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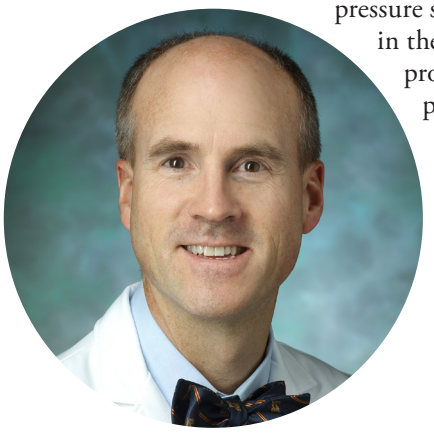
Will Osseointegration **Change the Future of Prosthetics?**

It has been projected that more than 2.2 million Americans will be living with limb loss in 2020.* **Jonathan Forsberg**, associate professor of orthopaedic surgery in the Johns Hopkins Division of Orthopaedic Oncology, is helping to introduce alternative types of prostheses for these patients.

Forsberg's current research focuses on osseointegrated implants, which attach directly to the residual limb's bone, eliminating the need for traditional, socket-based prostheses. "Our soft tissues were not meant to bear weight," Forsberg says, noting the shortcomings of traditional prostheses. "Patients can develop ulcerations, perspiration may disrupt the interface between skin and socket, and if the length of the residual limb is shorter, patients may have less control over the limb." Osseointegration can greatly improve quality of life by "increasing the amount of time patients wear a prosthesis throughout the day and enabling osseoproprioception (knowing where the limb is without looking at it) and osseoperception ('feeling' the differences between surfaces)," says Forsberg.

Osseointegrated limbs can also accommodate advanced prosthetic components, such as the Johns Hopkins Applied Physics Laboratory's Modular Prosthetic Limb, which uses pressure sensors embedded in the fingertips of the prosthetic hand to provide artificial sensory feedback.



"Osseointegration is a complex process that requires a long rehabilitation period and a multidisciplinary team, including orthopaedic and plastic surgeons, prosthetists, and rehabilitation and mental health specialists," Forsberg explains. As a large, collaborative academic institution, Johns Hopkins can provide every aspect of the care needed for these patients. Education is particularly important, given that osseointegration patients have a lifelong risk of infection.

"Osseointegration as an orthopaedic field is still in its infancy," Forsberg notes. "Several companies worldwide are developing osseointegrated implants, but only one of them has data beyond 10 years. Given the unique challenges, there are many areas that are ripe for research, such as the ideal patient population, ideal implant types for various bony anatomy, monitoring of bone health and the skin penetration site, and evaluating the ethics and costs associated with osseointegration."

To address these questions, Johns Hopkins will participate in an international registry to collect inclusion criteria, surgical information and outcomes data on osseointegrated implants at institutions worldwide. The registry will also improve transparency in the field of osseointegration by helping to identify implant designs at risk for early failure. Participants will be able to respond to questions from the Food and Drug Administration, which was involved in development of the registry, and from other investigators, as the field moves from first-generation prostheses to subsequent iterations.

"Once we address the ideal patient population and ideal implant types," Forsberg says, "we can turn our focus to other areas of research — in particular, deciding how best to convey the signals from the patient's own nerves and muscles to a robotic limb. I'm very excited to continue to develop this project at Johns Hopkins." ■

Osseointegrated limbs (like the one shown here) can accommodate advanced prosthetic components, such as the Johns Hopkins Applied Physics Laboratory's Modular Prosthetic Limb, which uses pressure sensors embedded in the fingertips of the prosthetic hand to provide artificial sensory feedback.

"Osseointegration as an orthopaedic field is still in its infancy…There are many areas that are ripe for research."
– Jonathan Forsberg

Ziegler-Graham et al. Arch Phys Med Rehab. 2008;89(3):422–429

Better Blood Management Improves Patient Outcomes After Joint Replacement

Harpal Khanuja

Knowing that infection is one of the most devastating complications for patients undergoing hip or knee replacement, **Harpal Khanuja**, Johns Hopkins associate professor of orthopaedic surgery, makes it his mission to address the issue through a multimodal approach to blood management.

