When the 'New Normal' Is Not Enough

Neurorestoration is an infant field, with life-changing potential for people like Bradford Berk '81M (MD/PhD).

Now he's on a quest to make Rochester an early leader.

By Karen McCally '02 (PhD)
Photographs by Adam Fenster

REHAB: Berk undergoes physical therapy at the Medical Center's Department of Physical Medicine and Rehabilitation. He's aided by physical therapist Tim O'Connor (left) and his personal assistant, Harley Bowman.


DELL

Bradford Berk '81M (MD/PhD) grew up immersed in science fiction. "I read science fiction as a kid, just endlessly," he says sitting in his Medical Center office. "I loved the ability to imagine other ways of being and of thinking. I believe it expands your mind."

Berk reaches for a glass of water sitting on the conference table next to him. He raises it to take a sip. It seems hard to imagine, but for the physician-scientist with more than 200 papers to his name, widely praised upon his appointment as Medical Center CEO in 2006 as one of the finest leaders in academic medicine, that simple motion was a daunting achievement.

In a split second during Memorial Day weekend in 2009, Berk, an avid cyclist, rounded a tight curve and encountered a car in his path. Skidding to avoid it, his tire popped and he flew over the handlebars. He heard a snap in his neck. Moments later, he began to lose feeling in his limbs. He struggled to breathe.

Berk was airlifted to the University's Strong Memorial Hospital, where he underwent emergency surgery to stabilize his neck. Paralyzed from his neck down, he remained in intensive care for 12 days and then was transported to the Kessler Rehabilitation Institute in New Jersey for 100 days of treatment.

His helmet did its job. He emerged from the accident with his mind unscathed, his intellectual faculties intact. He returned to his role as Medical Center CEO in February 2010, and has followed a rigorous course of physical therapy at Strong's Department of Physical Medicine and Rehabilitation ever since. Between his treatment in New Jersey and at Strong, he's made great progress, regaining enough movement to feed himself, brush his own teeth, and navigate a host of digital devices such as tablets and smartphones. Yet he remains mostly paralyzed, a quadriplegic with limited sensation and movement in his legs, arms, and hands.

A WELL-EQUIPPED OFFICE: Berk stands for an hour a day in a standing frame, which he says aids his bone, cardiovascular, and gastrointestinal health.

No doubt, life in a wheelchair is not among the alternative ways of being that the sci-fi enthusiast imagined for himself as a youth growing up in the Rochester suburb of Brighton. But since this condition has been thrust upon him, it's given him reason to think back to the realm of science fiction. Sometimes it really does foreshadow the future. Just this past summer, for example, the Food and Drug Administration approved the first wearable robotic exoskeleton, allowing people who've been paralyzed to stand, walk, and even climb stairs. As Berk sees it, developments like this one, combined with recent advances in pharmaceuticals and stem cell medicine, herald a revolution.

"I am watching with great interest the start of a revolution as new drugs, devices, and cellular therapies promise to improve the quality of life for people like me," he said in a public announcement in September. "As a clinician, scientist, and patient, I want to be part of that."

On January 1, Berk will officially step down from his role as Medical Center CEO. Then, after a six-month sabbatical of planning and writing, he'll return to head a new institute dedicated to neurorestoration—the emerging science that promises to lead to treatments of spinal cord injuries and a host of nervous system disorders.

Broadly speaking, neurorestoration is a means to recover central and peripheral nervous system functions that have been lost as a result of injury or disease. It describes a process in which the brain rewires itself, to work around connections that have been damaged or severed. Neurorestorative interventions in the realm of physical therapies, pharmaceuticals, and stem cell transplants, now at varying levels of development and accessibility, all have the potential to improve the lives of people living with a wide array of conditions, including spinal cord and traumatic brain injuries, Parkinson's disease, stroke, cerebral palsy, and others. But as of yet, neurorestoration remains more a goal than an established practice. We know *that* the brain can restore itself. We are only beginning to learn *how*, or to what extent, it can.

