The Spine Center: Relieving Neck Pain

When 62-year-old Mark Cowell woke up one Saturday morning with mild neck pain, he figured he had slept wrong on his pillow. But then he went to the kitchen to get a cup of coffee and discovered he couldn’t reach into the cabinet for a mug.

“My arm would only go about a third of the way up,” he says, “and the pain was so severe that I couldn’t grip.”

The following Monday, he visited his local primary care doctor, who recommended that he see an orthopaedist. When asked if he had a hospital preference, he said Beth Israel Deaconess. “Previously I had a highly successful procedure on my left ankle there,” says Cowell, “so it was my choice to return.”

The root of the problem

On April 15, he saw Ping Jin, MD, PhD, an anesthesiologist and pain management specialist in BIDMC’s Spine Center and the Arnold-Warfield Pain Center. “Mr. Cowell’s symptoms of acute neck pain with arm weakness clearly suggested nerve compression,” says Jin.

A magnetic resonance image or MRI revealed disc herniation—the rupturing of the tissue that separates the vertebral bones. Jin diagnosed Cowell with myelopathy in which the cervical spinal cord is compressed as a result of spinal stenosis or narrowing.

The first course of action was an epidural cortisone injection to deliver pain-relieving medication directly to the inflamed area around the nerve. But since Cowell’s pain was severe and accompanied by muscle weakness, Jin recognized the need for urgent surgical decompression and referred him for a surgical consult with a colleague in the Spine Center.

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Dear Colleagues and Patients:

Welcome to the Fall “Orthopaedic Connections.” In this issue, we feature the excellent care received in our Spine Center by a patient suffering from a sudden onset of cervical pain and arm weakness. This case underscores our integrated nonsurgical and surgical approaches to treatment. I am proud of the close collaboration of our orthopaedic surgeons with neurosurgeons and pain management specialists in the Spine Center. Their team effort ensures that patients receive top quality, efficient care.

I am also pleased to report on highlights of our recent clinical and lab research. Our investigators have gained significant new insights into bone formation, fragility, and pathology. In this issue, you will learn about a study evaluating vitamin D as a risk factor for wrist fractures and a multicenter randomized-controlled trial on antibiotic use after metallic prosthesis reconstruction for sarcomas of bone. You’ll also learn how diabetes can affect skeletal health in the young and how CT combined with computerized structural analysis is being developed to predict vertebral fracture risk in cancer patients.

In addition, I am excited to announce that Jack Wixted, MD, has joined our Orthopaedic Trauma Surgery Division. An expert in caring for acute fractures and post-traumatic deformity, he will help us expand our trauma surgery services and give patients more access to urgent care when they need it.

Sincerely,

Mark C. Gebhardt, MD
Chief, Department of Orthopaedics
A surgical solution

The next week Cowell saw orthopaedic surgeon Andrew White, MD, who specializes in cervical spine problems. After a residency in orthopaedic surgery, White completed a fellowship in spine surgery that combined both orthopaedic surgery and neurosurgery.

BIDMC’s Spine Center includes both orthopaedic surgeons and neurosurgeons as well as physiatrists, and pain management specialists. This multidisciplinary team works collaboratively to ensure patients receive the care they need.

Nurse practitioner Emily Derosier, MSN, NP, is dedicated to the orthopaedics team and sees patients in the Spine Center in conjunction with White and Spine Center Co-director Kevin McGuire, MD. She helps triage new patients to the best provider—surgical or nonsurgical—based on their doctor’s notes and MRIs. She also assists postoperative patients with any questions that might arise regarding medications, wound care, and physical therapy needs.

While most patients can be treated conservatively without surgery, others like Mark Cowell require an operation to relieve pain and stabilize their spine.

“What caused his neck pain and weakness was a disc herniation in between the bones of the neck,” says White. “The inside of the disc bulged outward, pushing on the spinal cord and the nerve roots.”

Nerve signals are like water flowing through a hose. If the hose is squeezed, the water doesn’t flow properly. Similarly, squeezing the spinal cord can interfere with nerve transduction. This isn’t the kind of condition that slowly creeps up on people, White notes. A nerve just suddenly stops sending impulses from the brain to the muscles.

