctors another reason to take time to redress.

All things considered, there are several downsides of conventional gauze treatments that are accepted as the standard, but don't have to be. Hydrogels can solve all these problems in one cohesive unit.

Advantages of Modern Hydrogels

Alternatively, hydrogels have the ability to maintain hydration, stay localized on the affected area, and induce autolytic debridement, which facilitates the elimination of dead tissue and increases collagenase production. Collagenase is an enzyme which breaks collagen peptide bonds to prevent the formation of bacteria. What's more, the expansion of crosslinked polymer chains results in an absorbent quality which can remove bacteria and waste molecules [11]. The impressively high water content found in hydrogels promotes oxygenation and vapor transmission to the injuries. These qualities align well with the characteristics of the optimal wound management treatment.

According to Baylor Scott & White Health, the most common and problematic wounds found in hospital patients are pressure ulcers, diabetic foot ulcers, arterial ulcers, and venous ulcers [1]. One case study compared the effects of a hydrogel with a standard gauze treatment—plain gauze impregnated with povidone-iodine—on pressure ulcers [14]. Researchers studied a group of 27 patients—24 males and 3 females—with spinal cord injuries and a combined total of 49 pressure ulcers. Each group was periodically treated with one of the two methods and the results were determined by measuring the rate of wound healing, in cm^2/day. 54% of wounds treated with the gauze treatment healed, while 84% of the wounds treated with hydrogel healed. The study concluded that wounds treated with hydrogels promoted greater epithelialization of pressure ulcers than the standard gauze treatment currently being used [15].

MARKET POTENTIAL OF THE HYDROGEL BANDAGE

With successful applications and marketed products of hydrogels in areas such as hygiene, optometry, and wound dressings, it is curious as to why the hydrogel bandage, or any drug-delivery product involving hydrogels for that matter, have not been able to establish adequate commercialization. According to the Journal of Biomedical Sciences, "many hydrogel-based drug delivery devices and scaffolds have been designed, studied and in some cases even patented, however not many have reached the market" [2].

Historically, some aspects that have inhibited the approval and commercialization of hydrogels have included the toxicity of cross-linking chemical agents as well as a limited understanding of the hydrogel's formation when subjected to physiological conditions [2]. Today, these issues have been remedied with new knowledge of polymer chemistry and a greater understanding of biological processes. Hydrogels require reapplication about 2-3 times a week, while other solutions must be reapplied daily [11]. The application of the hydrogel is a straightforward process which advances the recovery time, while the reapplication of gauze consistently extends the healing process.

The hydrogel bandage includes all the natural, proven hydrogel benefits while also incorporating the marketability. The sustained delivery of medication to the application area removes the need to reapply the hydrogel, which will only increase efficiency. The hydrogel still maintains all of its original properties, such as being mainly composed of water, which preserves the affected area's access to oxygen and other gases. The most significant function of the hydrogel in terms of its wound-healing properties is its ability to keep the area hydrated but not over-saturated. The addition of the elastomer was able to preserve this natural ability, so the product will still promote autolytic debridement and epithelialization.

Improving the Sustainability of Healthcare Systems

Replacing current wound-healing methods with this innovation would also be an environmentally-conscious decision, as it is sterile and can be reused, providing for a long shelf-life and thus greater sustainability. This factor is especially significant in hospitals, where there is a tremendous amount of waste. In fact, according to a WHO presentation titled "The Healthcare Waste Management System," total waste generated by hospitals amounts to 2-4 kilograms per hospital bed per day [16]. Waste categories include infectious waste, chemical waste, general non-hazardous waste, and sharps, which mainly consist of needles and syringes. "Dressings, bandages, gauze, and cotton contaminated with blood or body fluids" are considered infectious waste, which totals 0.2-0.4 kilograms per bed per day [16]. The following figure shows the average representation of healthcare material waste, excluding food.

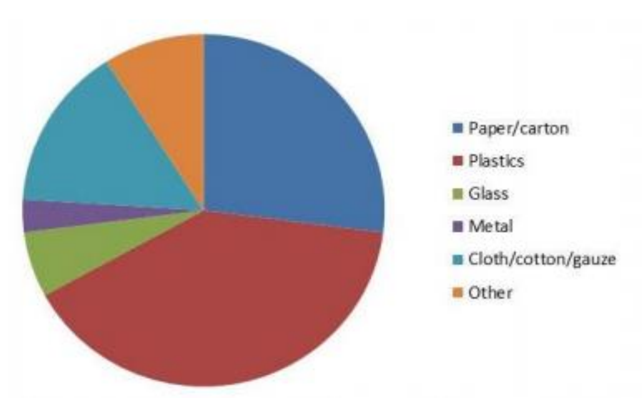

FIGURE 7 [16]
Typical breakdown of material components in healthcare waste

The substantial teal-colored section is representative of the healthcare waste due to cloth, cotton, and gauze. Disposal of infectious waste is often completed via incineration, which "poses a significant threat to the environment" [17]. Through this harmful process, pollutants such as sulfur, metals, acid gases, and "numerous substances of unknown toxicity" are released to the atmosphere, potentially resulting in "global warming, acidification, photochemical ozone or smog formation, eutrophication, and human and animal toxicity" [17]. These adverse effects could be reduced by paring down the amount of infectious waste that hospitals produce.

