



Fish Skin to Heal Wounds

This product shows promise
in helping chronic wound patients achieve closure faster.

BY CHRISTOPHER L. WINTERS, DPM, CWS-P

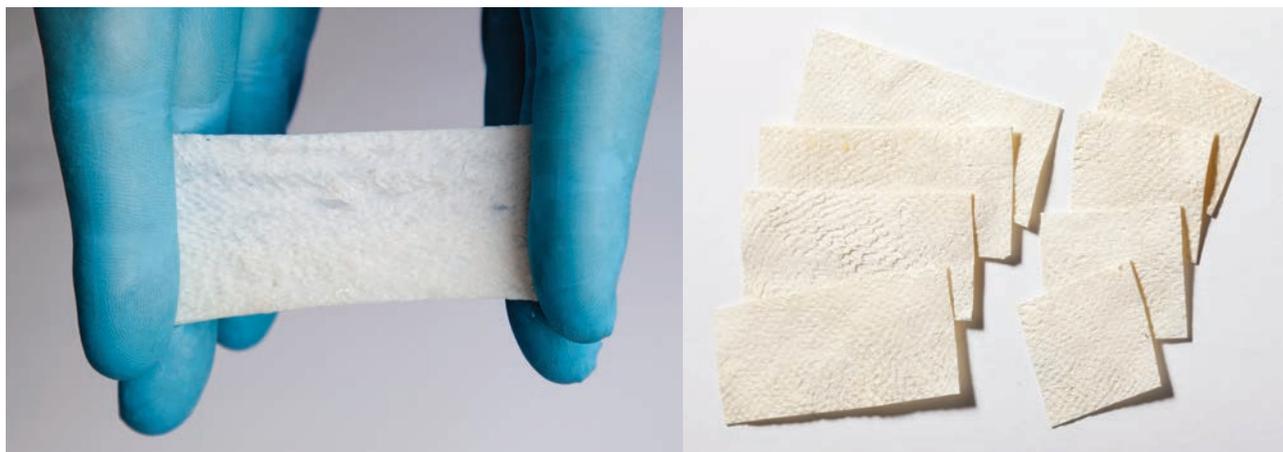


Figure 1: Kerecis™ Omega3 Fish Skin (photos provided by the author)

The field of wound care is ever-expanding with new and exciting products that have enabled physicians to be better able to heal challenging wounds in a timely and cost-effective manner. There are a plethora of products, both cellular and acellular, currently available to heal these ulcers; each has its own advantages. A novel and particularly

The Fish skin product helps the wounds that are stalled in the inflammatory state to move on to heal in the normal process.

promising technology has recently emerged from Iceland using fish skin. This is the only commercially available fish skin product on the market and is approved for human use in the United States by the Food and Drug Administration.

The company that developed this technology is Kerecis, which was established in 2009 as a research project based in Isafjordur, Iceland. Kerecis, with its headquarters and manufacturing facilities in Isafjordur and offices in Reykjavik, Iceland, and Arlington, Virginia, started commercial operations in 2013. The product is marketed as Kerecis Omega3 Wound. This author has had experience using the product since early 2014.

The fish skin is sourced from local fishermen located on the northwest coast of Iceland. The fish, Atlantic cod (*Gadus morhua*) are not farmed and are line-caught in a very sustainable manner that is thoroughly regulated by the Icelandic government. Atlantic cod is by far the most important marine resource in Icelandic waters and is probably the most common fish in northern Icelandic waters. The cold, pristine waters of the North Atlantic are the perfect breeding grounds for this fish. The fish skin is closely inspected for any defects or imperfections prior to processing.

According to the American Diabetes Association, more than 50,000 Americans undergo amputations due

Continued on page 120

New Concepts and Studies

“New Concepts” is a forum for the presentation of (1) new technologies and products and (2) new studies involving existing products. Readers should be aware that Podiatry Management does not specifically endorse any of the technologies, concepts, or products being discussed.

to diabetes each year. Fully 30 to 50 percent of amputees will undergo another amputation within the next one to three years. The Wound Reach Foundation has reported that diabetes-related amputations in the United States cost about \$3 billion per year and that another \$9 billion is spent on treating diabetic foot ulcers. According to the Centers for Disease Control and Prevention, an estimated

one in three U.S. adults could have diabetes by 2050.