At Rochester, one of the centers of that research is the Department of Brain and Cognitive Sciences on the River Campus. Greg DeAngelis, the George Eastman Professor and chair of the department, says that when it comes to clinical interventions in the brain, "I tell my students that it's a little bit like you're trying to fix an alien spacecraft that just landed. It has technologies in it that you don't fully understand. That's about where we're at. But as we learn more our ability to help heal the brain will increase dramatically."

Basic scientists now work directly, in some cases, with clinicians. And those are the types of relationships the institute is intended to foster. Brad Mahon is an assistant professor of brain and cognitive sciences with a secondary appointment in the Medical Center's neurosurgery department. His work is in understanding how the brain's networks function. He works with stroke patients, to understand how the brain recovers from a lesion, and with neurosurgeons to predict what functions could be compromised by surgery to remove tumors. After surgery, Mahon looks for patterns of damage and recovery. Although he's already enmeshed in intra-university collaborations, he sees the institute as an opportunity to build on those connections.

The value of an institute, he says, is that it "provides an infrastructure that's going to attract people from different fields who are interested in a common set of questions."

With research and clinical care in neurorestoration scattered across so many disciplines and subspecialties, it's not surprising that there are, at this point, few neurorestorative institutes as such. There are likely to be more in the future. But Rochester is making it a priority at an early stage, and a key reason Rochester can throw its hat into the ring is that neurorestoration draws on strengths the University already has.

Neuromedicine has been a strategic focus for several years, and in 2009, the late Ernest del Monte, then a life trustee, poured $10 million into the University's effort, expanding research and clinical care, and drawing both under the umbrella of what's now called the Ernest J. Del Monte Neuromedicine Institute. With a search under way for a new director, the institute will work closely, and share many resources, with Berk's neurorestoration initiative.

From a clinical standpoint, the Medical Center has already overhauled inpatient treatment of brain and spinal cord injury patients from admission to rehabilitation. The Kessler Trauma Center, serving Rochester, the Finger Lakes region, and western New York, received a Level One designation from the American College of Surgeons last spring, making it one of only two such trauma centers in the state.

Last summer, the Medical Center opened a brand new Neuromedicine Intensive Care Unit—long a goal of Webster Pilcher, the Ernest and Thelma Del Monte Distinguished Professor in Neuromedicine and chair of the neurosurgery department, and Robert Holloway, the Edward A. and Alma Vollertsen Rykenboer Chair in the Department of Neurology. They recruited two new directors to lead a specialized clinical team that operates 24/7. The unit is part of the Medical Center's Comprehensive Stroke Center, one of only three in the state. According to Berk, the unit, filled to capacity, is one of the Medical Center's major draws from regional hospitals. The unit will aid considerably in one of the most important aspects of treating traumatic injuries to the nervous system: working immediately to limit the damage of the injury.

On the research side, Rochester is a home to scientists of international distinction in stem cell biology, among the most promising


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avenues for treating brain and spinal cord injuries, as well as strokes, Parkinson's disease, and other nervous system conditions. They include Steven Goldman, the Dean Zutes Chair in Biology of the Aging Brain, and Maiken Nedergaard, the Frank P. Smith Professor of Neurological Surgery, both of whom hold joint appointments in the neurology and neurosurgery departments, and codirect Rochester's Center for Translational Neuromedicine; and Mark Noble, the Martha M. Freeman, M.D. Professor in Biomedical Genetics, and Margot Mayer-Proschel, and Christoph Proschel, also faculty members in the biomedical genetics department.

In short, distinguished clinical and research centers are rarely built from scratch. And with what's already been accomplished, the notion that Rochester can make a mark in the field of neurorestoration is well founded. That's even if the leader of the Rochester Neurorestoration Institute weren't a patient himself.

Riding in his motorized wheelchair, Berk is a regular presence in the corridors and atriums of the University's labyrinthine medical complex. With his personal assistant, Harley Bowman, always at his side, he works a busy schedule.

