Bringing Cut or Damaged Nerves Back to Life

Surgeons have been successfully reattaching limbs since the 1960s, but returning full function to the severed arm or leg remains the stuff of science fiction novels.

But surgeons at Vanderbilt University Medical Center hope their research will one day enable surgeons to apply a simple solution that begins to repair the nerves immediately while the limb is being reattached in the operating room.

Using a calcium-free polyethylene glycol (PEG) solution — think of this as a molecular gel — Wesley P. Thayer, M.D., Ph.D., and surgeons from the department of Plastic Surgery, were able to repair a severed nerve in a rat, returning movement in the leg in just minutes.

Thayer, assistant professor of Plastic Surgery and Orthopaedic Surgery, presented his work at the American Association for Hand Surgery annual meeting in January.

Nerves can naturally repair themselves by regenerating and reconnecting over time. Such repair in smaller extremities, such as fingers, can occur more easily because the distance between the nerves is short.

However, when an entire limb is cut or

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Vanderbilt Uses Virtual Animation to Perfect Oral Surgery Outcomes

By Craig Boerner, The Reporter

Nathan Cutright wasn’t supposed to be 6 feet 5 inches tall, but he grew so much during the summer between eighth and ninth grade — shooting from 5 feet 8 inches to 6 feet 3 inches — that his legs caused him a lot of pain.

And while his legs were growing, his jaw was growing too, forming a long “under bite” that not only dramatically affected his speech and appearance but also was potentially dangerous to his health.

Cutright, who also has attention deficit disorder (ADD) and Asperger’s syndrome, underwent corrective jaw surgery at Vanderbilt in September, 2011. The surgery involved moving his bottom jaw back 2 millimeters and his top jaw forward 7 millimeters.

To eliminate any guesswork in the operating room, Cutright’s surgeon Sam McKenna, DDS, M.D., chair of the Department of Oral and Maxillofacial Surgery, used a new technology known as virtual surgical planning to see the expected results and pinpoint measurements on the computer while planning the surgery.

“Virtual surgical simulation is taking surgical planning to the next level, where complex spatial changes can be

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Repairing Cut Nerves...

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damaged, it can take a year for nerves to regenerate at a rate of one millimeter per day. Unfortunately, by that time, muscle atrophy has set in, severely limiting any restoration of nerve function.

This new approach dramatically shortens the time for repair and regeneration, and has also been shown to work even after the nerves are cut, offering hope to patients who can’t immediately get to a hospital. These developments have far-reaching impacts on traumatic injury survivors who previously had little to no options in repairing nerve damage.

“I truly believe we can replicate our success in the lab in human patients. It’s just a matter of time,” said Thayer.

The PEG solution is applied to both ends of the severed nerve after bathing the nerves in a calcium-free solution. This solution acts to keep the nerve channel open, and the PEG brings the nerve bundles together. A follow-up calcium solution works to bind the proteins that medal the nerves in an unrepaired state.

In a calcium solution, nerve proteins that normally stay together are separated. In a calcium-free solution, these proteins knock against each other, causing the nerve to become damaged, coarse, and non-functional.

“By adding the calcium in the second step, we allow the nerve channels to remain effectively open before binding all of the critical elements in place,” he said.

Vanderbilt engineers are working with Thayer to develop a device that more precisely administers the PEG solution in the operating room. Launched in 2011, the Vanderbilt Initiative of Surgery and Engineering (VISE) has already developed new technologies in soft-tissue image-guided surgeries that enable surgeons to see exactly where critical structures such as blood vessels and nerves are located. Already, industry peers are taking note. In February, the Association for Academic Surgery (AAS) awarded Kevin W. Sexton, M.D., a research fellow who is working with Thayer, the Outstanding Resident Research Award in Basic Science and Best Manuscript by an AAS New Member prize for their paper on using polymers to bridge nerve gaps resulting from an injury.

The paper, “Hydrophilic Polymers Enhance Early Functional Outcomes after Nerve Autografting,” is also authored by Gabriel Del Corral, M.D., Lillian B. Nanney, Ph.D., and R. Bruce Shack, M.D., chair of Plastic Surgery at Vanderbilt. “I hope his visit and faculty appointment here will be the beginning of a long-standing relationship that is mutually beneficial to both Kijabe Hospital and Vanderbilt.”

