Putting an End to Chronic Pain

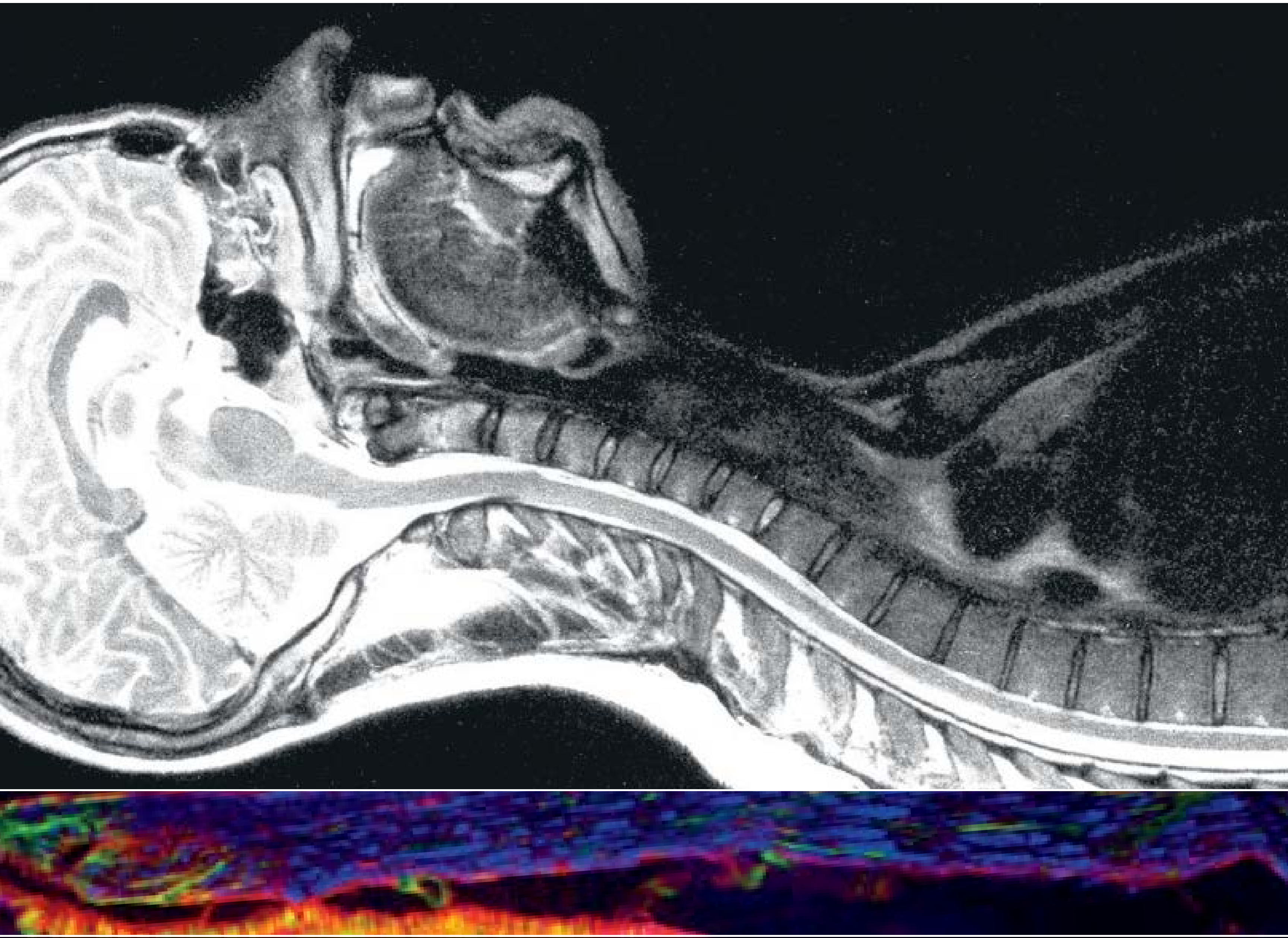
By Janelle Weaver

Chronic pain is the most common cause of long-term disability, and nearly one-third of all cases involve neck pain. Despite the prevalence of this condition, relatively little is known about the underlying molecular causes. Moreover, diagnostic imaging tools and biomechanical measures are often not sufficient for localizing painful injuries, and medical treatments are still not always effective.