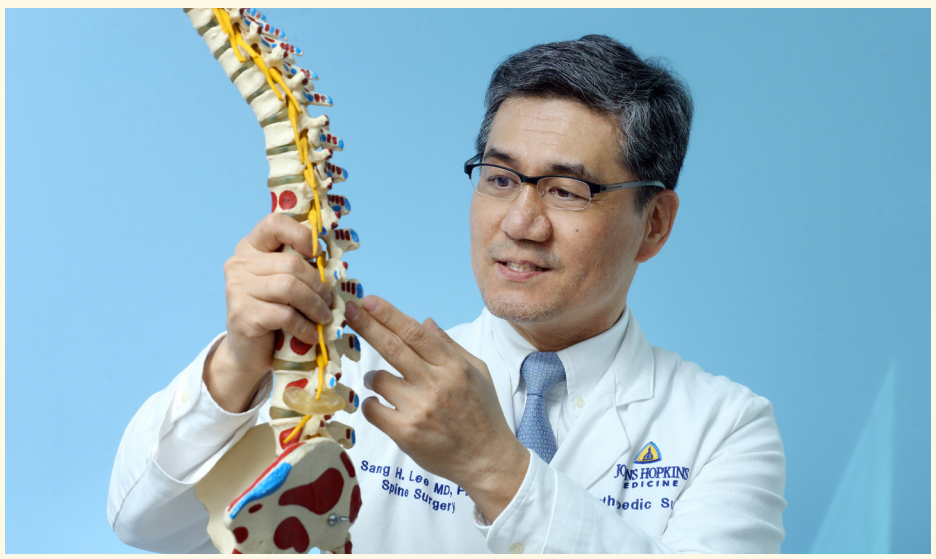
Blood transfusions can increase the risk of adverse outcomes, delay rehabilitation and extend a patient's hospital stay, so limiting blood loss is crucial. "Transfusions have inherent risks," says Khanuja. "There is the potential for complications, including infection and associated comorbidities."

The multimodal blood management approach instituted at Johns Hopkins involves treating patients who are hypotensive postoperatively with fluids first, then blood products as needed, using antifibrinolytic agents such as tranexamic acid, and lowering the restrictive threshold for transfusions from <10 g/dL to <7 g/dL hemoglobin in hemodynamically stable patients. In a study of patients with hip fractures, Khanuja found the new restrictive threshold of <7 g/dL was associated with the same or better outcomes compared with a threshold of <8 g/dL. Overall, the transfusion rate for joint replacements at Johns Hopkins dropped from 20% to 2%. This approach lowered infection rates and had the additional benefits of decreasing hospital costs and conserving blood.

With such progress, Khanuja says transfusion is no longer the primary concern in blood management. The new focus is on the extent of anemia after surgery and how anemia affects patient recovery. "Now most joint replacements are outpatient procedures in a hospital setting. We are trying to get patients up the same day and get them moving, so anemia is the better indicator of patient outcomes," says Khanuja. "We need to think of anemia in terms of how a patient feels postoperatively. How much energy do they have? How much better can we make them feel?"

Patient health optimization is a key component to addressing the effects of anemia. "Our department policy is to have all anemia examined if levels are not within a healthy range before surgery," says Khanuja. Typically, the primary physician would clear for surgery a patient who is slightly anemic because this low level is considered "the patient's normal." Khanuja encourages orthopaedic surgeons to question that assumption. "If a patient is slightly anemic, I'm wondering if they have an underlying condition that could be exacerbated with surgery," says Khanuja. "They could have a small bleeding ulcer made worse by the anti-inflammatories or blood thinners prescribed postoperatively. There are many reasons to address the anemia."

The same vigilance for anemia risks is applied to other risk factors as well, through diabetes control, weight loss, smoking cessation and nutritional screening. "We want to give patients the best outcome," says Khanuja. "That is something that is important to us, and that we will always be on top of at Hopkins." ■



The technique treats less complicated spine conditions such as disc herniation and spinal stenosis, and can be performed in an outpatient setting, says Sang Lee.

Endoscopic Spine Surgery: Rare Minimally Invasive Approach Now Available at Johns Hopkins

Surgeons in the Johns Hopkins Department of Orthopaedic Surgery's spine division are now providing minimally invasive endoscopic surgery, which is used frequently in other specialties but is uncommon in spine surgery. **Sang Lee**, assistant professor of orthopaedic surgery and director of complex cervical spine and spine tumor surgery, is leading implementation of this approach, which the department began to offer over the last several months.

"Endoscopic spine surgery has been historically more common in Asia and is recently gaining popularity in the United States. However, it is mainly performed by private surgeons, not academic practices," Lee says. He hopes to popularize endoscopic spine surgery among academic practices in the U.S. because of its many benefits. "It is the least invasive surgery and