Berk is more visible, friends and colleagues say, than before his accident. There are reasons for that. Getting out and about, greeting staff and visitors as he makes his way through his workdays, is all the more important to him now.

"A lot of people who have these problems," Berk says, alluding to traumatic brain and spinal cord injuries, or even partial paralysis from stroke, "disappear from view. The saddest thing about the community I'm part of is that people tend to be homebound."

Yet they're a sizable group. An estimated 15,000 people sustain a spinal cord injury in the United States and Canada each year, and at any given time, hundreds of thousands of spinal cord patients live with considerable handicaps. There are nearly 800,000 strokes in the United States a year, according to the latest statistics of the Centers for Disease Control and Prevention, and strokes are an even larger source of long-term disability.

Berk sees a parallel with the time, back in the 1970s, when he entered the field of cardiology. "When I was a student, somebody would come in with a major heart attack, and we would give them some oxygen, some diuretics, and some morphine for the pain, and then they either lived through it or died," he says. "A lot of them died."

A POWERFUL ADVOCATE: Lieberman, a University trustee and senior partner at the New York City law firm Skadden Arps, was a leader in the effort to restore state funding for spinal cord injury research.

Of those who lived, many would never regain enough strength to go back to work. And then, in the early 1980s, came angioplasty, followed by stents. And then implantable defibrillators and pacemakers. "These devices transformed cardiology," says Berk. "It was just this sudden wave over about a decade or two that totally changed the practice."

Today, the state of treatment for people with diagnoses like his is similarly rudimentary. Often patients are prescribed a course of physical and occupational therapy and told that after six months to a year, whatever state they are in is where they'll likely remain. They're told that's the "new normal." And Berk, speaking from personal experience, calls the new normal "unacceptable."

Aside from Berk, few people know this better than Nancy Lieberman '77.

Lieberman is not a scientist, but an attorney. She's known Berk since 1998, the year he came to Rochester to lead the Medical Center's Cardiovascular Research Institute. As a trustee, she served on the board's health affairs committee. Possessed of the same driven personality as Berk, Lieberman entered the University at age 16, and graduated first in her class, in three years. By age 22, she had earned a JD degree, and in 1987, at age 30, she became the youngest partner ever—of either gender—at the prestigious New York City law firm Skadden Arps.

In December 2007, on a ski trip with her husband and son, Lieberman, an experienced skier, slipped and lost control of her skis. She careened into a grove of trees, and heard a snap in her neck. "I had this horrible accident and, sadly, a year and a half later, he had his accident," she says of Berk. "I visited him in the hospital. I told him the world doesn't come to an end."

Lieberman had been a patient at Mt. Sinai Hospital. Although she was at a top facility, her progress had been slow and difficult. In five months, she'd gained only limited movement in her upper arms. Her doctors told her that she was unlikely to make much more progress.

Through her connections to Rochester, Lieberman was introduced to Mark Noble.

NEW LEADER: Taubman, who led the Medical Center during Berk's recovery in 2009 and early 2010, will become Medical Center CEO in January.

LEADERSHIP

Dean Mark Taubman to Lead Medical Center

Mark Taubman, who has served as dean of the School of Medicine and Dentistry since 2010, will become senior vice president for health sciences and CEO of the Medical Center, beginning January 1, 2015.

Taubman will succeed Bradford Berk when Berk transitions from those roles at the end of the year to launch the new Rochester Neurorestorative Institute at the Medical Center.

In announcing the appointment, President Joel Seligman praised Taubman as an "unflappable straight shooter" and "a man of unquestioned honesty and integrity."

"In his recent five-year review, Mark was praised for his strategic ability with the School of Medicine and Dentistry, his hiring and promotion of outstanding leaders, his implementation of operational plans, his integrity, and his ability to engage Medical Center leaders during the post-2008 recession period of financial challenges," Seligman said.