To correct Cowell’s problem, White performed an anterior cervical discectomy and fusion, a common surgery developed in the 1950s that allows troublesome discs to be removed through the front of the neck without disrupting the esophagus, trachea, large blood vessels, and other vital structures.

“Dr. Wayne Southwick, who was active during my residency at Yale, developed this elegant surgical approach that allows us to navigate in a very gentle way,” says White. “Patients who have anterior surgery are more likely to have less short- and long-term pain, less blood loss, and quicker recovery time. For patients like Mr. Cowell, whose spinal cord was pinched in the front, this is the best approach.”

The goal of the surgery is two-fold: first, to take the pressure off the nerves by removing the cervical discs, and second, to restore the spine’s stability with fusion. “In his case, I removed the disc connecting C-4 and C-5 and the disc between C-5 and C-6,” says White. “In place of each disc, we put a bone graft spacer—a plate with titanium screws—so that the bones will unite as they heal and become stable.”

Cowell had his operation on May 11 and was hospitalized for the next two nights. Hospital stay after this procedure is usually one to two nights to ensure patients can eat and drink normally, control pain with pills rather than intravenous medications, and walk well.

Rapid recovery

Mark Cowell was fortunate that his nerve compression, while severe, was not long lasting. Nerves that haven’t been pinched for a long time can recover quickly. By his first postoperative visit about two weeks after surgery, he had experienced complete pain relief and improvement in arm strength. Both his doctors, White and Jin, agreed that no additional treatment was necessary.

Immediately after surgery, Cowell wore a hard cervical collar exclusively and then began phasing into a soft collar, which he wore for two months. He returned to his job after 10 days. His accommodating workplace allowed him to work closer to home several days a week and adjusted his computer and seating to ensure ease of use and comfort.

“I’ve returned to my daily routine,” Cowell says. “I drive, take the train, and walk the dog. I’ve been extremely satisfied with my care.” When asked about the inch and a half long scar on his neck, he says, “I think it gives me roguish good looks.”

Dr. White compares the strength of Mark Cowell’s arms to ensure he has equal gripping power.
Today orthopaedic surgeons can save almost all limbs affected by primary bone cancer using one of several types of limb-salvage surgery, including replacing the diseased bones with large metal prostheses. This alternative to amputation, however, is a lengthy, complex operation that carries a high risk of surgical site infection. To prevent such potentially devastating deep infections, orthopaedic oncologists give patients intravenous antibiotics following surgery.

But there’s debate about how long to prescribe these antibiotics. One day? Five days? Sometime in between? Current concerns about overuse of antibiotics contributing to drug-resistant bacteria make the matter of determining the smallest effective dose critical.

To help settle this question, BIDMC oncologic orthopaedic surgeons are taking part in an international research study, known as PARITY or prophylactic antibiotic regimens in tumor surgery. This is the first-ever multicenter, prospective, randomized trial in the field of orthopaedic oncology. The goal is to compare short- and long-duration antibiotic treatments after surgery for primary bone cancer and decide which best prevents deep infections. Patients age 12 or older are eligible to participate in the clinical trial.

“The study is focused on the lower extremity, the most common location we deal with,” says BIDMC orthopaedic oncologist Megan Anderson, MD. “All patients receive the same broad-spectrum antibiotic, cefazolin, for either one or five days. The study is double-blinded, so neither the patient nor the doctor or nurse knows if antibiotic or saline solution is being given [during the last four days].”

Hospitals from throughout the world are participating in the clinical trial, sponsored by McMaster University in Canada and led by Michelle Ghert, MD. Anderson is the principal investigator for this study at the Dana Farber Harvard Cancer Center and oversees all participation by Harvard-affiliated institutions, including BIDMC. Mark Gebhardt, MD, Chief of BIDMC’s Department of Orthopaedics, is the co-principal investigator at BIDMC and Boston Children’s Hospital, while colleague Santiago Lozano Calderon, MD, PhD, is a co-investigator at BIDMC and MGH.

The risk of infection

Before the 1980s, amputation was the standard treatment for bone cancer. But with the development of effective chemotherapy, preserving limbs became possible. In recent years, limb salvage has been an option for more and more patients, thanks to improvements in imaging, surgical techniques, and prostheses.