300 Surgeons for 40 Million

With a population of 40 million, the people of Kenya struggle to find quality and affordable surgical care among the 300 surgeons in the country.

While most are found in the cities and large towns of the country, 30 percent of all healthcare in Kenya is provided by mission hospitals, such as Kijabe, as well as other non-governmental healthcare institutions, many of which are found in rural settings.

Already, Kijabe serves as a teaching and referral hospital. Nthumba says the training program with Vanderbilt will serve as a further stepping stone in preparing the next generation of surgeons in Kenya.

“What’s our current numbers and programs, we just can’t treat all the patients,” he said. “We must teach others how, as well.”

Nthumba specializes in plastic, reconstructive and hand surgery. He trained in Kenya, India and Spain before returning to Kijabe Hospital to address this critical shortage of surgeons. Each day, Nthumba sees patients who suffer from a host of life-threatening maladies requiring surgery, including massive tumors.

One such patient, a 22-year-old Kenyan man, could not adequately eat, breathe or see because the tumor covered most of his face. And the shocking appearance of the tumor led him to be ostracized and shunned by his family and village.

“As you can imagine, when we remove these tumors, it truly changes their lives,” said Nthumba. “But it’s distressful to know that so many of these tumors could be removed years earlier, as they are in the US, if access to surgical care were improved,” he said.

Why Global Healthcare?

At the annual meeting of the Royal Society of Medicine in London, John L. Tarpley, M.D., addressed the issue, saying “It’s time we realized that access to surgery is actually a public health issue. We all must do our part to improve access to quality healthcare across the globe,” said Tarpley, professor of Surgery and Anesthesiology, and program director of the General Surgery Residency Program at Vanderbilt.

Julia Shelton, M.D., a 4th-year surgical resident at Vanderbilt, was the first to participate in the program’s four-week, elective rotation in Kenya.

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Goldenring Named Takeda Distinguished Scientist of the Year

James R. Goldenring, M.D., Ph.D., vice chair of Research in the Section of Surgical Sciences, was named 2012 Takeda Distinguished Research Scientist by the American Physiological Society (APS).

The Takeda Award is given annually to an outstanding investigator who is internationally recognized for contributions to research in gastrointestinal and liver physiology.

Goldenring, the Paul W. Sanger Professor of Experimental Surgery, professor of Cell and Developmental Biology, and staff physician at the Vanderbilt Medical Center, will receive the award at the APS Experimental Biology meeting in San Diego on April 24, 2012.

Goldenring's ongoing research on the cell biology of epithelial cell vesicle trafficking and signaling, as well as precursors to gastric cancer have been published extensively in such journals as *Journal of Clinical Investigation*, *Proceedings of the National Academy of Sciences*, *Journal of Biological Chemistry* and *Gastroenterology*. His work is funded by grants from the National Institutes of Health and the Department of Veterans Affairs.

“The Takeda Distinguished Research Scientist Award represents well-deserved recognition of numerous important contributions that Dr. Goldenring has made in the fields of gastrointestinal epithelial cell biology and pathophysiology,” said R. Daniel Beauchamp, chairman of the Section of Surgical Sciences and the Foshee Distinguished Professor of Surgery.

As co-director of the Vanderbilt Epithelial Biology Center (EBC), Goldenring is a leader in the fields of epithelial cell biology and gastric cancer research. The mission of the EBC is to better understand and care diseases of epithelial origin, with an emphasis on gastrointestinal cancer.

Goldenring received his M.D. and Ph.D. from Yale University, and joined Vanderbilt in 2002. A member of the Vanderbilt-Ingram Cancer Center and the Medical Scientist Training Program, he was elected to the American Society for Clinical Investigation in 2004, and in 2006 was designated a Fellow of the American Gastroenterological Association. He received the 2004 Funderburg Award from the American Gastroenterological Association in recognition of his research into the origin of gastric cancer.