A highly respected leader at the Medical Center, Taubman was appointed dean following a nine-month stint as acting CEO while Berk recovered from his 2009 spinal injury.

A board-certified cardiologist, Taubman came to the Medical Center as chief of the Cardiology Unit and Paul N. Yu Professor of Medicine in 2003. He became chair of the Department of Medicine and the Charles E. Dewey Professor of Medicine in 2007 and served in that role until being named as dean.

Before joining the Medical Center, he was director of cardiovascular research at Mt. Sinai School of Medicine in New York City.

BRANDON VICK

STATE-OF-THE-ART: Amrendra Singh Miranpuri, surgical codirector of the new Neuromedicine Intensive Care Unit, gives a tour of the unit to (left to right) Berk, John Markman, associate professor of neurosurgery and of neurology, David Carmel, cofounder of New Yorkers to Cure Paralysis, and Lieberman.

Noble enjoyed a close collaboration with colleagues at the Burke Medical Research Institute in White Plains. For five years, he and the Burke Institute's director, Rajiv Ratan, were the codirectors of the New York State Center for Research Excellence on Spinal Cord Injuries—a communications and research hub for scientists from more than a dozen laboratories.

Burke researchers were recruiting spinal cord injury candidates for an experimental treatment in what's called mass practice therapy. With researchers from the Massachusetts Institute of Technology, Burke scientists had developed a series of robots—armbots, handbots, wristbots, and anklebots—that guide stroke and spinal cord injury patients through thousands of repetitions. The aim of the therapy was to re-educate the brain, to restore function to limbs that were themselves undamaged, but that the brain had forgotten how to use.

With Noble's help, Lieberman enrolled in Burke's experimental program. The results were significant.

"My arms are 60 to 80 percent back," Lieberman says. "This all has to do with the robots."

Among the first priorities of the Rochester Neurorestoration Institute is the replication of Burke's program, now fully operational in its new Restorative Neurology Clinic. Rochester's goal is to offer patients in the region access to this state-of-the-art rehabilitative therapy, which is itself a prerequisite for making use of any significant advances in research. For even if stem cell therapy could fully repair the spinal cord—the holy grail of research—the connections between the brain and the limbs would still have to be reestablished through extensive physical rehabilitation therapy. Which explains in part why Noble, a research scientist, has worked hard for the purchase of physical therapy equipment.

The initial goal of obtaining the robots is now within reach. But it was no easy process getting there. The challenges to improving the lives of patients like Berk and Lieberman aren't only scientific and technological, but also political and financial.

The main source of funding for medical research in the United

States has been the National Institutes of Health. After rising steadily for several years, NIH funding began to decline, adjusted for inflation within the biomedical sector, precipitously so since the financial crisis of 2007.

In 2013, President Barack Obama announced the Brain Research through Advancing Innovative Neurotechnologies, or BRAIN, initiative. NIH recently awarded $46 million in grants as part of the initiative, a relatively small amount for a major initiative in biomedical research. However, funding for the initiative is spread across multiple federal agencies, and Berk has his eye in particular on the Defense Advanced Research Projects Agency, or DARPA, part of the Department of Defense that has funded research leading to some of the most consequential technological innovations of our time, including the Internet.

With the decline in federal support, states and foundations have started playing more prominent roles in funding medical research. The result has been competition among states for top research talent and facilities.

For several years, spinal cord injury research in New York was funded to the degree that it helped scientists in the state to remain competitive, and attracted new ones as well. The money came from traffic tickets. Because motor vehicle accidents are the largest single cause of spinal cord injuries, in 1998, the New York state legislature established the Spinal Cord Injury Research Trust Fund, in which up to $8.5 million per year, collected from ticket surcharges, was to be deposited.

Those funds supported groundbreaking discoveries by researchers across the state, especially concentrated at the Burke Institute and at Rochester. In 2004, it helped support a groundbreaking study by Nedergaard. While many researchers were attempting to regenerate injured spinal cords, she took an alternate path, discovering how it might be possible to interrupt a series of molecular events that cause considerable damage in the immediate aftermath of an injury.