Surgery for malignant or benign aggressive tumors most often requires replacing a large section of bone with a metal “megaprostheses.” To remove the tumor, surgeons must take out the bone as well as any affected surrounding structures, such as the joint, muscles, or tendons. They also must separate the blood vessels and nerves from the bone in order to preserve the function of the leg.

“All that means much bigger skin incisions, much bigger surgical exposure, longer operations, and a greater risk of infections,” Anderson. “The risk for deep infection is at least 10 times higher in sarcoma reconstructive surgery than in non-cancer reconstructive surgery.”

A rare occurrence

Primary bone cancer, originating in the bone and not spread from elsewhere in the body, is rare. According to the National Cancer Institute, an estimated 2,970 new cases were diagnosed in 2015, compared to more than 200,000 each for breast, lung, and prostate cancer.

Having many centers participate is the only way to reach statistical significance, Anderson notes. The larger the sample size, the better the results. The clinical trial, which began in 2013, is expected to continue until 2019.

The researchers recently reached a milestone—enrolling their 100th patient. “It’s very exciting,” says Anderson. “Conducting a large study like this is incredibly difficult. We showed that logistically this can be done and in a safe way.”

At the forefront

Research is essential to top quality care. Yet randomized studies are difficult when surgery is involved.

“As a surgical specialty, orthopaedics doesn’t lend itself well to randomized controlled studies,” says Anderson. “This project puts us at the forefront of this kind of research. Hopefully, this will spawn more of these multi-institutional collaborative projects.”
New Trauma Surgeon

When John Wixted, MD, was deciding in which area of orthopaedics to specialize, his wife pointed him in the direction of trauma surgery. She had seen how he loved trauma surgery rotations and how excited he was about fracture cases. He realized she was right and pursued a fellowship in orthopaedic trauma surgery at Massachusetts General Hospital. After this training, he practiced for 11 years at UMass Memorial Medical Center in Worcester before joining BIDMC’s Orthopaedic Trauma Surgery Division in August.

At BIDMC, half of his practice relates to caring for acute fractures. As a Level One Trauma Center, BIDMC is equipped to care for a broad range of life- and limb-threatening injuries, including major pelvic fractures and threatened amputations.

The remaining portion of his practice is largely a mix of general orthopedics and limb reconstruction. Wixted’s experience includes complex limb deformity corrections and hip replacement surgery as well as the treatment of post-traumatic and post-surgical complications.

He notes that at BIDMC, an operating room is open exclusively for fracture surgery every day from 7 am to 5 pm. The medical center has a high volume of urgent care—for example, trauma surgeons fix an average of 250 hips a year.

A graduate of the University of Massachusetts Medical School in Worcester, Wixted trained as an intern at Virginia Mason Medical Center in Seattle. Then he returned to Worcester for his residency in orthopaedic surgery at the UMass medical center.

While in practice at UMass, he spent five years conducting bone-related research studies. The experience opened his eyes to research and academic medicine. He says, “I realized that after medical school, residency, and treating broken bones, I was just the bus driver. It’s the scientist who knows how the bus works.”

He was attracted to BIDMC by the “great research opportunities” and the excellent reputation of the biomechanics lab (the Center for Advanced Orthopaedic Studies). He also welcomed the chance to work with trauma surgeons Paul Appleton, MD, and Edward K. Rodriguez, MD, PhD, whom he has known for a decade.

“I’m looking forward to working on a team that has such a great local and national reputation,” Wixted says.

Outside of work, he enjoys spending time with his wife and three children. To make an appointment with Dr. Wixted in the Trauma Service, call 617-667-7671.

Diabetes May Affect Skeletal Health in the Young

Rarely seen in teens 10 years ago, obesity-related diabetes is not uncommon in adolescents today. In fact, the incidence of type 2 diabetes has risen dramatically from less than 3 percent to 45 percent of new pediatric diabetes cases. The onset of type 2 diabetes between ages 10 and 19 occurs at the same time that up to 90 percent of adult bone mass is developed. The question is: Does early-onset type 2 diabetes affect skeletal health and future fragility?

“Metabolic disturbances during that time can have profound, life-long effects on the skeleton,” says orthopaedic researcher Mary Bouxsein, PhD, senior author of a study on the skeletal effects in a mouse model published in Endocrinology in October 2014. Previous studies have suggested that adults with type 2 diabetes have a 30 to 100 percent higher risk of fracture.