Beth Winkelstein (B.S.E.'93), professor in the Department of Bioengineering, is determined to fix this problem. "The challenge with understanding painful conditions is that they often don't manifest with obvious signs on clinical imaging," she says. "We're never going to be able to prevent all injuries from happening, so one of our goals is to identify which tissues are injured, determine when that occurs, and define physiological signatures to identify them in the lab and the clinic."

Shortly after Winkelstein received her Ph.D. in Biomedical Engineering from Duke University in 1999, she decided to focus her research on combining biomechanical and neuroimmunological techniques to understand how injury causes chronic pain. Since joining the Penn faculty in 2002, she has developed

Beth Winkelstein

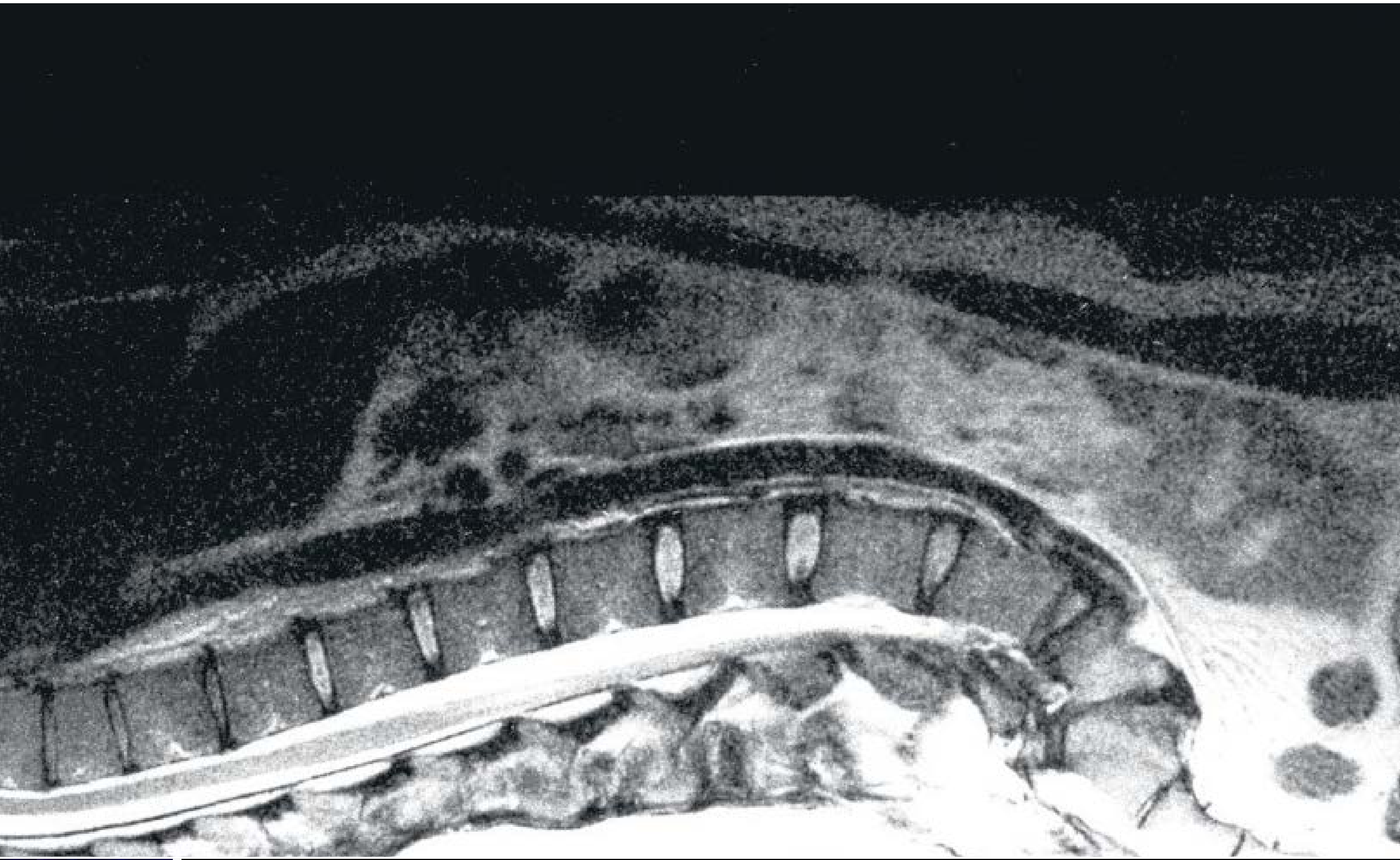


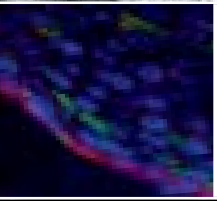
novel animal models to study the molecular pathways and cellular responses involved in chronic neck pain resulting from trauma and nerve damage in the spine and other joints in the body. She integrates engineering approaches to define tissue loads and strains, as well as the kinetic and kinematic relationships between macro- and microscale tissue responses.

"Beth has made a tremendous impact in understanding and translating treatments for chronic pain in the cervical area of the spine, which up until now has been poorly studied," says Kelly Jordan-Sciutto, chair and associate professor of Pathology at Penn Dental Medicine, who is working with Winkelstein to study the role of inflammation in pain cascades. "She has made therapeutic inroads into understanding the underlying mechanism, so she really walks the line between translational medicine and basic science."

Treatments Through Teamwork

To investigate the molecular and cellular causes of chronic pain, Winkelstein collaborates with experts in a range of fields. "This kind of interdisciplinary interaction exemplifies research at Penn," says David Meaney, the Solomon R. Pollack Professor and chair





Reversing nerve degeneration after axonal injury can help restore function and prevent the physiologic cascades that lead to chronic pain. In this slide, the injured axons are labeled in blue.

of Bioengineering. “Penn is a place where faculty in medicine and engineering naturally meet with a common goal,” he says. “Beth’s work is one of the great examples where collaborations between people with different backgrounds pave the way for accomplishing a major goal—understanding the mechanisms of chronic pain to develop new treatment strategies for one of the leading causes of disability in the population.”