Since gauze and other bandage materials make up a sizable portion of the total infectious waste, any efforts to curb the use of these materials would be greatly beneficial to the environment. The hydrogel bandage does not require gauze or any other material in order to operate and therefore its employment as a gauze replacement would diminish the harsh environmental impact, thus improving environmental sustainability.

Cost Effectiveness

While the cost of implementing the hydrogel bandage must be considered, it is also important to assess the need for a change. Is gauze a cost-effective option for treating wounds today? According to Travis Doering, a third-year medical student at the time, it is most definitely not. In his residencies, Travis was taught to "always use more tape, it's free," and if there was extra gauze, "toss it" [18]. This mentality, while also harming the environment, increases the bottom line of the hospital, making procedures more expensive than they need to be.

The other side of cost effectiveness is whether a price is worth the outcome. While gauze may seem cheap, is it doing its job well? An analysis of 3,047 wounds concluded that the infection rate for wounds treated with gauze is 7.1 percent, while the rate for wounds treated with moisture-retentive dressings was only 2.6 percent [19]. The increased infection rate only results in longer hospital stays.

According to the Wound and Hyperbaric Healing Center at Ridgeview Medical Center, the first evaluation of a patient's wound and care plan could take up to 90 minutes. Follow-up visits, which generally occur at least once a week, take 20-30 minutes each [20].

Each of these appointments costs the patient money, and while 20-minute sessions may not seem all that expensive, each one will start to add up quickly, especially if the patient's wound is severe and healing slowly. The hydrogel bandage could save the patient a great deal of money in the long run, as frequent clinical visits to get wounds redressed would be unnecessary. This money-saving benefit of the hydrogel bandage speaks to its economic sustainability.

ALTERING NATURE TO ALTER THE STANDARD

The hydrogel bandage has the potential to alter the current standard of wound care. Its natural water-based composition is its most utilitarian attribute, as it provides versatility to numerous avenues of scientific applications and additions. While hydrogel already has plenty of natural wound-healing benefits, Zhao proved that it is possible to alter its intrinsic characteristics to achieve even greater desired outcomes. For instance, Zhao improved the hydrogel's flexibility and robustness by modifying the mechanical dissipation to successfully distribute equal stress throughout the product. In addition, the cross-linkage imperfections were minimized by applying a below flaw-insensitive length scale and its effective strength was increased by creating identical polymeric chain lengths.

Furthermore, the creation of the macroporous ferrogel facilitated the stimulus-induced drug delivery that is crucial to the efficacy of the hydrogel bandage. The hydrogel is highly robust and adaptable, so that it can support both diffusion through microfluidic channels as well as electronic elements, such as indicator lights and temperature sensors.

Hydrogel, as an individual product, has shown success in the market and was proven to heal wounds more efficiently in a case study comparing hydrogel to a traditional chemically- treated gauze dressing. The hydrogel bandage has even more potential benefits which include a shorter recovery period due to sustained drug release and fewer visits to outpatient clinics for required redressing, which saves the patient time and money.

SOURCES

[1] R. M. Plemmons. "Wound Care in the Hospital." Wound Care and Hyperbaric Medicine Clinic Scott & White. Accessed 2.24.2018. http://healthcare-professionals.sw.org/resources/docs/division-of-education/events/hospitalist-medicine-conference/2013/1010_MON_WoundCare_Plemmons.pdf

[2] N. Chirani, L. Yahia, L. Gritsch, F.L. Motta, S. Chirani, S. Fare. "History and Applications of Hydrogels." Journal of Biomedical Sciences. 2015. Accessed 2.24.2018. http://www.jbiomeds.com/biomedical-sciences/history-and-applications-of-hydrogels.php?aid=7218

[3] "Xuanhe Zhao." Massachusetts Institute of Technology. Accessed 2.25.2018 http://meche.mit.edu/people/faculty/ZHAOX@MIT.EDU

[4] "Publication." Massachusetts Institute of Technology. Accessed 2.26.2018 http://web.mit.edu/zhaox/www/publication.html

[5] J. Sun, X. Zhao, W. R. K. Illeperuma, O. Chaudhuri Kyu Hwan Oh, D. J. Mooney, J. J. Vlassak, Z. Suo. "Highly Stretchable and Tough Hydrogels." Springer Nature. 9.05.2012. Accessed 2.24.2018 https://www.nature.com/articles/nature11409

[6] X. Zhao. "Designing toughness and strength in soft materials" Proceedings of the National Academy of the Sciences. 8.01.2017. Accessed 1.13.2018. http://web.mit.edu/zhaox/www/papers/100.pdf

