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Bones Reborn: 3D Printing Offers Amazing Options for Traumatic Bone Loss

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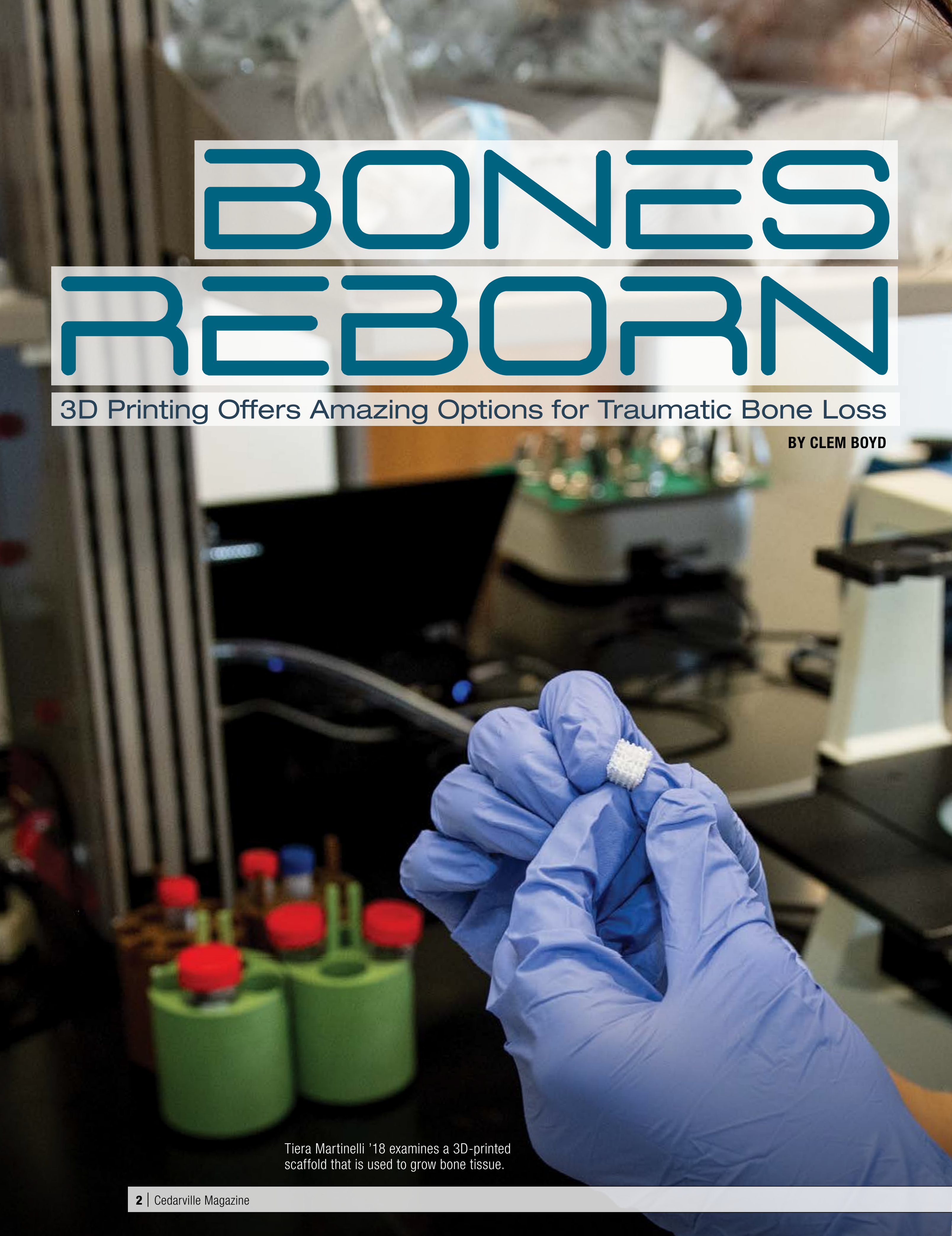
BY CLEM BOYD



Tiera Martinelli ’18 examines a 3D-printed scaffold that is used to grow bone tissue.