Researchers studied the bone mass, microarchitecture, and strength in male TALLYHO mice, a genetic model of early onset diabetes. “The mice had diabetes as juveniles, and the study showed diabetes clearly inhibited the normal gain of bone that is seen during growth,” says Bouxsein.

To make sure defects were not present in the bone-forming cells, investigators removed and grew cells from the bone marrow in a nondiabetic media. Outside of the body, these cells seemed to proliferate, differentiate, and behave like normal cells.

“There are many established complications of diabetes on different organ systems, including the eyes, kidneys, and heart,” says Bouxsein. “What we are learning is that the skeleton is also subject to diabetic complications. Our study suggests we need to pay attention to the skeletal health of adolescents who are developing diabetes.”

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When cancers, such as breast, lung, or prostate, spread to the bone, they most often travel to the spine, where they can weaken the vertebrae to the point of collapse. These spinal fractures can cause extreme pain and lead to muscle weakness, paralysis, and incontinence. Depending on the location and severity of the fracture, the patient may require costly surgery and a long period of convalescence.

To help predict when devastating fractures might occur Ron Alkalay, PhD, of BIDMC’s Center for Advanced Orthopaedic Studies, is working with David Hackney, MD, Chief of Neuroradiology, to conduct a series of novel NIH-funded investigations using computed tomography (CT) combined with computerized structural analysis. Their goal is to develop an objective method of estimating the risk of vertebral fracture in patients with spinal metastasis. The ability to predict risk of fracture could allow physicians to better manage patient treatment options, for example, to determine if surgery is needed to stabilize the spine and prevent vertebral collapse.

**Part one: Analyzing bone strength**

In the first of these studies, Alkalay and his research team tested the ability of human vertebral specimens with simulated bone defects to withstand force. They created holes of different shapes and sizes in normal bone to mimic the effect of destructive (or lytic) cancer lesions. “We developed a computed tomography-based approach that employs engineering principles in the analysis of image data and can predict whether a vertebral segment will fail,” Alkalay says.

The analysis involves taking a CT image of the spine, isolating the geometry of the complete vertebrae, computing the vertebral bone density, and assessing the bone’s architecture. Engineering principles are used to compute the load-carrying capacity of individual vertebrae. This new software allows users to rapidly segment the whole vertebrae in about 20 minutes. To test the accuracy of their predictions, the researchers used mechanical testing to compress the spine segments with defects until they failed. “We were able to fairly accurately predict the failures, independent of the type of defect or its location in the spine,” says Alkalay. “We now better understand the relationship between the image and the bone density.”

**Part two: How does cancer affect the bone?**

To improve their spine fracture risk predictions, Alkalay and his fellow researchers are currently studying the process of failure in the context of different lesion types. They are examining specimens of vertebrae with cancer to see how it affects the bone’s composition and strength.

Cancer metastases have two distinctive forms: lytic and blastic, which both reflect disruptions in the ongoing, natural process of bone being broken down and rebuilt. Lytic lesions, which can result in solitary or diffuse defects, occur when bone is broken down without being replaced by new bone. On the other hand, blastic lesions, which appear solid, result from bone overgrowth. Lung cancer, for example, leads mostly to lytic lesions, while prostate cancer generally leads to blastic lesions.

“With a blastic lesion, the bone becomes very dense and thick but is likely to be more brittle, leading to its failure during daily activities,” says Alkalay. “By contrast, in a lytic lesion lost bone tissue...”
osteoporosis, a common condition in postmenopausal women and the elderly, causes bones to become thinner and more likely to break. Bone mineral density (BMD) measurements are currently relied on to identify patients at risk for future fractures. But BIDMC hand surgeon Tamara Rozental, MD, points out, “Bone mineral density does not always identify everyone who will suffer a fracture. Up to 50 percent of those with fragility fractures do not have osteoporosis by BMD testing.”