“These staggering statistics demonstrate the importance of providing medical professionals the latest knowledge and tools to treat diabetic wounds effectively and efficiently,” said G. Fertram Sigurjonsson, CEO of Kerecis. “Kerecis is dedicated to working with these professionals

Continued on page 121

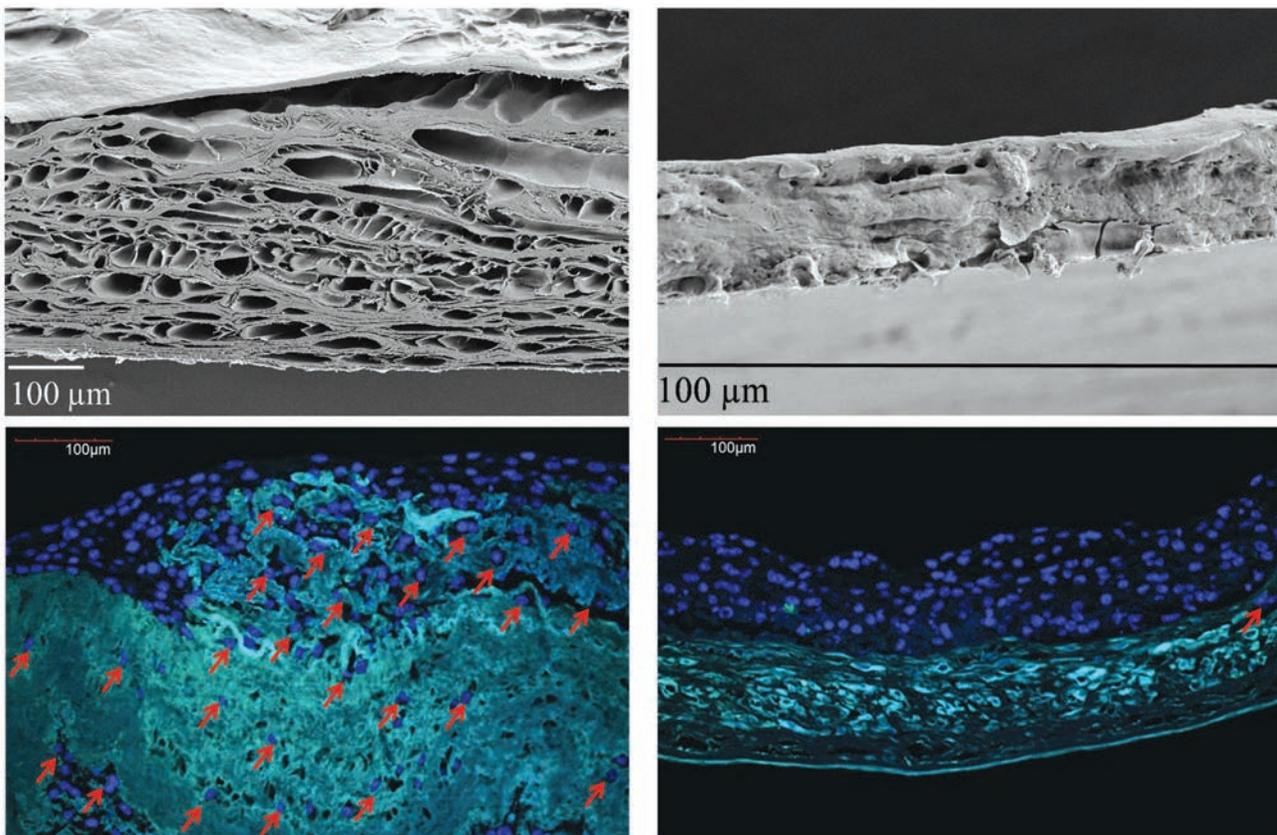
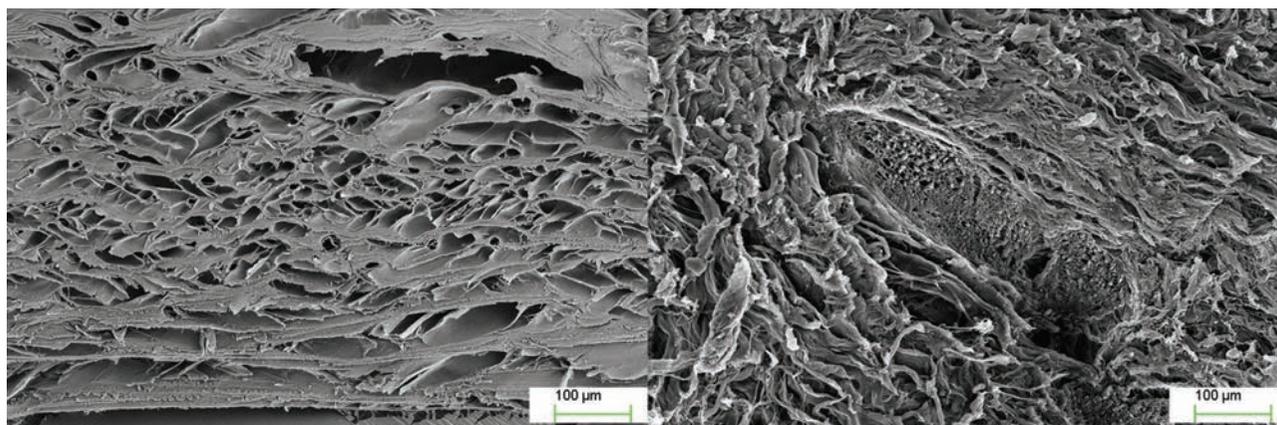


