A NOVEL LOW-ENERGY METHOD OF DEFIBRILLATION SHOWS PROMISE TO SUCCESSFULLY TREAT HEART ARRHYTHMIAS WITH LESS PAIN AND TISSUE DAMAGE THAN CURRENT DEFIBRILLATION METHODS

Like a big kick in the chest — that’s how people who have undergone defibrillation while conscious often describe it. Applied with “paddles” — as depicted in TV shows and movies — or by EMTs with AEDs (automated external defibrillators) or by implantable devices, defibrillation applies a brief burst of electrical current at energy levels many times higher than the human pain threshold.

“It’s a huge shock, 130 to 360 joules externally, about seven internally,” says computational scientist Elizabeth Cherry (as of this year at the Rochester Institute of Technology, formerly at Cornell). “Basically,” says Cherry, whose work has focused on the heart’s complex electrophysiology, “conventional defibrillation is for emergencies, most often ventricular fibrillation, which is almost always life-threatening and requires immediate resuscitation.”

Among many heartbeat irregularities, from the occasional skipped beat to various flutters and throbs, ventricular fibrillation (VF) is in a class by itself for rapid fatal consequences. Other cardiac arrhythmias, nevertheless, present serious health problems that could be treated effectively with defibrillation — if it didn’t involve serious pain and risk of lasting tissue damage.

With the goal of making that possible, Cherry and a large group of collaborators, including physicists Flavio Fenton (Cornell) and Jean Bragard (University of Navarra, Spain) and others at Cornell and the Max Planck Institute (Göttingen, Germany), have done experiments — correlated with simulations at PSC — that show the feasibility of defibrillation with much lower energy, less than one joule. Called far-field antifibrillation pacing (FFAP), their method appears to offer a realistic prospect for defibrillation below the pain threshold.

Many of their FFAP studies have focused on atrial fibrillation (AF), an arrhythmia in the heart’s upper chambers. Affecting more than 2.2 million people in the United States alone, AF incidence increases with age and, unlike VF, can persist for years. Although AF seldom requires emergency treatment, it increases risk for stroke and heart failure. Current treatments — primarily antiarrhythmic drugs and sedated defibrillation in a clinical setting (called cardioversion) — aren’t especially effective and often have serious side effects. “There’s a big clinical hole,” says Cherry, “in how to treat this type of disease.”

Their experiments with FFAP have shown a success rate comparable to conventional defibrillation, higher than 90 percent, in stopping AF and restoring normal heartbeat. Their computational simulations (using up to 500 processors on PSC’s BigBen) confirm the theory underlying FFAP and allow the researchers to test many possibilities. They reported their findings last year in Circulation (August 2009), a leading cardiology journal, and newer publications are in press. “Based on human pain threshold values in the literature,” says Cherry, “we believe our approach is currently at the threshold and that with optimization of parameters such as shock waveform and electrode placement, guided by computer simulation, we’ll be below it.”
SCROLL WAVES IN A FAR FIELD

The steady lub-dub we call the heartbeat is regulated by a built-in pacemaker—the sinusoidal node. This cluster of cells at the top of the right atrium emits electrical pulses about once a second that excite nearby cells, generating a cell-to-cell electrical wave that in milliseconds becomes the smooth and concerted muscular contraction that pumps blood.

Arrhythmias occur as these propagating waves break apart and form “reentrant waves”—in effect, a mistimed pulse that loops back through the heart’s muscle fibers like a dog chasing its tail. Called “spiral waves,” they meander through the heart and play havoc with its normal rhythmic pattern. VF is believed to involve multiple scroll waves, and AF may or may not require multiple waves. “A single wave might be tachycardia or flutter in the atria,” says Cherry, “or it might be fibrillation.”

Before the work of Cherry and her collaborators, research on low-energy defibrillation focused on a single spiral or scroll wave, investigating how a low-energy field could move the wave to the edge of tissue, where it would disappear (since with this kind of wave there’s no reflection at edges). “People were looking at what we call ‘pinned waves,’” says Cherry, “such as when there’s scar tissue from a heart attack. A wave can confine itself within that tissue and circulate repeatedly.”

Cherry and her colleagues took the low-energy approach much farther, starting from the same basic “far field” idea: “You have field electrodes,” she explains, “so you’re not injecting a current directly into the tissue, but letting the tissue respond to changes in the field around it.” “With a series of experiments, they are investigating how the low-energy field affects more complicated arrhythmias, beginning with AF.”

Their computational models, developed over a period of years, have allowed them to do basic research on how arrhythmias get started and evolve, both as a function of the electrical properties of heart cells and larger-scale heart anatomy. Because of the great range of scales involved—spatially (from a single cell to the full-size heart) and over time (microseconds to minutes)—these simulations require large amounts of computing. For their whole-organ model of cardiac electrical dynamics, they relied on PSC’s BigBen until it was decommissioned this year. “This system worked well for us,” says Cherry. “It was easy to use and convenient. They are now moving their code to Purdue’s Storito system. Their whole-heart model is well suited to simulating FFAP because of its characteristics as a ‘bidomain’ model. Some models of current flow are ‘monodomain,’ a simpler mathematical formulation. Basically you’re representing the membrane potential with no extracellular medium where current can flow,” says Cherry, “as opposed to a bidomain model, which represents intercellular space as distinct from extracellular space.”

This difference, says Cherry, is not only critical to accurate modeling of FFAP but also tied to how it works. “The idea of FFAP,” says Cherry, “is that you apply a pulsed electric field, and as the current produced by this field encounters discontinuities—blood vessels, for instance, or collagen and other features of the extracellular matrix—it recruits these discontinuities as ‘virtual electrodes.’”

These discontinuities—whose electrical effects can’t be represented with a monodomain model—function essentially as physically implanted “real” electrodes would. They activate nearby cells, and with successive pulses, the far-field current activates increasingly larger regions of tissue, which synchronizes electrical activity throughout the heart and restores normal rhythm. The FFAP findings of Cherry and her colleagues demonstrate feasibility and offer the prospect of more effective treatment for AF. Along with antiarrhythmic drugs, which work by varying success— and less frequently—catheter intervention to isolate a problematic region of atrial tissue, standard therapy for AF is cardioversion.

“Because the patient’s rhythm corrects whenever this pathological rhythm occurs. And the response would be immediate demand whenever it senses fibrillation, not causing you to have atrial fibrillation, the longer it’s been there, the more difficult it is to keep it from coming back.”

Like cardioversion, FFAP could be applied externally, but also could function as an implantable device, which Cherry envisions as a more convenient, more personalized approach to cardioversion: “You can usually restore rhythm, but the more you’ve had atrial fibrillation, the longer it’s been there, the more difficult it is to keep it from coming back.”

How it Works

With computational simulations, Cherry and her co-workers corroborated their experimental findings and gained clearer understanding of how FFAP works. “With experiments,” says Cherry, “we use dyes that bind to the tissue, and fluorescence in proportion to changes in membrane potential, but you still can’t see everything you want to see. With modeling and simulation studies, you can vary parameters and elucidate the changes systematically, which is hard to do in experiments.”

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