LifeCell introduces skin replacement for burns

AlloDerm, an acellular dermal matrix produced from human cadaver skin, doesn't require FDA marketing approval because it's made from human skin.

NEW YORK—Surgeons have long sought a skin replacement for severely burned patients, since the sole treatment for these patients involves transplanting a layer of their intact skin to their burn sites, a painful procedure that often results in severe contracture at the transplant sites. These surgeons may have finally found such a skin replacement, as LifeCell (The Woodlands, TX) recently started U.S. sales of AlloDerm, an acellular dermal matrix produced from human cadaver skin. Indeed, AlloDerm—which, because it is produced from human skin, doesn't require marketing approval from the Food and Drug Administration (FDA, Rockville, MD)—could minimize burn patient skin transplants and reduce transplant-site contracture.

Skin is largely made up of two layers, the outer epidermis and the underlying dermis. The epidermis—a thin layer composed mostly of keratinocytes—forms a physical barrier against the environment. The dermis—which is about three times thicker than the dermis and is vascularized—is composed predominately of fibroblasts locked in a collagen matrix. Severe burns, or third-degree burns, destroy both the epidermis and the dermis. When surgeons transplant a patient's intact skin—containing both the epidermis and the dermis—to the burned area, they first punch holes in the skin to expand its area. Yet since the dermis doesn't regenerate, these holes fill with scar tissue, causing transplant-site contracture.

LifeCell produces AlloDerm by first removing the epidermis from cadaver skin and then removing the fibroblasts from the cadaver-skin dermis, leaving intact the collagen bundles of the dermal matrix, as well as the dermis' basement membrane. The basement membrane anchors the epidermis' keratinocytes to the dermis and also influences keratinocyte differentiation into stratified layers. The product is then freeze-dried for storage and shipping and is rehydrated just before use.

AlloDerm's basement membrane, according to LifeCell, is what separates it from the competing skin-replacement products of Advanced Tissue Sciences (La Jolla, CA), BioSurface Technology (BST, Cambridge, MA), and Organogenesis (Canton, MA), none of which contain basement membranes and all of which are in clinical tials, since they're composed of more than just human skin. LifeCell believes that skin-replacement products without basement membranes won't adequately anchor epidermal keratinocytes, resulting in the epidermis peeling away from the dermis.

AlloDerm underwent 18 months of clinical testing in 60 patients at 10 U.S. burn centers, with results showing that AlloDerm takes to full-thickness burn wounds without immune rejection. In one study, AlloDerm had a 93 percent take rate in 18 patients with third-degree burns, a rate statistically equivalent to control sites grafted with the patient's own skin. Moreover, patient keratinocyte-supplying epithelial grafts had an 88 percent take rate when applied simultaneously to the grafted AlloDerm's surface. Analysis at 15 days following surgery revealed keratinocytes migrating from the patient epithelial grafts onto AlloDerm's surface. Fifteen-day analysis of the AlloDerm dermal matrix revealed infiltration by host fibroblasts, along with evidence of neovascularization without inflammatory-cell infiltration.

In conducting AlloDerm's trials, LifeCell adhered to FDA protocols, in case the FDA decides to regulate the product as a medical device. The FDA has already classified as medical devices certain human tissue used for transplantation, including heart valves and corneal lenticules. The FDA, furthermore, recently announced new regulations for tissue banks—from which LifeCell obtains cadaver skin—to ensure that all tissue donors are properly screened for transmitted diseases. LifeCell, though, already requires such screening, so the new FDA regulations shouldn't affect it, says Jane Lea Hicks, LifeCell's vice president of business development. Yet Marc Klee, a biotech analyst at Renaissance Research Department (RRP, Carle Place, NY), cautions that if the FDA "chooses to require LifeCell to undergo clinical trials for AlloDerm, it would nullify the firm's two-year marketing window over its competition in the skin-replacement market."

Another skin-replacement product has also escaped FDA regulation to reach the U.S. market, since it, too, is made from human skin. BST's Epicel—which the firm intoduced in 1988—is an epidermal graft grown from a patient's own skin, as BST uses its cell-culture know-how to expand in three to four weeks a postage-stamp size epidermis biopsy about 10,000 times, generating enough epidermis to cover a patient's whole body. Yet Epicel—with a shelf life of 24 hours and a price of $15,000 a square foot—is generally used only on those patients who are so badly burned they don't have enough intact skin to graft onto their burns, a patient population that annually totals about 200 in the U.S. and 400 worldwide. Epicel sees such limited use because it doesn't contain a dermal layer and, thus, doesn't reduce wound contracture and improve wound durability as well as conventional skin grafts. Epicel, in fact, racked up sales of just $7.7 million in 1992 and $5.7 million in 1993. Despite these limitations, Toho Pharmaceutical (Tokyo) has signed on to market Epicel in Japan, with sales slated to start later this year.

For its part, LifeCell will market AlloDerm—which has a one-year shelf life and will sell for $10,000 a square foot—to U.S. burn centers through its own sales force, a force that, over the next two years, should grow from its current level of two people to six people. Such a small sales force should be effective, though, since AlloDerm's user market is made up of just 146 burn centers, with 80 of these centers accounting for 80 percent of all burn patients. RRD's Klee, for one, believes that AlloDerm will achieve sales of at least $4 million this year, as this projection calls for AlloDerm treatment of just three patients a week. LifeCell, moreover, expects to broaden AlloDerm's use, with AlloDerm clinical trials already underway for chronic skin ulcers and coming up for reconstructive plastic surgery. **—B.J. Spalding**