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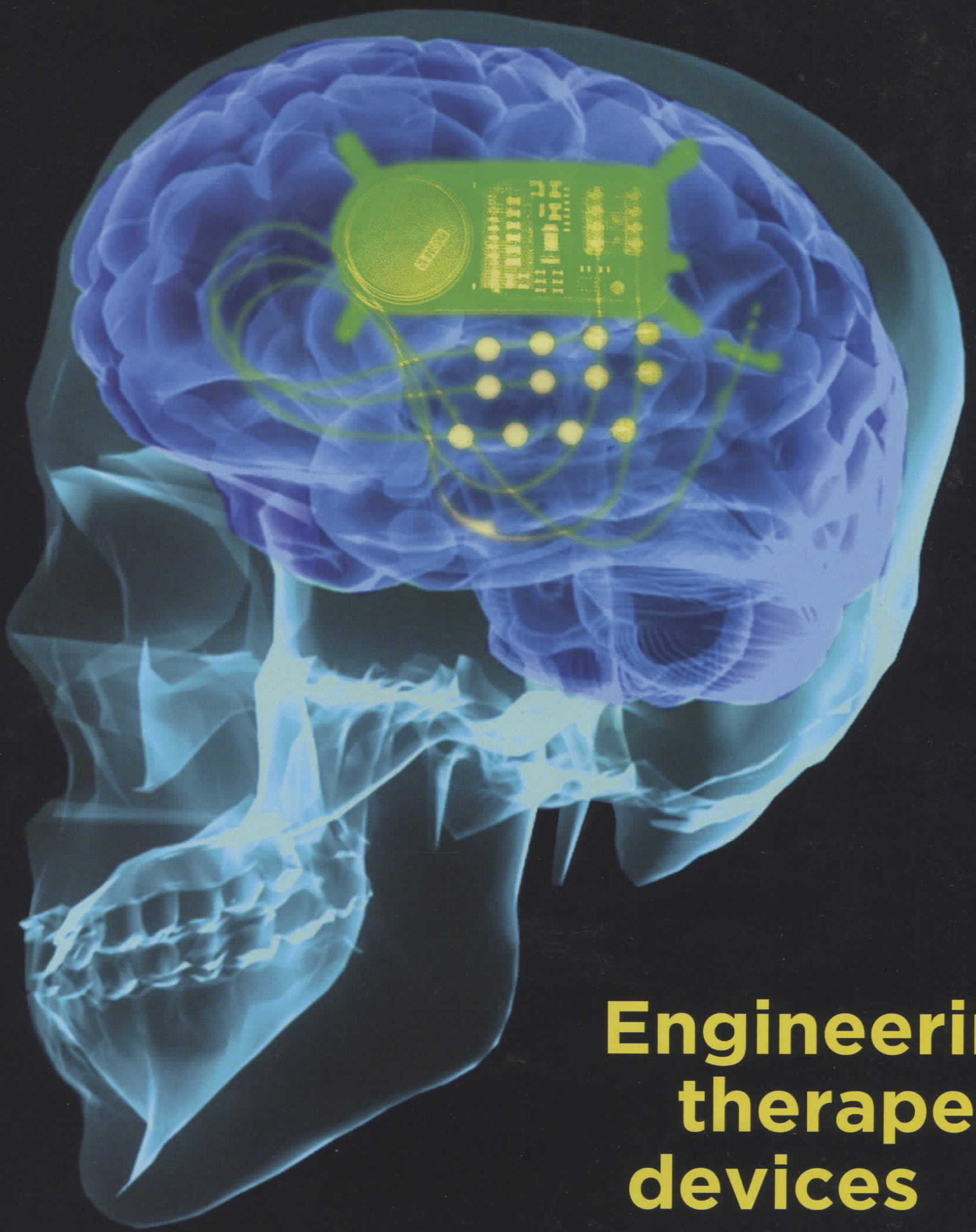

Engineering therapeutic devices

UNIVERSITY OF PENNSYLVANIA

In

BY JESSICA STEIN DIAMOND

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Soul of vention

Brian Litt's Quest to Bring Moore's Law to Therapeutic Devices

Though his work promises to transform medical care for the brain and heart, Brian Litt is motivated by a less scientific realm: his soul.