Through collaboration with Paul Janmey, professor of Physiology, Winkelstein recently discovered that proteins found in fish blood could alleviate chronic pain when applied to the site of injury. Unlike its mammalian counterpart, fibrin derived from salmon is non-toxic, and it lasts longer and promotes more neuron growth.

“Current clinical treatments involve using joint injections or radiofrequency to ablate damaged neurons, but those treatments usually require repeated dosing and multiple hospital visits, and they give only temporary relief,” Winkelstein says. “Using novel biomaterials is promising because we can develop treatments that are non-immunogenic, simple and very safe, and you can tune their mechanical properties to promote recovery, making them even more effective.”

Beth Winkelstein with Ph.D. student Sijia Zhang

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Another branch of the Winkelstein lab focuses on developing a new optical technique to track in real time the onset and location of ligament damage well before a rupture can be seen. This method involves passing polarized light through ligament tissue and collecting images to create a map showing abnormalities in the alignment of collagen fibers. Unlike traditional approaches based on mechanical measures, Winkelstein’s method can directly localize microstructural damage in tissue as it occurs.

“Our goal is to develop quantitative polarized light or other imaging techniques for clinical use in humans,” she says. “The potential impact is that it could reveal damage that would otherwise be undetectable and make it easier for clinicians to know where in the body to treat.”

Admirable Advisor

Beyond discovering better ways to detect and treat painful injuries, Winkelstein is on a mission to improve undergraduate education. Through her role as Associate Dean for Undergraduate Education at Penn Engineering, she has revamped the year-long Senior Design project to encourage students to think more creatively, work more independently and take more risks. She is also teaming up with Dennis DeTurck, Dean of the College of Arts and Sciences, to lead an undergraduate STEM education initiative at Penn to enhance learning in science, technology, engineering and mathematics, in part by increasing online course options, bringing active learning to the classroom and developing more facilities on campus for laboratory and hands-on activities for students and faculty alike.

Winkelstein’s enthusiasm and commitment to students has not gone unnoticed. In 2006 and 2013, she earned the Ford Motor Company Award for Outstanding Faculty Advising. “She is really dedicated to and passionate about education, and she really wants to do the best by students,” Jordan-Sciutto says. “Her level of commitment to students is what all mentors should aspire to achieve.”