Engineers, doctors develop novel material that could help fight arterial disease

November 25 2009

A fortuitous discovery that grew out of a collaboration between UCLA engineers and physicians could potentially offer hope to the nearly 10 million Americans who suffer from peripheral arterial disease.

Also known as hardening of the arteries, peripheral arterial disease, or PAD, is a common circulatory problem in which narrowed arteries reduce blood flow to the limbs. The condition is considered a red flag for vascular disease, heart attack and stroke, and its progression can result in the loss of limbs or death.

While there are currently several treatments for PAD, including balloon angioplasty, stenting and bypass surgery, devices used in the latter two can frequently cause thrombosis, in which clots form inside blood vessels, obstructing blood flow and leading to serious complications.

Now, a team from the UCLA Henry Samueli School of Engineering and Applied Science, in collaboration with researchers from the David Geffen School of Medicine at UCLA, is working to develop a PAD treatment device that can prevent thrombosis in small-diameter blood vessels.

Their research centers on stents that incorporate a material known as Nitinol, a superelastic nickel and titanium alloy that has the ability to be deformed and to recover its original shape upon heating.

In recognition of the potential of the research, the National Institutes of

Health's National Heart, Lung and Blood Institute recently awarded the team a $1 million Challenge Grant.

"What we've been doing at UCLA for the last five to 10 years now is working with thin-film Nitinol," said Greg Carman, a professor of mechanical and aerospace engineering and lead investigator for the multidisciplinary research team, which was organized under the umbrella of the UCLA Center for Advanced Surgical and Interventional Technologies.

"Nitinol, discovered back in the 1960s, is a shape-memory material. They thought it was going to revolutionize the engineering field. It wasn't until 1985 that people began to think this material would probably be great to use in a stent," Carman said. "The reason they liked it for a stent is because you could bend the material a very large distance and it would return back to its original shape. Other metals, such as surgical steel, do not allow such a large shape recovery and, as such, cannot be used in many stenting devices."

In the early 2000s, Carman's group started looking into making thin-film Nitinol and accidently stumbled across a way to fabricate what they believed was very high-quality, uniform-composition Nitinol.

"That's when we started producing thin-film Nitinol. We weren't sure where the applications for this novel, very low-profile material would go until we ran into someone in the medical school," Carman said.

"I immediately saw the promise that thin-film Nitinol had for intravascular and cardiac applications," said Dr. Daniel Levi, a pediatric cardiologist at Mattel Children's Hospital UCLA and a principal investigator on the team. "Greg and I started working together immediately on stents and a heart valve."

Carman and Levi's team looked into producing stents that incorporated thin-film Nitinol on the exterior. Originally, the team considered it a possible treatment for neural vascular disease. They then discovered that their thin-film Nitinol, at only 5 microns thick — compared to commercial stents, with a covering 100 microns thick — could be placed into much smaller tubes or catheters and used on much smaller-diameter blood vessels, like those found in limbs.

While this was a boon to treatment delivery, the main concern with PAD treatment was thrombosis. During testing, the team soon discovered their new stent possessed several attributes that could combat thrombosis.

When a blood vessel is injured, the body uses blood platelets to form clots as a first step in repair and to prevent further blood loss. Initially, the researchers found that blood clots formed on the surface of the thin-film Nitinol they tested in animals. But a student of Carman's, Youngjae Chun, reviewed the literature and discovered that the thrombosis might be related to the hydrophobic nature of the material's surface. He measured the film and found it to be slightly hydrophobic.

"Hydrophobic means when you put a drop of water on a surface, it beads up like water on a freshly waxed car," Carman said. "This is typically undesirable in reducing thrombosis. We wanted it to be hydrophilic, the opposite of hydrophobic."

The team began an elaborate study, exploring various treatments that would modify the surface structure of the thin-film Nitinol. During one test, Chun discovered a treatment that produced not just a hydrophilic response but a super-hydrophilic response, meaning the wetting angle goes to zero and there are no water beads on the surface.

The team conducted in vitro studies to see if platelets would adhere to the surface of their new chemically treated material. The tests were a

success: Virtually no platelets adhered.

But they also realized that in vitro testing alone wouldn't convince the medical community that their material was definitely non-thrombogenic.

"With the Challenge Grant, we are beginning to do tests in animals again and have already seen that our film does remain patent," Carman said. "It's our understanding that very few, if any, covered stents out there that are put into 3- or 4- millimeter vessels will remain patent. We need to show with statistical relevance that our material stays patent longer than other systems commercially on the market. If we can do that, we would have something that could impact the world quite dramatically.

"While we are very optimistic it will work, we also understand that biology does not always behave how you would like it to. All of our results to date point to a very promising conclusion."

"At this point, we need to deploy the stent grafts and have them stay open," said Dr. David Rigberg, a vascular surgeon at the Geffen School of Medicine and the third principle investigator on the team. "We also want to see that under examination many of the things that we look at to determine if something is going to thrombose are decreased. I think the study has a real shot at clinical application."

"PAD is a huge problem," Levi said. "The ability to produce an advance in this field would help millions of Americans. Clearly, the potential impact is the most exciting aspect of the project. As a pediatric cardiologist, I hope that similar thin-film technology will produce stents that can benefit adults with coronary disease and children with pulmonary venous and arterial disease."

Both Carman and Levi believe the multidisciplinary research environment at UCLA has helped them achieve so much success in their

work and that the unique interactions between seemingly disparate disciplines — like medicine and engineering — permit revolutionary discoveries to be made.

"My career at UCLA has been made possible by the ability to work closely with engineers," Levi said. "It is a huge advantage for me to be at UCLA; this sort of collaboration is not possible at a free-standing children's hospital."

Funding for the two-year Challenge Grant comes from the American Recovery and Reinvestment Act of 2009. The NIH has identified a range of challenge areas that focus on specific knowledge gaps, scientific opportunities, new technologies, data generation and research methods that could benefit significantly from an influx of funds. The research in these challenge areas, according to the NIH, should have a high impact on biomedical or behavioral science or public health.

Source: University of California - Los Angeles