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Developing advanced tissue products

Innovative technology addresses unmet needs

Dr. Paul F. Gratzer does not mince words when it comes to the use of amputation as a means of treating chronic diabetic wounds.

"In this day and age of modern medicine and technology, it really is unacceptable," he says. "This is an issue that hasn't had a good solution to it."

Thanks to Dr. Gratzer, that may be about to change. For more than a decade, the associate professor with the School of Biomedical Engineering has been developing advanced tissue products for use in wound healing and surgical reconstructions. His work has resulted in a groundbreaking process that removes the cellular components – the source of tissue graft rejection – from donated human tissue. The result is a safe, sterile, effective scaffold that promotes tissue regeneration when the processed tissue is implanted on patients.

"People have been trying to conduct decellularization of tissues for years, but it's difficult to achieve a high level of removal of the cellular component and maintain the other components of the tissue that you want," explains Dr. Gratzer. "It's like trying to remove the white and the yolk from an egg without damaging the shell."

Through his company, DeCell Technologies, Dr. Gratzer has been very successful in achieving that aim, having developed a patent-pending technology that removes up to 95-97 per cent of cellular material from donated human skin. Competing processes, he notes, remove significantly less cellular materials – as little as 50 per cent. Given that cellular material can impede or prevent tissue regeneration in patients, the more you can remove without altering the structural matrix of the original tissue, the better.

"By maintaining the structural components of tissues and removing all of the donor cells, after implantation in animal trials, we found we were able to get cells from the recipient to grow back in and start to repopulate and regenerate tissue. Ultimately, you can get the recipient's body to replace the implanted material, turning it into tissue that is 100 per cent of the recipient's tissue."

It isn't just the amount of cellular material removed that makes Dr. Gratzer's technology innovative; it's also the fact that it is fully automated. "Other companies rely heavily on manual processing of the tissue. Once we put the donated tissue into our system, it's treated, sterilized, packaged and not touched again until the patient receives the graft. Also, the process is simple enough that we can do the decellularization treatment and sterilization at the same time. As a result, there are some significant safety and cost advantages there."

Dr. Gratzer's decellularized skin product has other significant advantages over competing products in that it doesn't require re-hydrating or thawing. Many competing products require freezing or dehydration to increase shelf-life. "Freezing and dehydration require considerable forethought for the clinician in terms of preparing products for use since it takes extra time to rehydrate or

thaw. Also, if you don't use the tissue after rehydrating or thawing, it can't be kept and is wasted. Most significant is that freezing and dehydration can alter tissue properties and impede wound healing. We've been able to produce our tissue so that it can be stored in a hydrated state at room temperature with an anticipated five-year shelf life."

This spring will see the biggest test to date of Dr. Gratzer's technology: a Canada-wide clinical trial involving 40–60 patients with diabetic foot ulcers. There were many reasons he chose foot ulcers for the first major human trial. For one, diagnoses of diabetes are on a sharp rise worldwide, with 550 million people expected to have the disease by 2030 – approximately 10 per cent of the world's adult population. Up to 25 per cent of people diagnosed with diabetes will develop a foot ulcer in their lives, and 20 per cent of those wounds will eventually result in amputation.

"If you look at amputations that are done in a therapeutic way – to prevent the loss of life – the majority of these are done on diabetic patients who have had a chronic ulcer," says Dr. Gratzer.

"Some tissue products on the market do well, but they're expensive, require multiple applications to heal, and are utilized as last-case salvage before amputation comes into play. What we're trying to do is encourage people to use our decellularized tissue early in treatment in order to minimize the risk of infection and give patients the best care from the start. That way, you get better outcomes with faster healing and that means less expense for our healthcare system."

"We want to provide the best quality solution that we can, taking into account the needs of the healthcare system, the clinician and the patient so we deliver something highly effective, but also with limiting costs to the healthcare system in mind."

Ironically, Dr. Gratzer has a vested interest in the outcome of this trial, having been diagnosed with diabetes himself over the course of his research. "I would be happy to know that, if I did have a problem like this, there would be an effective method of treating and healing the ulcer. That's reassuring."

The next year is likely to be a busy one for Dr. Gratzer. In addition to the clinical trial, he is preparing to set up a for-profit manufacturing facility at the Innovacorp Enterprise Centre. He's beginning a Pilot Clinical Trial this spring to demonstrate the effectiveness and safety of the product. Once completed, he will be securing more grants and equity investments to conduct a larger patient treatment trial in healthcare centres across North America to obtain approval for product reimbursement by public and private insurers. He's also been chatting with clinicians about applying his technology to meet other tissue needs – everything from treating burns to surgical reconstructions.

"The possibilities are limitless," says Dr. Gratzer. "But the key as always is to do it well. We want to provide the best quality solution that we can, taking into account the needs of the healthcare system, the clinician and the patient so we deliver something highly effective, but also with limiting costs to the healthcare system in mind."