# Replacing Worn Out Joints: New Materials and Designs Come to Artificial Hips and Knees

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Now that baby boomers are embracing artificial hip and knees, their ''golden'' years might be more appropriately renamed the titanium years.

At one time, the typical joint replacement patients were 70 years or older. Now, members of the 40+ generation choose not to live with the pain and decreased mobility of arthritis and are opting for hip or knee replacements. Younger patients also want to return to an active lifestyle with their artificial joints. Such desires pose a challenge both to the surgeons who need to choose and implant the appropriate replacement joint and to the engineers who design artificial hips and knees.

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''Baby boomers have different expectations than our grandparents had,'' says Stuart Goodman, M.D., Ph.D., professor of orthopedic surgery at Stanford University, Palo Alto, California. ''You can't tell someone who is 45 years old and had an arthritic hip replaced to stop living their life.''

Joint replacement surgery restores function and relieves pain. Goodman adds that both surgeons and patients alike are starting to see that implants have good outcomes and are lasting longer; still, he tells his patients that even though the procedure is more common, it is major surgery that needs significant rehab and that some adjustments in activity will be required.

By the time people opt for hip or knee replacement, their joints have been damaged by trauma, osteoarthritis, or by a rheumatoid disease such as rheumatoid arthritis. In osteoarthritis, the most common form of arthritis, the cartilage deteriorates to the point where the damage reaches the bone. Orthopedic surgeons refer to this condition as end-stage joint disease. Mobility decreases, quality of life deteriorates, and pain often wakes people in the night.

Twenty years ago, the industry focused on getting people out of a wheelchair and getting them mobile again, says Cheryl Blanchard, Ph.D., Senior Vice President and CSO at Zimmer, a company headquartered in Warsaw, Indiana, that designs and markets joint replacement technologies as well as biologics for early intervention. She also notes that, as patients, boomers are more educated and engaged in their healthcare decision, so they are much more data driven. ''I think that's a good thing.''

The Nex Gen knee is Zimmer's flagship product. The science and engineering that goes into designing, developing, and commercializing a clinically successful replacement joint takes collaboration between engineers and orthopedic surgeons. A replacement for a joint that moves needs to imitate the motion and sliding (articulating) surfaces. The design process brings together multifaceted disciplines such as mechanical engineering, design engineering, and materials science, as well as quality engineers, ''all while working in close collaboration with clinicians who understand what they need surgically to make this happen and what their patients need,'' says Blanchard. Designing instrumentation that goes along with putting implants in is just as important as getting the implant right. ''It's like carpentry in the operating room,'' says Blanchard.

In a total knee replacement, for example, surgeons remove the damaged tissue and fix the artificial knee with a stem, commonly made of titanium, which replaces the ends of the long bones, such as the femur. Stems come in various lengths and are either placed into long bones without cement or fixed with polymethylmethacrylate or PMMA.

The moving articulating surfaces are most commonly high molecular weight polyethylene (PE), cobalt chrome, or ceramic. These materials are sometimes used in combination with one another; for example, one articulating end can be PE and another can be metal, so the joint would be PE gliding against metal. In the end, the artificial joint needs to withstand weight bearing and mimic the smooth glide that cartilage provides for a healthy joint. One of the changes to materials over the past decade has been the advent of PE made from highly cross-linked polymers. The cross-linking adds another chemical bond in the polymer chain that improves wear resistance.

Replacement joints don't last forever. One of problems plaguing replacement joints has been the generation of what is called wear debris. As the articulating surfaces move against one another day after day, year after year, the friction generates microscopic particles that set off a chain reaction which can lead to implant failure.

## Microscopic Particles, Major Issues

In about 10% of total hips and knee replacements, a piece of fibrous tissue forms between the implant and the titanium stem. That tissue, full of active cells, contributes to loosening of the implant; worse, cells in the tissue cause a cascade of damage that leads to a significant amount of bone loss. Eventually, the implant loosens to the point so that the surgeon needs to take the patient back to the operating room for revision surgery, which is far more complicated than implanting a primary hip or knee.