Jackson Appointed Chair of National Library of Medicine Committee

The National Library of Medicine recently appointed Gretchen P. Jackson, M.D., Ph.D., as chair of the Literature Selection Technical Review Committee (LSTRC), from July 2012 through June 2013.

The committee advises on matters related to the evaluation and recommendation of biomedical publications to be considered for indexing and inclusion in MEDLINE, an online database of journal articles containing more than 14 million references.

The National Library of Medicine began indexing journal articles in 1879. The practice of cataloging medical publications was referred to as America’s greatest contribution to 19th century medicine.

Jackson, assistant professor of Pediatric Surgery and Biomedical Informatics, has served on the committee since 2009. As chair, Jackson and a team of physicians and surgeons from across the U.S. will review journals for selection in the MEDLINE database.

“I am extremely proud of this achievement for Gretchen,” said Kevin B. Johnson, professor and chair of the department of Biomedical Informatics. “This committee is an important component of our biomedical education and research process. Gretchen is one of the few surgeons with a Ph.D. in biomedical informatics, and, as such, is an ideal chair for this committee,” he said.

Jackson’s interest in evolving communication technologies as a powerful tool in patient care and her leadership role on this committee. Her appointment as chair is appropriate recognition of her expertise in medicine combined with informatics.

She is an outstanding representative of Vanderbilt University, Surgical Sciences and Biomedical Informatics,” said R. Daniel Beauchamp, M.D., chair of the Section of Surgical Sciences and the Foshee Distinguished Professor of Surgery.

Jackson joined the Vanderbilt Department of Pediatric Surgery in 2006, after completing her chief residency in General Surgery at Duke University Medical Center and a fellowship in pediatric surgery at Children’s Hospital of Pittsburgh.

She completed her medical degree from Stanford University and her Ph.D. in Medical Information Sciences from Stanford University.

“The National Library of Medicine was founded in 1836 and is a part of the National Institutes of Health (NIH). As the world’s largest health sciences library, its mission is to translate biomedical research into clinical practice.

Goldenring's interest in advancing communication technologies as a powerful tool for patients and their families led to the development of self-management tools on the MyHealthatVanderbilt patient portal. In January, she was appointed medical director of MyHealthatVanderbilt.

In 2010, a pilot program using the MyHealthatVanderbilt web site showed a dramatic improvement among patients with severe hypertension. While only 35 percent were in compliance with their blood pressure management when the study started, 83 percent were in compliance after just weeks using the web-based management tool.

“This appointment is another accomplishment reflecting Dr. Jackson’s dedication and passion for biomedical informatics,” said Dai H. Chung, chair of the department of Pediatric Surgery.

Jackson joined the Vanderbilt Department of Pediatric Surgery in 2006, after completing her chief residency in General Surgery at Duke University Medical Center and a fellowship in pediatric surgery at Children’s Hospital of Pittsburgh.

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“The National Library of Medicine was founded in 1836 and is a part of the National Institutes of Health (NIH). As the world’s largest health sciences library, its mission is to translate biomedical research into clinical practice.
Penson Appointed to National Advisory Council for Healthcare Research & Quality


Penson joins a 21-member panel comprised of private-sector experts, representing healthcare plans, providers, consumers and researchers. The panel offers real world insights into healthcare research and those critical topics AHRQ should address in promoting improvements in quality, clinical outcomes and cost effectiveness of healthcare in the US.

“Dr. Penson’s appointment to this important national committee is a well deserved high honor. This is an important national service commitment and it is wonderful to have outstanding representation from Vanderbilt University at this level,” said R. Daniel Beauvillain, chair of the Section of Surgical Sciences and the Foster Distinguished Professor of Surgery.

Penson, professor of Urologic Surgery and director of the Center for Surgical Quality and Outcomes Research, was awarded a $7.6 million grant in U.S. Stimulus funds in 2009 to study the effectiveness of various treatments for prostate cancer.

Funded by AHRQ, the three-year grant is already providing valuable information on which treatments work best for each patient.