[7] H. Gao, B. Ji, I.L. Jager, E. Arzt, P. Fratzl. "Materials become insensitive to flaws at nanoscale: Lessons from nature." Proceedings of the National Academy of the Sciences. 5.13.2003. Accessed 2.27.2018. http://www.pnas.org/content/pnas/100/10/5597.full.pdf

[8] J. Chu. "Tough new hydrogel hybrid doesn't dry out." MIT News. 6.27.2016. Accessed 2.10.2018. http://news.mit.edu/2016/tough-hydrogel-hybrid-artificial-skin-0627

[9] X. Zhao, J. Kim, C.A. Cezar, N. Huebsch, K. Lee, K. Bouhadir, D.J. Mooney. "Active scaffolds for on-demand drug and cell delivery." Proceedings of the National Academy of Sciences of the United States of America. Accessed 2.23.2018. www.pnas.org/content/108/1/67?ijkey=10ddfd43f4a0d5ff6b088cca529e0edc8dff58fa&keytype2=tf_ipsecsha

[10] H. Yuk, T. Zhang, G.A. Parada, X. Liu, X. Zhao. "Skin-inspired hydrogel-elastomer hybrids with robust interfaces and functional microstructures." Nature Communications. 6.27.2016. Accessed 2.23.2018. https://www.nature.com/articles/ncomms12028

[11] E.Calo, V.V. Khutoryanskiy. "Biomedical applications of hydrogels: A review of patents and commercial products." ScienceDirect. 4.2015. Accessed 2.24.2018. https://www.sciencedirect.com/science/article/pii/S0014305714004091

[12] "Burns." World Health Organization. 1.2018. Accessed 3.28.2018. http://www.who.int/mediacentre/factsheets/fs365/en/

[13]"A WHO Plan for Burn Prevention and Care." World Health Organization. 2008. Accessed 3.28.2018. http://apps.who.int/iris/bitstream/handle/10665/97852/9789241596299_eng.pdf?sequence=1&isAllowed=y

[14] A. Sood, M. S. Granick, N.L. Tomaselli. "Wound Dressings and Comparative Effectiveness Data." US National Library of Medicine National Institutes of Health. 8.1.2014. Accessed 2.22.2018. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4121107/

[15] A.Z. Kaya, N. Turani, M. Akyuz. "The effectiveness of a hydrogel dressing compared with standard management of pressure ulcers." US National Library of Medicine National Institutes of Health. Accessed 2.25.2018. https://www.ncbi.nlm.nih.gov/pubmed/15656468

[16] "Module 1: Definition, Sources and Characteristics of Healthcare Waste."World Health Organization. Accessed 3.28.2018. http://www.who.int/water_sanitation_health/facilities/waste/module1.pdf

[17] R. Sharma, M. Sharma, R. Sharma, V. Sharma. "The impact of incinerators on human health and environment." US National Library of Medicine National Institutes of Health. 2013. Accessed 3.28.2018. https://www.ncbi.nlm.nih.gov/pubmed/23612530

[18] T. Doering. "Use More Tape-It's Free." Costs of Care. 2015. Accessed 3.29.2018. costsofcare.org/use-more-tape-its-free/
[19] G. Motta. "The True Cost of Gauze." Ostomy Wound Management. 3.2008. Accessed 3.29.2018. http://www.polymem.com/articles/pearls4practice0308.pdf
[20] "Wound & Hyperbaric Healing Center FAQs." Ridgeview Medical Center. Accessed 3.30.2018. https://www.ridgeviewmedical.org/services/wound-care-hyperbaric-oxygen-therapy/wound-care-hyperbaric-healing-center-faqs#FAQ3

ADDITIONAL SOURCES

Kamoun, Kenawy, Chen. "A review on polymeric hydrogel membranes for wound dressing applications: PVA-based hydrogel dressings." Journal of Advanced Research. 2.03.2017. Accessed 3.28.2018. https://www.sciencedirect.com/science/article/pii/S2090123217300243
Marra. Conversation regarding hydrogel research. University of Pittsburgh Department of Plastic Surgery and Bioengineering. 3.02.2018
"Hospital Incinerators." INCINER8. Accessed 3.28.2018. https://www.inciner8.com/hospital-incinerators.php
Liu, Tang, Tham, Yuk, Lin, Lu, Zhao. "Stretchable living materials and devices with hydrogel-elastomer hybrids hosting programmed cells." Proceedings of the National Academy of Sciences of the United States of America. 2.2017. Accessed 2.24.2018. www.pnas.org/content/114/9/2200

ACKNOWLEDGEMENTS

We would like to thank our conference co-chair Claire Kraft for providing valuable feedback during our weekly meetings that helped us shape our paper into something that was ready for the conference. We would also like to thank our chairs Hannah Smith and Natalie Rutkowski for helping us find new information as we finished our research, including connecting us with Dr. Kacey Marra, an associate professor who has published several peer-reviewed articles on hydrogels.