Memories of patients with epilepsy whose lives were tragically altered by uncontrollable and unpredictable seizures drive Litt's determination to find new therapeutics. Recalling, for example, the mother who drowned in the bathtub she filled for her child, part of the one percent of the world's population who suffers from epilepsy, Litt asks, "How can you not be compelled by that? Ninety-eight percent of the time they spend their lives just like we do, except for that unpredictable two percent when they're suddenly unconscious or having convulsions."

Urgently-needed devices that would anticipate and override epileptic seizures are currently under review for approval by the FDA. These devices integrate patents by Litt and were developed by NeuroPace (a privately-held company). The firm's technology development team includes former Litt graduate students.

"When people look back on Brian's research, he will be viewed as a real pioneer in advanced biomedical devices," says John A. Rogers, professor of Materials Science and Chemistry at the University of Illinois at Urbana-Champaign, MacArthur Foundation "genius grant" recipient in 2009 and Litt collaborator.

Litt joined the Penn faculty in 2000 and became the first dually-appointed professor in both Penn's School of Engineering and Applied Science and School of Medicine in 2007. He received tenure in both schools in 2008. An associate professor of Neurology and Bioengineering, Litt juggles at least four professional lives: translational research, teaching, patient care, and mentoring graduate students and clinicians-in-training.

Commercializing his work doesn't count as a separate professional life, says Litt. His focus is on bringing therapeutics to patients as quickly as possible. Initially, he intended to devote himself to full-time epilepsy patient care in Baltimore, his hometown. Five years into clinical practice, Litt redirected his career after a painful realization. "For the most severe epilepsy cases, nearly 30 to 40 percent of our patients, I could do everything I was taught to help them, and I wasn't affecting the natural history of their disease," he says.

Litt then began a career-long quest to use engineering techniques to improve patient outcomes, focusing on outdated technologies that created diagnostic and therapeutic bottlenecks in epilepsy care. He holds an undergraduate engineering degree from Harvard, a medical degree from Johns Hopkins University, and completed a neurology residency and fellowship in epilepsy and clinical neurophysiology at The Johns Hopkins Hospital.

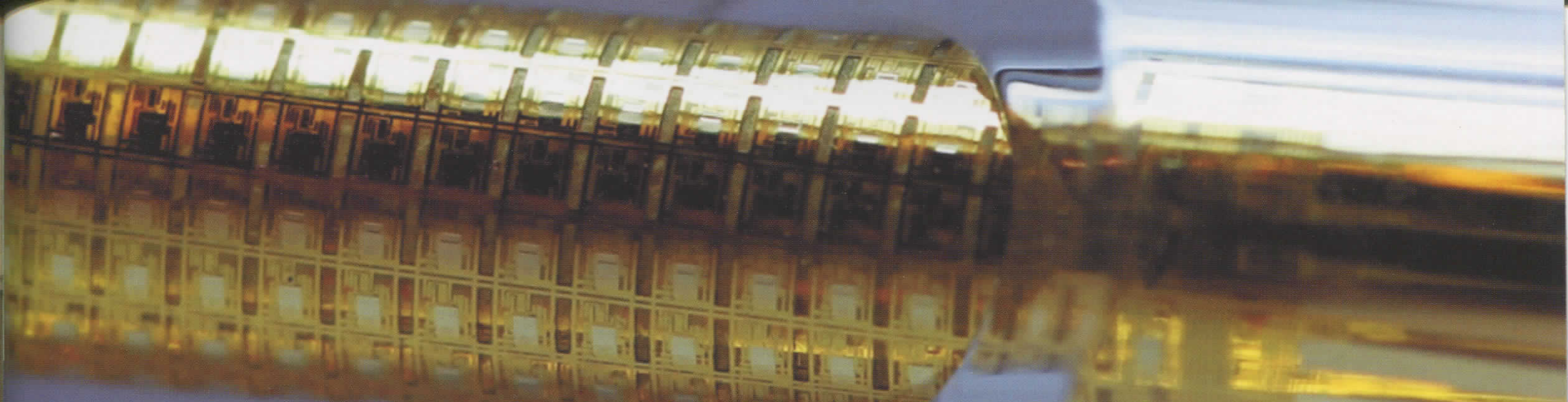
While he isn't a neurosurgeon, Litt designs operations for epilepsy surgeries at Penn. The challenge is, says Litt, "You have to find a way to disable seizure networks without resecting a hunk of brain that's going to cause deficits."