Goodman has been studying this phenomenon since his surgical residency more than 30 years ago. His surgical mentor at the time was implanting a

  

"metal on plastic" hip in young trauma patients. Goodman says the concept was good, but the new joint was essentially a wear debris machine that failed after 2 to 5 years; however, it provided Goodman's mentor and collaborators with a bounty of wear particles to study. He continued investigating biological and molecular processes that leads to aseptic loosening when he moved to Stanford in 1985.

Researchers have come to understand more over the past 30 years about wear debris. One thing they do know is that wear particles will never go away; the idea is to find the right combination of materials and design that generates fewer particles.

Many different cells are involved: macrophages, mesenchymal stem cells, osteoblasts, and osteoclasts. Goodman's research in animal models shows that macrophages can be recruited from distant sites in the body. His team has also shown that cytokines and chemokines inhibit the response that can repair bone. Clinically, Goodman says the idea is to modulate the local reaction and to boost local tissues to make more bone. For example, Goodman is a participant in a clinical trial of Biomet's E1, an antioxidant-infused polyethylene. Biomet, also headquartered in Warsaw, Indiana, specializes in orthopedics, sports medicine, and dental implants. Bill Kolter, Corporate Vice President of Government Affairs at Biomet, says the objective of E1 is to increase wear resistance by reducing oxidative degradation of the PE and to maintain mechanical properties. Cross-linking PE via high-dose radiation provides good wear resistance, says Kolter, but any active free radicals residually left in the material can become progenitors for oxidative degradation. By doping PE with vitamin E, Biomet aims to quench those free radicals.

## One Step Ahead

Revision rates for joint replacement are tracked in several joint registries in Europe and in Australia. Typically, revision rates at 1% per year are the standard for hip replacements set by NICE (National Institute for Health and Clinical Excellence, UK). At 5 years, for example, the revision rate should not exceed 5%. Joints can fail for reasons other than aseptic loosening such as implant position and the many individual differences in patients, including weight, degree of joint damage, level of activity, and dedication to rehab.

Pam Plouhar, Ph.D., world-wide Vice President of Clinical Affairs at DePuy Orthopaedics, says the company's Pinnacle Hip System has a long history of clinical performance and is designed to work well with the younger, active patients who receive hip replacements today. The revision rates are less than 4% at 5 years and comparable or better to this class of hip implants overall. Recently, DePuy had a "ceramic on metal" hip system approved by the FDA.

"We're always trying to understand how current innovation impacts the marketplace and how we can leverage that to develop better products to meet the needs of both the surgeons and the patients," says Plouhar. "Even though the performance of the Pinnacle systems shows less than a 4% revision rate at 5 years, and that is a very good outcome, we're always looking to improve the performance of our products."

Zimmer also has a new bone and growth implant surface called trabecular metal, which goes on a number of hip and knee implants in which no cement is used. The surface that's exposed to bone is made from a specialized material that mimics the microstructure of bone and is conducive to bone growth. Edward Greenfield, Ph.D., Professor and Director of Orthopedic Research at Case Western Reserve University, is working on the osteointegration with Zimmer on their trabecular metal. Greenfield's team is focusing on the hypothesis that bacteria contribute to aseptic loosening. When Greenfield first started mentioning his hypothesis at meetings, his colleagues took a while to warm to the idea. Now, many labs have data in data cell culture and mouse models consistent with that hypothesis.

A number of other labs have looked at implants in patients with aseptic loosening and found that many patients have bacterial biofilm on their implants even though there are no clinical signs of infection. That's why it's called aseptic. "That doesn't prove that the biofilm is contributing to loosening; at least it tells you the bacteria are there and the PAMPS [pathogen associated molecular patterns] that bacteria make are presumably there," says Greenfield.

Greenfield's team also really wants to understand how signaling in wear debris works in cell culture and mice and is investigating the role the toll-like receptors (TLRs) play. The researchers are also investigating other bacterial recognition molecules—some downstream of TLR receptors and some that work in parallel. "If, some day, we really show that bacteria are important contributors to aseptic loosening, that suggests that antibacterial strategies might be useful. We're a long way from there," says Greenfield.

Data from the Norwegian Arthroplasty Registry support the bacterial hypothesis. In a study of more than 10,000 primary cemented hip replacements, patients who were given intravenous antibiotics and had antibiotics embedded in the bone cement had fewer revisions.

"It may be that you just have to win the race," says Greenfield.

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