Figure 2 (at bottom of left pix): A. Acellular fish skin graft; (at bottom of right pix): B. Human amnion/chorion membrane allograft



Kerecis™ Omega3 Wound

Human Skin

Figure 3: Scanning electron microscopy images of the fish skin (left) and human skin (right) cross-sections show the structural similarities between the skin types (photos provided by the author)

so that they can help wounds heal and ultimately lower the number of amputations.”

This product has a wide variety of uses and indications but certainly one of the most promising uses is for diabetic foot ulcers.

Kerecis Omega3 Wound offers improved economics and clinical performance, as well as reduced disease transfer risk.

Recruiting the Body's Cells

Kerecis Omega3 is intact fish skin rich in naturally occurring omega 3 polyunsaturated fatty acids. When grafted onto damaged human tissue such as a burn or a diabetic wound, the material recruits the body's own cells and is ultimately converted into living tissue. This is an acellular dermal matrix that allows the body's own cells to incorporate into the fish skin tissue.

Compared to mammalian-based skin substitutes, the fish skin offers improved economics and clinical performance,

as well as reduced disease transfer risk and no cultural constraints on usage. It has powerful anti-inflammatory properties that help the wounds that are stalled in the inflammatory state to move on to heal in the normal process.

The utilization of Kerecis™ Omega3 fish-skin graft (Figure 1) transplantation technology (especially designed for transplant into damaged tissue such as in chronic wounds) has been proven to enhance the wound care clinician's ability to heal wounds and potentially improve the lives of some 6.5 million patients living with chronic wounds in the United States¹ while potentially reducing healthcare costs. Additionally, studies show fish-skin grafts harbor many bioactive properties due to their natural lipid content and preservation of the native structure.² The product also recruits human-adipose stem-cell ingrowth,⁷ acts as a bacterial barrier, and promotes significantly more three-dimensional (3-D) cell ingrowth compared to human amnion allograft.^{3,4} In a randomized, double-blind clinical trial, the omega-3 wound care application has promoted significantly faster healing compared to a porcine small intestinal submucosa (SIS) product (P=0.041).⁵ Furthermore, the fish skin reduces the need for use of analgesic medication in recent case studies^{6,7}

Continued on page 122



Figure 4: Diabetic patient with underlying osteomyelitis. Healed after 33 days and three applications with the Kerecis Omega3 acellular graft.

and, because there are no known religious and cultural barriers to its use, the fish-skin acellular graft can help potentially underserved communities.⁸ These advantages further strengthen the product's and the wound care clinician's ability to improve the lives of patients and potentially reduce healthcare costs.