Recent research efforts have focused on finding better ways to predict fracture risk. A number of studies have linked low levels of vitamin D and high rates of bone turnover—the breaking down of old bone and building of new—to an increased risk of hip fracture. So Rozental and Mary Bouxsein, PhD, Director of the Center for Advanced Orthopaedic Studies at BIDMC, wondered if the same could be true for wrist fractures. Wrist fractures tend to occur 10 years earlier than hip or spine fractures and can be the first warning sign of osteoporosis.

In a novel study, Rozental and Bouxsein along with researchers from the University of Connecticut Health Systems set out to see if levels of 25 hydroxyvitamin D and 25(OH)D—an accurate measure of vitamin D—were, in fact, lower in postmenopausal women with distal radial (wrist) fractures than in women of a similar age with no fracture. The investigators also compared indicators of bone formation and resorption measured from blood samples from women with wrist fractures and those without.

In this study, researchers found vitamin D deficiency was not linked to wrist fractures.

Compared to the control subjects with no prior fracture, those with wrist fractures, on average, were slightly older (67 vs. 63 yrs), had lower a body mass index (26.4 vs. 28), and more commonly had a prior fracture (52% vs. 31%).

“Since a new fracture can influence blood serum indices of bone metabolism,” says Bouxsein, “we assessed serum markers of bone metabolism three months after the injury.”

The results

The next step will be a clinical trial to test whether this CT-based analysis can predict vertebral fractures in patients living with cancer. “Ultimately, we want to create a protocol by which we would be able to objectively quantify changes in three dimensions and tell the physician if the patient’s risk is getting higher or lower and if treatment is successfully preventing the onset of fracture.”

This could prove to be a powerful tool in tracking fracture risk and planning individualized treatment. Automating this process may enable physicians to achieve faster, more accurate results and patients to receive better care.
Student Researchers

Student researchers helped BIDMC orthopaedists with clinical studies this past summer. The students worked along side Drs. Edward Rodriguez, Paul Appleton, Santiago Lozano Calderon, and Ayesha Abdeen. They assisted with such tasks as data collection, literature reviews, and manuscript submissions.

Here with Paul Appleton, MD, are (left to right): Kayva Crawford, Tufts University School of Medicine; Oatade Iyoha-bello, Case Western Reserve University; and Paolo de Angelis, Cornell University.

Summer Interns

This summer 19 students, interested in future careers in biomechanical engineering or medicine, had the opportunity to experience lab and clinical research first-hand. The interns came from 15 different universities, both near and far, including Rensselaer Polytechnic Institute, Johns Hopkins, Bowdoin, Duke, Harvard, Cornell, and McMaster. For 8 to 10 weeks, the students worked closely with orthopaedic research investigators on a variety of projects.

To apply for next year’s summer intern program, contact Paula Cohen at pcohen@bidmc.harvard.edu.

News and Notes

Mary Bouxsein, PhD, Center for Advanced Orthopaedic Studies, was recently selected to lead a NASA-funded study to examine bone loss in U.S. astronauts who have spent at least six months on the International Space Station.

John Kwon, MD, Foot and Ankle Surgery, and others published “Damage control orthopaedics: Variability of construct design for external fixation of the lower extremity and implications on cost” in the August issue of Injury.

Ara Nazarian, Dsc, Center for Advanced Orthopaedic Studies, published “Treatment Planning and Fracture Prediction in Patients with Skeletal Metastasis with CT2-based Rigidity Analysis” with Megan Anderson, MD, and Mark Gebhardt, MD, Orthopaedics Oncology; Brian Snyder, MD, Center for Advanced Orthopaedic Studies; and others in Clinical Cancer Research in February.

In addition, Nazarian and others published “Hierarchical analysis and multi-scale modelling of rat cortical and trabecular bone” in the May 6 issue of the Journal of the Royal Society Interface.

Ryan Porter, PhD, Center for Advanced Orthopaedic Studies, spoke on “Beyond development: how can we direct a patient’s endogenous regenerative potential to address large skeletal defects?” at the Harvard School of Dental Medicine in May.


Harris Yett, MD, Joint Replacement and Reconstruction, was named the 2015 Massachusetts Orthopaedic Association’s (MOA) Orthopaedist of the Year. This is the highest honor given to a member of the association who demonstrates commitment to Orthopaedics in both professional and academic settings. Yett has a long history with the association, serving as a board member of MOA since its founding in 1981 and as president in 1991.