Mayer-Proschel used the funds to build on nearly 10 years of research she'd conducted in stem cells with partners Noble and Proschel. At the University of Utah, where she, her husband, Proschel, and Noble worked together before coming to Rochester, she discovered a new central nervous system precursor cell—that is, a cell that lies on the path of embryonic development between undifferentiated stem cells and fully developed spinal cells. She began to cultivate the precursor cell population in vitro, turning the cells into a very specific kind of astrocyte—the major support cells of the brain and spinal cord that perform many functions, among them, tissue repair. In 2011, she, Proschel, and Noble completed a study in which the cultivated astrocytes were implanted into injured spinal cords of adult rats. Their results showed significant healing in those rats, compared with the control.

The Spinal Cord Injury Research Trust Fund dispersed approximately $70 million. But in 2010, the research funds were diverted when the state faced a $7.5 billion budget gap. Among those who mobilized to restore the funding was Lieberman. She cofounded New Yorkers to Cure Paralysis, a lobbying coalition bringing together most of the state's centers for medical research, as well as several foundations, and at least one pharmaceutical company.

Last May, Berk, Lieberman, her cofounder, New York investor David Carmel, and Noble traveled to Albany to press their cause. "They had a pretty hard time saying no," Berk says. The funding was restored at $7 million. When the board doled out multiple grants in the aftermath of the new budget, Rochester's Medical Center received the state's largest, at more than $1 million. An equipment grant, it will go toward the purchase of multiple tools for research and treatment, including the robotics rehabilitation devices pioneered at Burke.

Noble sees it as a good omen. And in August came further good news, as Gov. Andrew Cuomo announced the release of $14 million to support stem cell research.

New York still has a way to go. California is the national leader in state funding on stem cell research, including research on brain and spinal cord injuries. Scientists under pressure to find grant money to support themselves, their labs, and the graduate students and postdoctoral fellows on which research relies tend to go where the funds are.

Noble, a member of the team that reviews stem cell grants for the California Institute for Regenerative Medicine, says New York will have to continue its leadership, lest it end up becoming "a farm team."

Philanthropy will also play a role.

And Berk's leadership will be key.

"There's an aspect to Brad that I can point out, but Brad wouldn't," says Noble. "This field needs articulate advocates. And there are far too few of them."

Lieberman, who has also become an articulate advocate, agrees. "Most people with these injuries aren't the head of a major medical center, or like me, a senior partner in a law firm. They can't go to Albany and talk the talk." Spinal patients are often young—the victims of car crashes, sporting accidents, gunshots, and increasingly, blasts from military combat. The late actor Christopher Reeve, who was paralyzed in a horseback riding accident in 1995, raised the profile of spinal cord injury patients considerably. But although the Christopher Reeve Foundation remains an important force for publicity and fundraising for research, since Reeve's death in 2004, there have been few compelling spokespeople.

Berk is not a movie actor. But he's a distinguished medical leader, clinician, and scientist. Personable, photogenic, and at home before an audience, he's ready to write, speak, and travel to educate the public and raise money—for the Rochester Neurorestoration Institute, and for the cause of patients more broadly.

Lieberman will continue to be an important partner. "I have felt for myself—and I think Brad probably feels this way—that's it's incumbent on us. Incumbent on the people who have had accidents later in their lives to do for all the others who can't do for themselves."

To her, it really is a matter of saving lives. "We warehouse—and I use that word deliberately—warehouse human beings in nursing homes and institutions." But even small advances can make a big difference to people like her. Her goal is to walk again. Nearly six-and-a-half years after she was expected to make no progress, she continues to work on her arms. Whether you consider her progress modest or significant can depend on what chair you're sitting in.

"Every notch that you're able to get back makes a huge difference," she says. "If I were simply a paraplegic, meaning I couldn't walk, but I had my arms, that would be transformative for me." R