The side of a house covered with a vine. We've all seen one. Sometimes it's a sign of neglect; sometimes it's intentional. Regardless the reason, the effect is memorable: a living organism, working from the foundation to the roofline, slowly covering and swallowing up an entire side of a home till only the vine is visible and not what's beneath.

Biomedical engineering and pharmacy students at Cedarville are attempting to replicate that effect on a microscopic level, but for a different purpose — to restore missing bone in individuals who have suffered a traumatic injury.

During the 2016–2017 academic year, Tim Norman, Distinguished Professor of Mechanical and Biomedical Engineering, and Rocco Rotello, Associate Professor of Pharmaceutical Sciences, began cutting-edge research with 3D-printed scaffolds that could support cell life. The scaffolds are made of polylactic acid, a type of plastic very similar to that used in children's construction toys.

Thought of a different way, the scaffolds are like tiny plastic trellises, but instead of vines or roses growing on them, microscopic cells cling to them, dividing and multiplying, and eventually producing living tissue. But the outcome would be the same as a trellis — the cells would cover the entire scaffold, like a vine covering a trellis, so that only new living tissue would be visible.

But different than a trellis on the side of your home, which remains till the homeowner removes it, this "trellis" will biodegrade over time, leaving only tissue. Voila! The scaffold disappears; new bone remains.

RESTORATIVE OUTCOME

Although Norman and Rotello's research is not for application yet, the final outcome could help people who've experienced a severe physical impact and lost bone. Think of a veteran who lost part of a leg bone from an explosive device.

"You're inserting a piece of material into a vertebra or a bone in your hip and providing an environment for the cells that are naturally in the person to invade it," noted Rotello. "This will replace the gap or the vacancy with tissue of the same strength and quality as the person was born with."

Norman and Rotello's research is strictly limited to replacement tissue. "It won't regrow a limb or reproduce a lot of different types of tissue because it's just a scaffold with one type of cell growing on it right now," said Norman. "It's not really designed for the kind of genetic information inside a cell to be triggered to transcribe genes and send signals that would grow a body part."

Even still, the thought of replacing damaged tissue where the body would have created a scar, deformation, and maybe even impairment, is nothing short of remarkable.

SCAFFOLD SCIENCE

While the image of a vine slowly engulfing a trellis or the side of a home is easy enough to grasp, recreating that process in the miniature world of cells is tedious and meticulous.

For instance, cells won't grow on just anything. The scaffolds that might be placed in a person's bone must be like a hothouse for cells, a structure to which they will hold and proliferate. Or to borrow the language of Genesis, Norman and Rotello's scaffolds must be like tiny Gardens of Eden, where the cells can be fruitful and multiply.

What makes a fruitful scaffold? One important factor: stiffness. The scaffolds must be pliable enough to flex under the normal loads that a person would put on that area of bone. But not so pliable the scaffold will easily break down and the growing tissue lost.

"Bone varies in stiffness depending on where it's found in the body and from person to person," noted mechanical engineering major Jacob Cole '18, team leader on the project. "We had to find a way to customize the stiffness of the scaffold based on the patient and the location in the body."

"We know that bone cells like a certain amount of stretching to go on," Norman said. "If you put a bone cell in an area where no load is being applied, it may die because it's not needed. Bone cells need activity that causes them to thrive. Thriving causes them to actually proliferate."

Imagine the bone cells are like teens checking out a youth group. They want to grow somewhere, but if the "ministry" is stiff and there's not much happening, they won't go. The cells want a structure that is flexing, moving, and dynamic, acting like bone even though it isn't bone.

Surface roughness and porosity also play a part in where cells attach. They aren't attracted to a smooth scaffold; they like a roughened surface, similar to how green moss flourishes on a rocky shoreline or microscopic coral attaches to objects to create a reef.

"Once they're stuck, they start to secrete other molecules to multiply and divide," Rotello said. "Some materials you put in the presence of the cells will cause them to quiet down and sort of go to sleep. Great for babies, not so great when trying to create new tissue. But the material Dr. Norman's lab has generated is conducive to growth. These scaffolds promote cell survival and regenerate tissue."