“The study just closed enrollment after accruing more than 3,600 participants with newly diagnosed localized prostate cancer from six tumor registries. When completed, this unique study will address “what works, in which patients and in whose hands” and will be the largest of its kind in localized prostate cancer. “David Penson’s status as an international leader in health services research is enhanced by his clinical and surgical skills, which give him a practical understanding of the issues,” said Joseph A. Smith, Jr., M.D., chair of the department of Urologic Surgery. “He will be an extremely valuable member of this advisory board. Moreover, he is a dedicated and unselfish mentor to many other investigators in our department and throughout the institution who benefit from his capabilities,” he said.

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Surgical Residents Take Top Honors at Academic Surgical Congress

Kevin W. Sexton, M.D., a research fellow in the department of Plastic Surgery, and Michael James Osgood, M.D., General Surgery resident, received top honors by the Association for Academic Surgery (AAS) in February.

They received their awards at the 7th Annual American Surgical Congress in Las Vegas.

Sexton received the Outstanding Resident Research Award in Basic Sciences for his research with Wesley P. Thayer, M.D., Ph.D., on nerve regeneration and repair. He also received the Best Manuscript by an AAS New Member prize for Vanderbilt’s submission, “Hydrophilic Polymers Enhance Early Functional Outcomes after Nerve Autografting.”

Osgood received the Best Presentation by a New AAS Member prize for his discussion of “Inhibition of Vein Graft Intimal Hyperplasia with a Non-toxic Blue Marking Dye in a Rabbit Carotid Interposition Model.”

In 2011, Osgood also received a resident scholarship to travel to the Annual Vascular Meeting of the Society of Vascular Surgeons.

At this meeting, he was named the General Surgery Resident winner of the Vascular Surgical [Saturating] Skills Competition, leading 80 other residents.

“Certainly, we are all proud of Drs. Osgood and Sexton and their many accomplishments,” said Kyla Tvershke, M.D., assistant professor of Surgery, division of General Surgery, and associate program director, General Surgery Residency Program. “They both have been exceptionally productive during their research years and it’s nice to see them duly recognized for their efforts, she said.”

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Senator Frist Addresses Surgical Residents on Changes in Healthcare

Former Tennessee Senator and adjunct professor of Surgery William H. Frist, M.D., made a surprise visit to Vanderbilt in January when he addressed the Surgical Residents’ Teaching Conference.

Though routinely geared toward specific surgical procedures, Frist’s lecture provided a long-term view of the both the wonders of innovation and the challenges of how to pay for them.

He addressed the healthcare needs of an aging population, medical reimbursements and the national debt crisis.

“It was an eye-opening experience of real world challenges surgeons will face on a daily basis,” said Michael D. Holzman, M.D., associate professor of Surgery. “We are, indeed, fortunate to be able to learn from his vast healthcare experiences,” he said.

Frist founded the Vanderbilt Transplant Center and served as its director from 1989 to 1993, and then served as assistant professor of Surgery in the then combined department of Cardiac and Thoracic Surgery from 1984 to 1994. In 2011, he was appointed adjunct professor of Surgery in the department of Cardiovascular Surgery.

He has traveled the world over leading emergency medical response teams in the Sudan, New Orleans, Sri Lanka, Haiti and, most recently, Kenya/Somalia.

While Traumatic Brain Injury Month may only come once a year in March, the surgeons, nurses and staff at Vanderbilt know that recovering from such a trauma requires a lifetime of hope, hard work and the kindness of family and friends.

Treating more than 3,000 trauma patients every year, Vanderbilt recognized the need for a clinic that specializes in the unique rehabilitation needs of patients starting a new life after a traumatic brain injury.

Opened in 2011, the Traumatic Brain Injury (TBI) Clinic is a multi-specialty center offering free follow-up for patients recovering from a major injury to the head.

Less than a year after opening, the Brain Injury Association of Tennessee chose Vanderbilt’s TBI Clinic to receive its Professional of the Year award for 2012.

The award is given annually to the individual or program that has provided quality care or service to both patients recovering from a brain injury and their families.

“The TBI clinic offers expert resources from trauma physicians and surgeons, social workers, speech-language pathologists, as well as former trauma patients returning to the hospital as peer visitors, helping guide others on the road to recovery.”