Improved Economics and Clinical Performance

The size of the fish skin tissue is much thicker than that of the porcine SIS. Compared to mammalian-based skin substitutes, Kerecis Omega3 Wound offers improved economics and clinical performance, as well as reduced disease transfer risk and no cultural constraints on usage.

Other tissue-transplant products are based on tissues of human and porcine origin. These are not ideal substitutes

There is remarkable similarity in the cellular structure of human skin compared to fish skin.

because heavy processing is needed to eliminate the risk of disease transmission. This harsh antiviral treatment removes most of the material's natural components, making it dissimilar to human skin. This does not occur with the processing of the Kerecis Omega3 Wound product. The scales are also removed during the processing. The technology includes a very gentle processing technique that keeps the majority of the native fish skin structure intact.

The fish skin has been shown to have superior cellular ingrowth in comparison with a human amnion/chorion tissue¹⁰ (Figure 2).

There is also remarkable similarity in the cellular structure of human skin compared to fish skin (Figure 3). It is thought that this may explain some of the rapid incorporation of the human cells into the fish skin as the body may recognize the fish skin as similar to its own skin.

A unique property of this product is the omega 3 content that is native to the fish skin. The Kerecis Omega3 Wound product is an acellular intact fish skin that contains proteins, lipids (including omega-3), and other skin elements in its natural structure that fundamentally differ from other biologic products due to its structural preservation and bioactive lipid content. The omega-3 in the fish-skin graft may also help the wound escape the chronic inflammatory state by giving rise to pro-resolving lipid mediators, in the opinion of this author. The Kerecis Omega3 wound product is used to reconstruct human tissue in wounds. Kerecis Omega3 fish skin is marketed in the U.S., Europe, and Southeast Asia and has been cleared by the U.S. Food and Drug Administration (FDA).

The porosity of the fish skin structure and natural omega-3 content are likely to play a key role in its regenerative properties. Another *in vitro* study done at the U.S. Army Institute of Surgical Research showed fish skin is able to recruit ingrowth of human-adipose-derived mesenchymal stem cells.¹¹

A recent study by Yang *et al* showed promising results in a 18-patient prospective study with 5 weekly applications of the fish skin. The results showed that there was a 40% decrease in wound surface area ($P < 0.05$) and a 48% decrease in wound depth seen with 5 weekly applications of the fish-skin graft and secondary dressing.⁷

There are many examples of the clinical application of this product. It is indicated for use on wounds including diabetic, venous, burns, surgical buttress that can be used in lung, bariatric, gastric, colorectal, and other surgeries including dura matter repair. It is also indicated for use in pressure ulcers, arterial and venous insufficiency and vasculitis.

It comes in multiple sizes, making it ideal for starting with a larger wound and decreasing to a smaller size as the wound is healing. The currently available sizes range from 7x10 cm to 1.75cm x 1.75 cm. It is available for use in the office, wound clinic and operating rooms, making it a very versatile product in that sense. It also has its own Q code allowing for reimbursement to occur.

Continued on page 123

The fish skin product can be used over bone, tendon and muscle as well as under negative pressure wound therapy. It is relatively thick and thus can stand up to the NPWT pressure as well as plantar foot pressure.

Application Technique

The application technique of Kerecis Omega3 is straightforward. The product has a long shelf life of 3 years and is stored at room temperature. It is hydrated for about 60 seconds in saline. The product should be trimmed to the size of the wound with very slight overlap. It is recommended that the scale side goes up. Fixation is physician's preference and could be steri strips, sutures or staples. The cover dressing is also physician

A recent study by Yang *et al* showed promising results in a 18-patient prospective study with 5 weekly applications of the fish skin.

preference but should be something that can absorb drainage and prevent significant biofilm formation. The dressing can be left on for up to one week.

At one week the dressing would be changed and the wound inspected. There likely will not be any visible product left in the wound bed. At this point it is the physician's choice where to debride or re-apply. Normally the wound would be cleansed and debrided as needed and a second piece would be applied at the end of the first week. This process is continued weekly with further applications at week two or three based on clinical appearance and physician preference. It is normal to have 3-5 applications per wound and most wounds would not need many more than five based on the size and clinical appearance of the wound.