While Norman and his team are creating the right structures for life to take hold, Rotello and his pharmacy students are responsible for creating the right context. This is the biology of the research — what kind of cells to use, the composition of the solution in the petri dish where the cells will live, whether to stir or not to stir the solution. Once these decisions are made, the cells are introduced to the solution, or media, and everything is placed in an incubator.

"Without all of those things, it does not work," Norman said. "We're trying to figure out the right combination, and there are a lot of variables."

A STEP UP

For both Norman and Rotello, 3D human tissue scaffold research is more than cutting edge, it's cutting educational. Students are being pushed to think in ways no textbook can duplicate.

"This is something they can't look up," said Norman. "There's not a real good example of what they're doing; they have to think outside the box. Every day, it's kind of like, 'Where do we go from here?'"

Students who worked on the 3D project with Tim Norman, Professor of Mechanical and Biomedical Engineering, second from left, include (L-R) Daniel Sidle '18, Stephen Smith '18, and Jacob Cole '18.

They're also learning to collaborate across professional fields. "How many engineering students in an undergrad institution get to spend time with a pharmacy professor in a cell culture lab?" Norman added. "That's really unique. They're talking to someone in a different discipline, learning to speak in his 'language.' That's necessary in a field like biomedical engineering."

For Cole, he and the other engineering students learned to lean on the expertise of their pharmacy teammates. "We have a basic knowledge of cells from biology, but they bring a depth of knowledge that allows us to be more efficient in evaluating our scaffolds," Cole said. "They recommended we use fibroblast cells because they divide and multiply normally and are part of the connective tissue family that includes bone-forming cells."

The processes involved are an education in themselves. "They're learning the value of good sterility," said Rotello. "These are living things; you can't introduce foreign substances, which requires careful monitoring."

That was part of the education for mechanical engineering major Sarah Seman '21. Teammate Tiera Martinelli '18 and she cultured cells onto scaffolds, dyed the scaffolds, and counted the number of cells on each. "Early in the project we learned that we needed to follow specialized sterilization procedures to prepare the scaffolds for a living environment," she added.

"They aren't following a cookbook — just do this and you'll get that," Rotello added. "They're learning to alter their methods and problem-solve. It can be frustrating; it isn't just a matter of showing up each day, adding cells, and you see a result. You're babying things along, hoping for a result."

"These engineers are learning how to design for biological systems," Norman added, "making something that has to be agreeable to the way the body works. They don't do that typically."

TINY WINDOW INTO CREATION

The ability to recreate bone and provide a place for muscle attachment that trauma had removed — that's heady stuff. But for Norman and Rotello, this research goes beyond powerful scientific inquiry. It is a window into the ways of the All-Powerful.

"I always tell students, 'We are engineers trying to figure out how God created the world,'" Norman said. "Everything I've discovered and learned shows that Someone designed it. It is not random but very orderly with rules and formulas. Discovering God's creation is part of everything we do."

"We're just looking at one cell, one piece of material," added Rotello. "I appreciate the growth and the science behind it, but we're not even at the molecular level yet. The unique molecules binding to that surface is further proof God did this. He did that inside someone; it didn't just happen by chance."

Tiera Martinelli '18 and Rocco Rotello, Associate Professor of Pharmaceutical Sciences, check out cell growth in the School of Pharmacy lab.

Seman echoed this thought. "Whenever you study biology or physiology, it just gives you a greater sense of awe about how God has created us," she said. "Even at the cellular level, it's so complex. God put all those systems in place, and we're trying to help those systems work as God intended."

The research led to an apologetics application for Cole. During two weeks of training in Germany for his job after graduation, he had an evangelistic discussion with a fellow trainee from Russia. "I was talking with him about the origin of life," he explained. "I told him that, based on my studies so far, I can't see how it's possible for complex structures to evolve by random mutation. This has really given me a better appreciation for creation."

For Norman, the 3D human tissue project ultimately leads to worship. "It's a manifestation of what He created us to do," he said. "Getting to know what He's created is part of getting to know Him."

Clem Boyd *is Managing Editor of* Cedarville Magazine.