

# Researchers Offer Sutureless Method Of Joining Blood Vessels

Reconnecting severed blood vessels is mostly done the same way today — with sutures — as it was 100 years ago, when the French surgeon Alexis Carrel won a Nobel Prize for advancing the technique. Now, a team of researchers at the Stanford University School of Medicine has developed a sutureless method that appears to be a faster, safer and easier alternative.

In animal studies, a team led by Stanford microsurgeon Geoffrey Gurtner, MD, used a poloxamer gel and bioadhesive rather than a needle and thread to join together blood vessels, a procedure called vascular anastomosis. Results of the research are published online in *Nature Medicine*. Lead authors of the study were Stanford post-doctoral scholar Edward Chang, MD, and surgery resident Michael Galvez, MD. The big drawback of sutures is that they are difficult to use on blood vessels less than one millimeter wide.

Gurtner began thinking about alternatives to sutures about a decade ago. "Back in 2002, I was chief of microsurgery at Bellevue in New York City, and we had an infant — 10 to 12 months old — who had a finger amputated by the spinning wheel of an indoor exercise bike," said Gurtner, senior author of the study and professor of surgery. "We struggled with re-attaching the digit because the blood vessels were so small — maybe half a millimeter. The surgery took more than five hours, and at the end we were only able to get in three sutures. "Everything turned out OK in that case," he continued. "But what struck me was how the whole paradigm of sewing with a needle and thread kind of falls apart at that level of smallness."

Sutures are troublesome in other ways, too. They can lead to complications, such as intimal hyperplasia, in which cells respond to the trauma of the needle and thread by proliferating on the inside wall of the blood vessel, causing it to narrow at that point. This increases the risk of a blood clot getting stuck and obstructing blood flow. In addition, sutures may trigger an immune response, leading to inflamed tissue that also increases the risk of a blockage.

The new method could sidestep these problems. "Ultimately, this has the potential to improve patient care by decreasing amputations, strokes and heart attacks while reducing healthcare costs," the authors write in the study. Earlier in his career, Gurtner contemplated whether ice could be used to fill the lumen, the inner space of the blood vessel, to keep both ends open to their full diameter long enough to glue them together. Not feasible, he concluded. "Water turns to ice quite slowly and you would have to drop the temperature of the surgical site a lot — from 98.6 degrees to 32 degrees Fahrenheit," he said.

Shortly after arriving at Stanford in 2005, Gurtner approached fellow faculty

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member Gerald Fuller, PhD, professor of chemical engineering and the Fletcher Jones II Professor in the School of Engineering, about whether he knew of a substance that could be turned easily from a liquid to a solid and back to a liquid again, and that would also be safe to use in vascular surgery. Fuller immediately suggested a Food and Drug Administration-approved thermoreversible poloxamer called Poloxamer 407. It is constructed of polymer blocks whose properties can be reversed by heating.

Fuller teamed up with Jayakumar Rajadas, PhD, director of the Stanford Biomaterials and Advanced Drug Delivery Laboratory, to modify the poloxamer so that it would become solid and elastic when heated above body temperature but dissolve harmlessly into the bloodstream when cooled. The poloxamer then was used to distend both openings of a severed blood vessel, allowing researchers to glue them together precisely.

The researchers used a simple halogen lamp to heat the gel. In tests on animals, the technique was found to be five times faster than the traditional hand-sewn method, according to the study. It also resulted in considerably less inflammation and scarring after two years. The method even worked on extremely slim blood vessels — those only 0.2 mm wide — which would have been too tiny and delicate for sutures. "That's where it really shines," Gurtner said. Dermabond, a surgical sealant, was used to attach the ends of the blood vessels together.

Poloxamers have been used before as a vehicle for delivering drugs, including chemotherapeutics, vaccines and anti-viral therapies. Researchers have used Poloxamer 407 to occlude blood vessels in experimental animals for the purpose of evaluating the gel's safety and efficacy in so-called "beating heart surgery," in which certain vessels need to be temporarily blocked to improve visibility for the surgeons performing a coronary artery bypass.

Although other sutureless methods have been developed, they generally have not produced better outcomes, the authors said. "Often, the use of microclips, staples or magnets is itself traumatic to blood vessels leading to failure rates comparable to or higher than sutured anastomoses," they wrote. "This approach to anastomosis could play a valuable role in microvascular surgery," said Frank Sellke, MD, chief of cardiothoracic surgery at Brown University Medical Center and associate editor of the *Journal of Thoracic and Cardiovascular Surgery*, who was not involved in the study. "But it really needs to show that it holds up in clinical trials."

The authors say further testing on large animals is needed before human trials can begin, but they note that all of the components used in the technique are already approved by the FDA. "This technology has the potential to progress rapidly from the 'bench to bedside,'" they write. Gurtner said he believes the new technique could satisfy a huge unmet need and prove especially useful in minimally invasive surgeries, in which manipulating sutures takes on a whole new level of difficulty.

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