IMPACT

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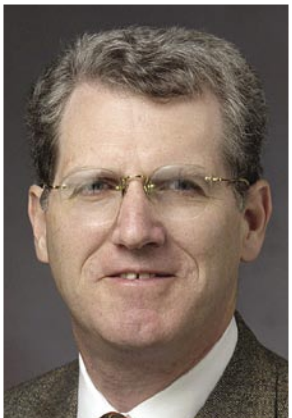


L. ANDREW KOMAN, M.D.

Research Can Directly Benefit Orthopaedic Practice

OREF's Annual Campaign supports current research projects that can directly impact orthopaedists' daily practice.

"Most basic science research can be extrapolated to design operations, or to defend operations," said **L. Andrew Koman, M.D.** "It's difficult to obtain CPT® codes, but using resultant data from research that began with an OREF grant, we were able to do just that," he said.

Current Procedural Terminology (CPT®) codes enable doctors, including orthopaedists, to report medical services and procedures. According to the American Medical Association, the uniform language provides accurate information to agencies concerned with insurance claims and allows evaluation of current diagnostic and operative procedures.

Since 1962, OREF has awarded nine research grants to the Department of Orthopaedic Surgery at Wake Forest University School of Medicine. Three recent grants, in which Dr. Koman was an investigator, have aided in approving CPT® codes for surgical procedures and methods of simple treatment and diagnosis.

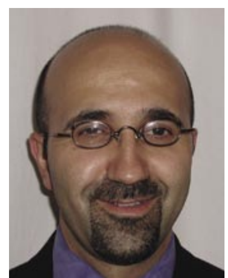
With funding from an OREF Basic Science Grant, Dr. Koman investigated the effects of sympathectomy — removing the nerves from the arteries to decrease the impulses that make them constrict — on blood flow in rabbit ears. This research enabled him to verify that the human digit behaves much like the rabbit ear. Because of these results, Dr. Koman was able to clinically test sympathectomies, confirming that they're effective on human patients.

Sympathectomy can be used to manage patients who have significant Raynaud's Disease — extreme cold sensitivity in the fingers — if those patients have ulcers or sores or do not respond to medication. *(continued on page 14)*

STUDY TO FOCUS ON PERIPROSTHETIC INFECTION

Smart Implants Could Eradicate Joint Replacement Infections

By Amy Kile, Public Relations Specialist



JAVAD PARVIZI, M.D.

Joint replacements enable patients to return to activities they once enjoyed. But for some, infections require treatment that can hinder recovery. To fight infection without causing further stress to the patient, orthopaedic researchers are investigating new treatment methods that directly employ artificial joints to eradicate infections.

"Periprosthetic infection is a very difficult problem to deal with," said **Javad Parvizi, M.D.**, Assistant Professor in the Orthopaedic Department of Thomas Jefferson University. "It is associated with immense psychological cost for the patient and high financial burden for the health care industry."

Each year in the United States, according to Dr. Parvizi, about 600,000 patients undergo joint replacement surgery. Although many measures are taken to minimize the risk of infection, about 1% to 3% of joint replacement patients become infected.

Scientists from a multitude of disciplines, including bioengineering, chemistry, and life sciences, will help Dr. Parvizi to research new means of preventing and treating periprosthetic infection. *(continued on page 10)*

INSIDE

Smart Implants Could Eradicate Joint Replacement Infections (continued from page 1)

Dr. Parvizi is one of three clinician scientists to receive an OREF Clinician Scientist Award in 2004. Funded by the *Journal of Bone and Joint Surgery*, Dr. Parvizi's award will provide him with a $100,000 per year salary stipend for three years.

"Without the OREF award, I would not have been able to dedicate the time to this research, and thanks to the Clinician Scientist Award, now I'm able to dedicate 50% to 60% of my time to research without having to endure a huge economic penalty by losing my clinical revenue," said Dr. Parvizi.

Infection of prostheses has been studied extensively, and, although the total number of infections has decreased, problems of successful salvage with current treatment methods still remain.

The most common strategy to deal with infection is to remove the prosthesis and place a dynamic or static methylmethacrylate cement spacer impregnated with antibiotics. The antibiotics in the spacer can leach out over time in the local environment of the joint. The patient also receives weeks of intravenous antibiotics. Later, the prosthesis is reimplanted if possible. This protocol to eradicate infection is successful between 80% and 90% of the time, but even if the infection is successfully eliminated, there are problems inherent to this method of treatment.

"The cost is immense. You can imagine the psychological trauma of the first surgery, taking out usually well-fixed components, the interim of two to three months requiring intravenous antibiotics, some with potentially serious side effects, and the second stage surgery," said Dr. Parvizi.

There are other problems with this method of treatment, too. Antibiotic contained within the methylmethacrylate cement often eludes out at an unpredictable rate, meaning the amount of antibiotic released and the period over which this elusion occurs is unpredictable. The cement can also inactivate some of the antibiotics, rendering them useless against bacteria.

Dr. Parvizi and his group of researchers are working at Thomas Jefferson University at Rothman Institute to identify a treatment method that will not only fight periprosthetic infection, but also solve the problems intrinsic to current treatment methods.

"The analogy is to a land mine. The organism steps on it and it explodes and delivers enough antibiotics to kill the organism."