Case Study

A case study here is of a 47 year old diabetic African-American male with a chronic (over 30 days) ulcer at the medial aspect of the first metatarsal head. It probed to bone and showed early radiographic changes of osteomyelitis. The infectious disease physician recommended amputation and the patient refused. The Kerecis Omega-3 Wound product was applied (Figure 4) three times in less than 5 weeks and the ulcer achieved complete closure. The ulcer remained healed at one year.

Summary

In summary, Kerecis Omega-3 Wound is a very versatile product with unique properties unlike anything else on the market. It is the only commercially available fish skin product that is used in wound care. Benefits include the rapid incorporation of the cells, relatively lower cost, omega-3 anti-inflammatory properties, multiple sizes, minimal process-

ing with harsh chemicals and thus the advantage of preserving the native structure of the product. This product offers the physician a "new tool in the toolbox" to help chronic wound patients achieve wound closure faster and to avoid potential amputation or prolonged wound care. **PM**

References

- ¹ Sen CK, Gordillo GM, Roy S, et al. Human skin wounds: a major and snowballing threat to public health and the economy. *Wound Repair Regen.* 2009;17(6):763-71.
- ² Magnusson S, Baldursson BT, Kjartansson H, et al. Decellularized fish skin: characteristics that support tissue repair. *Laeknabladid.* 2015;101(12):567-73.
- ³ Magnusson S, Baldursson BT, Konradsdottir F, Kjartansson H, Rolfsson O, Sigurjonsson GF. Regenerative and antibacterial properties of acellular fish skin grafts and human amnion/chorion membrane: implications for tissue preservation in combat casualty care (unpublished data).
- ⁴ Magnusson S, Baldursson B, Konradsdottir F, Rolfsson O, Sigurjonsson G. Acellular fish skin reduces wound area and allows for significantly more cell ingrowth than human amnion / chorion membrane allograft. Presented at SAWC Fall. September 2015; Las Vegas, NV.
- ⁵ Baldursson BT, Kjartansson H, Konradsdottir F, Gudnason P, Sigurjonsson GF, Lund SH. Healing rate and autoimmune safety of full-thickness wounds treated with fish skin acellular dermal matrix versus porcine small-intestine submucosa: a non-inferiority study. *Int J Low Extrem Wounds.* 2015;14(1)37-43.
- ⁶ Trinh TT, Dünschede F, Vahl CF, Dorweiler B. Marine omega3 wound matrix for the treatment of complicated wounds. *Phlebologie.* 2016;45(2):93-98.
- ⁷ Yang CK, Thais O, Polanco, MD, Lantis II JC. A prospective, postmarket, compassionate clinical evaluation of a novel acellular fish-skin graft which contains omega-3 fatty acids for the closure of hard-to-heal lower extremity chronic ulcers. *Wounds.* 2016;28(4):112-18.
- ⁸ Eriksson A, Burcharth J, Rosenberg J. Animal derived products may conflict with religious patients' beliefs. *BMC Med Ethics.* 2013;14:48.
- ⁹ A Prospective, Postmarket, Compassionate Clinical Evaluation of a Novel Acellular Fish-skin Graft Which Contains Omega-3 Fatty Acids for the Closure of Hard-to-heal Lower Extremity Chronic Ulcers. Chun K. Yang MD; Thais O. Polanco MD; and John C. Lantis II MD FACS. *WOUNDS: A Compendium of Clinical Research and Practice,* 2016 Apr;28(4):112-8.
- ¹⁰ Structure of Acellular Fish Skin is Conducive for Cell Ingrowth Compared to Human Amnion/Chorion Membrane Allograft. Skuli Magnusson BSc, Baldur Tumi Baldursson MD PhD, Hilmar Kjartansson MD, Ottar Rolfsson PhD.
- ¹¹ Magnusson S, Baldursson B, Konradsdottir F, Rolfsson O, Sigurjonsson G. Acellular fish skin supports stem cell ingrowth: acellular fish skin graft facilitates ingrowth and proliferation of stem cells. Presented at: Military Health System Research Symposium. August 2015; Kissimmee, FL.



The author is in private practice with the American Health Network in Indianapolis, IN. He serves as the podiatry residency director at St. Vincent Hospital in Indianapolis and is the current Chair of the American College of Clinical Wound Specialists. Dr. Winters is a speaker for Kerecis.