“This peer visitor program was developed as part of the Trauma Survivors Network at Vanderbilt (TSN), a fully-integrated program started in 2009 as a resource for patients and their families seeking encouragement, hope and community resources following a traumatic injury.”

“When a critically injured patient is first wheeled onto our floor, our first priority is in saving his life,” said Oscar Guillaumondegui, M.D. “But that’s just the very first step. These patients and their families must then begin the very challenging task of beginning a whole new chapter in their lives. The TBI Clinic is just one way we can ease that burden,” he said.

When Zach Phillips was hit by a car in 2006, he suffered a traumatic brain injury and was left with limited speech and the loss of his left arm. Today, he has returned to school and to competitive cavaledoring through the TBI clinic. While his dexterity is less than 10% of what it was before, he is thankful for the care he’s received.

The TBI clinic serves more than 50 patients a month who are facing the challenges of their injuries.

Less than a year after opening, the Traumatic Brain Injury (TBI) Clinic is a multi-specialty center offering free follow-up for patients recovering from a major injury to the head.

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Vanderbilt Links Deficiencies in Protein Tumor Suppressor with Colorectal Cancer

Researchers have long known that colorectal cancers usually develop as the result of inappropriate activation of the Wnt signaling pathway. Additionally, progression of these cancers often involves inactivation of TGF-β/Bone morphogenetic family signaling.

But the mechanisms of interaction between these important signaling pathways remain unclear.

A new study reported by medical student Tanner J. Freeman in the Medical Scientist Training Program, and Surgery Resident J. Joshua Smith, M.D., Ph.D., working in the laboratory of Vanderbilt’s chairman of Surgical Sciences, R. Daniel Beauchamp, M.D., may shed light on how these activities are connected and what role they play in the development of cancer.

Adenomatous polyposis coli (APC) is a protein that helps regulate cell growth through modulating levels of β-catenin, a central mediator of the Wnt signaling pathway best known for its role in the development of cancer.

When APC is inactivated by mutation the result is decreased protein, or breakdown, of β-catenin and increased levels of β-catenin signaling activity.

Known tumor suppressors, such as transforming growth factor β, bone morphogenetic protein (BMP) and mediators of Smad signaling are also frequently mutated and inactivated in colorectal cancers, decreasing their ability to suppress tumors and promoting tumor progression.

Penson Appointment...

Penson joined Vanderbilt University Medical Center in 2009 after serving as associate professor of Urology and his Master of Public Services, supporting research that improves the quality, safety, efficiency and effectiveness of healthcare in the U.S.

He completed his medical degree from Boston University School of Medicine, and his Master of Public Health from Yale University School of Public Health. He completed residencies at the University of California, Los Angeles Center for Health Sciences, and a fellowship at Yale University School of Medicine.

To better understand the overall interaction of the seemingly divergent Wnt and Smad4 pathways, Beauchamp and his colleagues studied the effects of deficiencies in the transcription factor Smad4 expression on levels of β-catenin.

By studying gene expression data from 250 human colorectal tumor samples, Beauchamp et al. were able to demonstrate an inverse correlation between Smad4 and β-catenin mRNA transcripts in stage I and stage II cancers.

This suggests that as Smad4 levels drop, β-catenin levels rise, which enhances the Wnt signaling pathway and increases the invasive behavior of cancer cells.

They then used molecular techniques to genetically deplete or overexpress Smad4 in human embryonic kidney and colon cancer cells, and found that manipulation of Smad4 expression alters β-catenin mRNA and protein levels along with downstream Wnt signaling in predictable ways.

The most novel observation of this study was that loss of Smad4 expression increased the rate of transcription of the β-catenin gene, resulting in increased β-catenin mRNA, protein and activation of downstream target genes.

This differs from the dominant paradigm that β-catenin protein levels are regulated primarily at the level of post-translational alterations in protein stability.

“These findings provide potential insight into the important relationship between Smad4 loss and amplification of Wnt signaling in colorectal cancer and may help to explain how loss of Smad4 promotes tumor progression, and why such loss is associated with poor prognosis,” said Beauchamp.

