SOUTHWESTERN NEWS

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UT SOUTHWESTERN ENGINEERS BUILDING BETTER HEART SURGERY

DALLAS — December 6, 1994 — Biomedical engineers at UT Southwestern Medical Center at Dallas are building a new device that will keep coronary arteries open and possibly prevent the need for repeated operations.

Balloon angioplasty, where physicians unclog a blocked coronary artery, was a lifesaving procedure for nearly 400,000 Americans with heart disease in 1993. But as many as 40 percent of them may have to have their coronary arteries reopened in 1994, researchers say.

Dr. Robert Eberhart, chairman of the biomedical engineering program, and his colleagues in the surgery, molecular cardiology and cardiac catheterization laboratories at UT Southwestern are developing a new vascular stent to deliver healing gene therapy to the patient.

"Our stent is both a mechanical support and a drug-delivery device," Eberhart said. "It's a very appealing combination." Eberhart and his colleagues published their findings in a recent issue of the *ASAIO* (American Society for Artificial Internal Organs) *Journal*.

When performing balloon angioplasty, surgeons insert a catheter with a deflated balloon on its tip into an artery narrowed by plaque. The balloon is inflated, widening the clogged artery. However, inflating the balloon stretches the wall of the artery and may damage it. Another complication of angioplasty is restenosis, in which the artery becomes constricted again. Restenosis occurs in about 40 percent of the angioplasty cases and commonly develops about three to six months after the angioplasty. Currently, surgeons insert a metal stent to prevent restenosis.

The UT Southwestern stent is fabricated from a resorptive polymer and is designed to dissolve after gene therapy has been delivered to the artery and sufficient healing has occurred. The stent is made from a blend of Poly-L-lactide and caprolactone polymers. The polymer — or plastic — gives the

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stent sufficient strength to keep the artery open. It is also porous, which will allow surgeons, including Dr. G. Patrick Clagett, professor of surgery and a research collaborator, to load genetic material or drugs into the stent for direct delivery to the artery.

"We've combined materials-science technology with gene-therapy technology," said Eberhart, whose research is being partially funded by a five-year, $1 million grant from the National Institutes of Health. "Ideally we could mix a genetic cocktail to meet the specific needs of a particular patient and deliver that medicine to a precise location at the precise time to produce optimum results." Drs. Robert Meidell, Charles Landau and John Willard, assistant professors of internal medicine and molecular cardiology researchers, are testing several drug- or gene-therapy strategies to treat restenosis.

Metal stents pose a number of complications, Eberhart said. First, the stent has to be surgically removed or bypassed if it fails. Even more troublesome, Eberhart said, is that the metal stents can promote blood clotting and blockage in the artery. "Metal stents just don't do very well in the blood vessels."

As an alternative to metal stents, researchers are looking at polymer-coated (plastic-coated) metal stents to give the support of the metal stents without the complication of blood clotting. They also have studied composite stents that are made of both plastic and metal. However, Eberhart said, those versions also must be treated surgically if they fail, and they are not capable of delivering gene or drug therapy.

"Our objective," he said, "is to make a stent that provides the support the artery wall needs to heal" after it has been stretched by the angioplasty. "Then to help the healing process, we deliver genes to the vessel and see how they can accelerate the process."

The UT Southwestern stent is made of a material that was first proposed for use in medical devices 20 years ago. The stent is from a class of polymers

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that can be broken down by the body's normal metabolism. Polymers like the one used to make the stent have been used for a number of years in vicryl sutures. These sutures hold long enough for the tissue to heal before the knot dissolves.

By applying that technology to an arterial stent "the body can naturally absorb the stent. All that's left is carbon dioxide and water," he said. "Ideally the medicine will be delivered to the critical site, and none of the stent will remain in the artery."

While the potential medical applications are significant, Eberhart, the materials engineer and director of the joint graduate program in biomedical engineering at UT Southwestern and The University of Texas at Arlington, also is excited about the technological innovations made to develop the stent. "We've shown how to make these stents in a porous form to deliver medicine," he said. "We can control the size and distribution of the pores throughout the stent" to ensure even delivery of the medicine or genetic material. The stents are being manufactured at Eberhart's UT Arlington laboratory.

Another significant engineering breakthrough was to take a traditionally "water-hating polymer" like the Poly-L-lactide-caprolactone blend and build into the stent a system Eberhart calls an "inter-penetrating" network that allows physicians to load medicine into the gene evenly. "Our system lets us put more drugs in the artery under better loading conditions."

Eberhart said the next step is to refine the fabrication of the stent and learn more about the ability of the stent material to hold and deliver genetic material. The stent must then be tested for use in humans.

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