Axon Regeneration to Restore Function After Injury

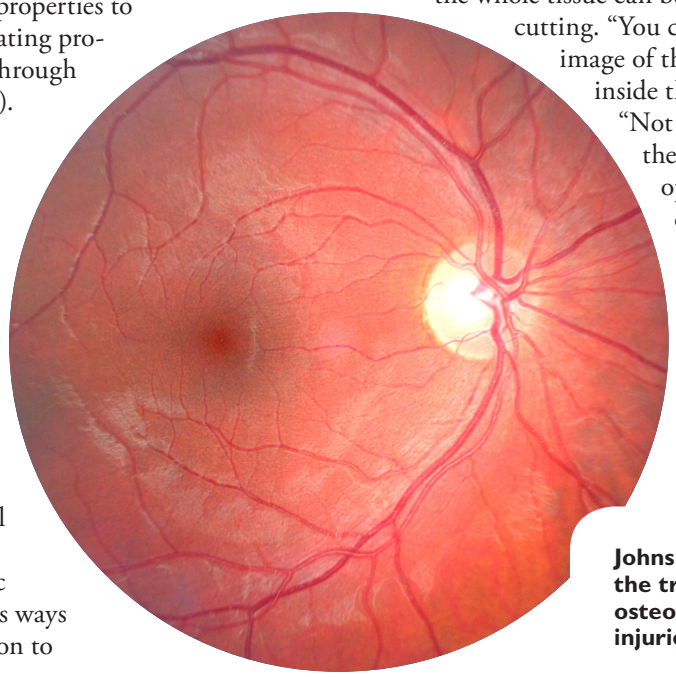
Feng-Quan Zhou, associate professor of orthopaedic surgery, and his basic science lab at The Johns Hopkins University are performing leading-edge neuronal morphogenesis research — specifically, how to promote axon regeneration after injury. Zhou's current focus is optic nerve regeneration for treatment of glaucoma, but his research applies to several devastating diseases including osteoarthritis, Alzheimer's and Parkinson's disease, and paralysis caused by spinal cord injuries.

Zhou's lab uses a two-pronged approach to study nerve regeneration. One involves examining the optimal environment for regrowth (the peripheral nervous system, which — unlike the central nervous system — can regenerate). The other involves manipulating intrinsic properties to stimulate growth (activating pro-regenerative pathways through epigenetic modification).

"At my lab, we are familiar with not only the peripheral nervous system, but also the central nervous system, and that is important," says Zhou. "So we have the unique ability to compare the two systems and apply knowledge from the peripheral to the central nervous system." To manipulate the intrinsic properties, Zhou studies ways to alter gene transcription to "switch on" the capacity to regrow, which means he must first identify changes in gene expression that occur after injury.

Using a machine that can perform single-cell RNA sequencing, Zhou can create a library of chain transcriptions for 10,000 neurons. "Now you can find out if some neurons regenerate better than others or if some cannot regenerate at all. Isolating functionality was not possible when you were only able to get a summary of sequencing of a lot of neurons together," explains Zhou.

Using cultured cell models, Zhou can then change gene expression in the neuron and monitor the effects on regeneration. New technologies make the tissue transparent, enabling visualization of the axon, so the whole tissue can be imaged without any cutting. "You can reconstruct a 3D image of the axon regeneration inside the nerve," says Zhou. "Not many other labs around the world can create an optic regeneration model, change gene expression and do imaging of the nerve." Zhou's collaborators at the Johns Hopkins Wilmer Eye Institute analyze the raw data Zhou's experiments generated.



Johns Hopkins researchers are working on regeneration of the optic nerve for the treatment of glaucoma. This research applies to other diseases including osteoarthritis, Alzheimer's and Parkinson's, and paralysis caused by spinal cord injuries.

Zhou believes this collaboration is key to translating his research because physicians typically understand patients' experiences with glaucoma better than basic scientists do. "Maybe the physician can put the pieces of my data together," he says.

In addition to stimulating optic nerve regeneration after injury, Zhou's lab is also interested in identifying markers for early detection of glaucoma. In asymptomatic patients without increased intraocular pressure, glaucoma can go undetected, leading to irreversible vision loss. An early detection system could enable patients with glaucoma to retain their vision longer by delaying the disease's progress.

> "Not many other labs around the world can create an optic regeneration model, change gene expression and do imaging of the nerve."
> – Feng-Quan Zhou

The groundwork this research laid could be used as a model to treat spinal cord injuries — a future area of research for Zhou. "All the genes supporting optic nerve regeneration are very likely to support spinal cord regeneration," says Zhou, suggesting hope that paralysis may someday be reversible. ■

uses an incision of less than 1 centimeter," Lee says. "Outcomes are similar to traditional open surgeries, but there are quicker recovery rates, shorter hospitalization times, and it is the better option cosmetically." Endoscopic surgery is used to treat less complicated spine conditions such as disc herniation and spinal stenosis, and can be performed in an outpatient setting.

This endoscopic discectomy procedure uses a transforaminal approach with access through the flank. The incision is less than 1 centimeter long.

Incorporating this technique will also provide valuable learning opportunities for surgeons in the spine division's residency program. "There is a steep learning curve of at least 20 initial cases. It requires a steadier hand," says Lee. Surgeons training in endoscopic surgery participate in cadaver training courses to refine their techniques. Initially, the endoscopic approach may take one to two hours longer than more invasive procedures. However, the skills required are similar to those needed for open surgery. "I explain to students that you need to be able to see every anatomical characteristic in your mind's eye," Lee explains. "When you see a patient in the clinic, you should be able to picture the spinal cord, nerve roots, vessels, and all the critical structures."

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> – Sang Lee

Lee is excited by the opportunities available in the spine division, which he says "have expanded greatly in the past two years." He is eager to help Johns Hopkins become a leader in endoscopic spine surgery among academic institutions, and to provide an option with less tissue damage, less blood loss, and shorter hospitalization and recovery. ■

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