"We thought why not design a new treatment method that allows the surface of a metal implant to act as an antibiotic carrier? If we were able to attach antibiotics to the surface of the implants and control their release, a prosthesis made of this material could be used to possibly prevent infection in those patients at risk and for treating those patients who do develop infection," Dr Parvizi said.

To make these "Smart Implants," as Dr. Parvizi calls them, he and his team have developed a method to attach antibiotics to the surface of titanium. Because the antibiotics are attached chemically to the implant in a covalent manner, they are stable and are only cleaved from the implant surface when bacteria threaten them.

"The analogy is to a land mine. The organism steps on it and it explodes and delivers enough antibiotics to kill the organism. The antibiotic land mine will not go off unless the organism is present and steps on it," said Dr. Parvizi.

This specific approach, as far as Dr. Parvizi and his team know, has never been attempted before, although the delivery of antibiotics from implant surfaces is not new.

"People have used biodegradable materials such as poly-lactic acid (PLA), poly-glycolic acid (PGA), or a combination of both (PLAGA), to deliver antibiotics. The problem with these materials is that the diffusion kinetics over time are not known, and diffusion occurs regardless of whether an organism is present or not. In other words, after a given time period no antibiotics will be around," Dr. Parvizi said.

The attraction of the Smart Implant technology is that the antibiotic-prosthesis bond is stable and the antibiotic will be around for years to combat later infections. Presently it is not uncommon for patients to undergo procedures, such as tooth extractions, that introduce bacteria to the blood. This may result in infection of a hip or knee prosthesis many years after the joint replacement. The Smart Implant, which only releases antibiotics when provoked, would still be able to combat the later infections.

Smart Implants may also have applications beyond fighting off and preventing infections. Implant components can loosen with time, and osteolysis, or bone loss may occur. After repeated loading of the bearing surfaces, where the motion occurs, wear particles develop. This triggers an inflammatory process as cells are recruited to digest these wear particles. The cells engulf the particles, secreting enzymes that harm the surrounding bone. As the bone is lost, the prosthesis may loosen. During revision surgery there is less bone to hold

Dr. Parvizi is shown in the laboratory where he performed tests to confirm that antibiotics covalently attach to Smart Implants.

the prosthesis in place, and replacing it would be difficult, similar to placing a heavy bookshelf in a wall made up of drywall without struts.

Currently, to address this problem, orthopaedic surgeons use cadaver bone or bone substitutes such as growth factors, demineralized bone matrix, calcium sulfate, or other bone graft substitutes. To aid in stimulating bone growth, Smart Implants could have growth factors attached to their surface.

“The titanium could deliver growth factors to the native bone and stimulate bone regeneration, making it possible to use the titanium as a vehicle for delivery of growth factors to deal with the problems of aseptic loosening and osteolysis,” said Dr. Parvizi.

The main emphasis, however, is on an implant that would be self-protective against infection.

“That’s the Smart Implant. If it is successfully developed, it might have a revolutionary effect on the treatment of periprosthetic infection. It could make a huge difference to patient care by either reducing the risk of infection or treating infection when it does occur,” Dr. Parvizi said.

Dr. Parvizi and his team have already accomplished the first stage of developing these Smart Implants. They have proven their method, on which they have a patent pending, of covalently bonding antibiotics to the titanium surface. These results were presented at the Hip Society last year and a manuscript based on these findings will be published in *Clinical Orthopaedics and Related Research* this December.

With the preliminary research completed, Dr. Parvizi soon will move to an animal model. He will place antibiotics bonded to titanium cylinders in infected rat femurs. If, as Dr. Parvizi anticipates, these tests are successful, they will move on to a larger animal model to test Smart Implants.

“We’re working on hip implants because currently 70% to 80% of the femoral components and nearly 100% of the acetabular components that are being implanted in North America are uncemented,” said Dr. Parvizi. “We feel that Smart Implants will have application in the hip first.”

Dr. Parvizi credits OREF for the success of the preliminary research. “Because of the OREF grant, early work on this research was possible, and we believe that the research is now receiving much more favorable reviews by other organizations,” he said.

One of those favorable reviewers was the Department of Defense, which is also funding research on Smart Implants. This is a testament to the importance this research has to the medical community.

“All surgeons benefit from the results of research. This particular research will benefit an orthopaedic surgeon implanting artificial joints,” said Dr. Parvizi. “This is a classical example of how the development of a unique technology in the basic research laboratory can have direct patient application for the practicing surgeon that will minimize problems and complications that can occur.”

With Smart Implants battling infections, more total joint replacement patients will realize the benefits of the procedure without the pain and expense of revisions. ■

Dr. Zachary B. and **Mrs. Kathleen Friedenberg** established an endowment, making the first Clinician Scientist Award possible.

Because of the example set by Dr. and Mrs. Friedenberg, the ***Journal of Bone and Joint Surgery*** and **Dr. Dane** and **Mrs. Mary Louise Miller** have also established endowments.

The *Journal of Bone and Joint Surgery*’s donation to OREF’s 2003 fund made **Dr. Javad Parvizi**’s Clinician Scientist Award possible. This award will provide Dr. Parvizi with a salary stipend of $100,000 per year for the next three years.

For information about making endowment gifts to OREF or funding a Clinician Scientist Award, please contact **Tom Coffman**, OREF Senior Vice President, Endowments, at (847) 384-4349 or coffman@oref.org.