Further investigation into the precise mechanisms underlying our observations may provide new avenues to identify therapeutic targets,” he said.

The study, which appeared in the March issue of Gut and the Gut, was co-authored by Tanner J. Freeman, J. Joshua Smith, Xi Chen, M. Kay Washin-ington, Joseph T. Roland, Anna L. Means, Steven A. Eschrich, Timothy J. Yeatman, Natasha G. Deane and R. Daniel Beauchamp.

Virtual Oral Surgery...

(Continued from page 1)

simulated, visualized and verified by the surgical team and patient before we go to the operating room,” McKenna said.

“We not only have more control over desired surgical changes but also a better idea of what our results are going to be. And we are able to share this with the patient beforehand, and then actually go to the operating room and achieve the planned changes,” McKenna said.

McKenna said his patients are typically teenagers and young adults age 16 to 20 who have acquired facial deformities.

“Kids are very self-conscious of facial deformity,” McKenna said. “As teens, they don’t feel like they fit in. They are very motivated young people with deformities that impact both function and appearance so, by correcting deformity, we are able to restore both function and self-esteem.”

Nathan’s father, Ed Curlington, said he is very pleased with the end result.

“Initially I was concerned that the physical effect of the surgery would be very difficult for him, a lot harder than it ended up being,” he said. “If we didn’t do anything it would only compound the issues that he faces in life anyway.”

“Seeing the end result, and the change in his ability to communicate, has been astounding. It was pretty dramatic in the fact that they didn’t do any exterior cutting at all. And that they could plan it out virtually and visually and get it to match up within a half millimeter is amazing”

McKenna said he primarily uses the virtual surgical planning when preparing for corrective jaw surgeries and other oral and maxillofacial surgeries that require pinpoint measurements.

“Certainly, prior to virtual surgical planning, you couldn’t manipulate the facial bones in a virtual manner and actually see how things fit together,” he said.

“It gives us more control over where we are placing various parts of the skeleton in space, a better idea of what the outcome is going to be, and we are learning ahead of time whether the planned surgical changes are technically feasible.”

Nathan Curlington said what he remembers best about the procedure, and having his jaw wired shut for a couple of weeks, is that “when you sneeze it hurts! And I sneeze at least five times a day.”

He notices the little differences here and there in both his appearance and his speech. His bite was also dramatically improved.

“It was something that I wanted to fix but a lot of me was saying, ‘Oh, I’ll just leave it for a while.’ And then when the jaw got fixed, I was like ‘Hrm, it was sort of the same until I looked sideways and I said ‘Oh wow I do have a differ-ence,’” Nathan said.

“And when I talked before it sounded like I was saying something different than what I was actually saying,” he added.

Now he is focusing on going back to school to pursue his dream of becoming a pastry chef, a pursuit made a bit easier by the corrective procedure.

“It has just been amazing,” Nathan’s father said. “Knowing the end result, without question, I would not hesitate to tell anyone about our experience.”

TBI Clinic...

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injury and didn’t even wake from an accident-induced coma until five weeks later.

After receiving treatment at George Washington University Hospital and The Shepherd Center, he returned to Nashville to continue rehabilitation at Pi Beta Phi.

Today, he is back running marathons and now volunteers as a peer visitor for TSN, as well as for the TBI Clinic.

“Having been through this myself, I have complete faith that others recovering from similar trauma can get through this,” said Phillips. “You just have to know it takes time, but you can get there;” he said.

Housed in the Bill Wilkerson Center’s Pi Beta Phi Rehabilitation Institute on the Vanderbilt campus, TBI patients meet once a week to go over their reha-
New to the Section

The Section of Surgical Sciences welcomes its newest additions.

**Mayur B. Patel, M.D.**

Mayur B. Patel, M.D., has been promoted to assistant professor of Surgery, within the division of Trauma & Surgical Critical Care. He previously served as instructor within the division.

**Chong Y. Shin, B.D.S., D.D.S., M.S.**

Chong Y. Shin, B.D.S., D.D.S., M.S., joins the division of Orthodontics in the department of Oral & Maxillofacial Surgery as assistant professor. He comes from Southern California where he was in private practice.