Standard procedure to identify seizure-affected, treatment-resistant regions of the brain involves placing arrays of electrodes one centimeter apart directly onto brain tissue (accessed through the skull via a burr hole or craniotomy). This protocol has remained virtually unchanged for decades: each electrode was previously hand-soldered to a wire connecting to a cable outside the head. "People being monitored have a spaghetti of wires coming out of their head," says Litt. "Sometimes you have 256 plugs that you have to manually put in the right place. Imagine the potential for error."

Four years ago Litt asked graduate student Jonathan Viventi to find a way to place thousands of smaller electrodes on the brain that would connect with a single USB plug. In addition to reducing error and pressure on the surface of the brain, smaller electrodes would allow clinicians to obtain more detailed data, better reflecting the scale of functional units in brain tissue.

After hearing Rogers give a talk to Penn's Electrical Engineering department, Viventi suggested the two labs collaborate. In partnership with a research team from Tufts and Northwestern, they have since developed flexible, stretchable microelectronics for clinical use. Rogers, who hadn't previously worked on biomedical devices, says, "Brian's group has been absolutely essential to defining the most clinically relevant modes of use for our advances in electronics. Together, we have laid the groundwork for something that could be a really big deal. I don't think there is anything approaching this level of sophistication in bio-integrated electronics. Our collaboration has opened up a whole new world for doctors and researchers alike."

Compared to 40 years ago, consumer electronics are virtually unrecognizable. Clinical and surgical devices look primitive by comparison, says Rogers. "However, our work on biocompatible electronics may eventually enable Moore's Law types of advancements to map directly to biomedical devices. Even if you could do that only to some degree it would be a huge win."



“More recent discoveries by the Litt Lab and research collaborators include flexible active electronics that could serve as a biocompatible platform for new diagnostics and therapeutics for the brain, heart and other organs.”

In February, Litt received a $6 million grant from the National Institutes of Health (NIH) to create an international database to understand seizure generation and epileptic networks—linking a diverse group of investigators from Penn’s medical and engineering schools.

Litt reflects, “There is such a desperate need for the application of engineering to everyday medical problems. We started out asking a simple question: How and where do seizures begin and what does an epileptic network look like? And we ended up with new medical technologies and commercialization, new training programs, and a ton of ideas pending patent disclosure. There has been a tsunami of ideas because Penn has tremendous scientific strengths and is a medical powerhouse. We need more conduits like me.”

That idea is circulating at the highest levels. George J. Pappas, Deputy Dean for Research for Penn Engineering, says, “Strengthening the ties between engineering and the medical school through more such dual appointments will give us a competitive advantage over other universities and lead to medical breakthroughs. We’re working to create an environment between engineering and medicine that would help people who are dually appointed to be intellectual leaders.”

The Litt Lab is a hub for broad collaborations, a small subset of which includes a customizable cognitive neuroprosthesis to compensate for damaged brain tissue, working with Michael J. Kahana, director of Penn’s Computational Memory Lab; organic neuroprostheses with Cherie R. Kagan, associate professor of Electrical and Systems Engineering; and a cortical auditory prosthesis with Yale Cohen, associate professor in ENT and Neuroscience.

David J. Callans, electrophysiologist and Penn Medicine professor, is exploring ways to use Litt’s advances to increase the functionality of cardiac devices such as pacemakers. “We started thinking about heart disease because of its prevalence, but there’s certainly a lot that could be done with Brian’s approach in many different organ systems,” says Callans.

Having just turned 50, Litt thinks about his legacy. “There’s so much to accomplish. I plan to train as many good people as I can in this collaborative image.”

Litt’s protégés are influential in academia, government and industry. And his postdoc trainees are being offered joint positions in Neurology and Bioengineering. “Perhaps the idea is catching on a little,” says Litt. His 15-member research team is comprised of bioengineering graduate students paired with neurology and neurosurgery residents and junior faculty.

Amidst the deadlines and the pulls between medicine and engineering, the patients and the science, Litt strives to keep it all in perspective. He still makes house calls to terminally ill patients and tries to balance work with family—his wife, Lisa, an occupational therapist, and sons (twins) Dan and Brad, 17, and Ben, 15.

And he remembers the advice of his late father, who never went to college: Do work you enjoy, that can support a family, and that will leave the world a better place after you are gone. “If I could just take the refractory rate of people who have epilepsy down from 38 to 28 percent, that would be a life well spent,” says Litt.