Taking Skeletal Muscle to Heart

By RICK WEISS

"Would you have your songs endure? Build on the human heart," advised Robert Browning in the mid-1800s.

Day in, day out, the human heart endures — leaving physiologists, as well as poets, marveling at its dependability. No other type of muscle has the stamina of that fist-sized, four-chambered pump.

But the heart can fail. And medical researchers who deal with failing hearts are now taking Browning's advice: Rather than replace an injured heart with a mechanical device or a transplant, they are learning how to build on the human heart.

For building materials, they rely mostly on skeletal muscles taken from elsewhere in the body. Using a variety of approaches — only a few of which have been tried on humans — scientists increasingly are finding that skeletal muscle can be wrapped around a damaged or overworked heart and rhythmically stimulated to provide valuable assistance. Indeed, while skeletal muscle may never match the heart for its ability to inspire lilting couplets, scientists can now train even the most mundane contractile tissues to do much of the work that was once considered the heart's exclusive domain.

"There's a tremendous clinical need to treat patients with 'end-stage' or irreversible heart failure," says Stephen F. Badylak, who specializes in the use of skeletal muscle for cardiac assistance at Purdue University in West Lafayette, Ind. Each year, he notes, 400,000 people in the United States develop end-stage heart failure — a serious weakening of the heart due to the death of some portion of cardiac muscle. Nearly half these individuals die within one year.

About 30,000 to 50,000 U.S. heart-failure patients could have benefited from heart transplants last year, but because of the shortage of donors, only 1,400 received them, Badylak says. And scientists developing artificial hearts, although perennially optimistic, remain plagued by a variety of problems — including the risk of infection from body tubes connecting the device to its external power supply.

"I don't think this will replace the field of artificial heart development, nor will it at this time replace transplantation," says George J. Magovern, the only person to perform the experimental surgery on humans in the United States. "But it's a third modality we're looking at, and one that could help a tremendous number of people."

Four of Magovern's five cardiac-assist patients remain alive — including the first, operated on three years ago (SN: 5/3/86, p.284). Their failing hearts are now securely wrapped in skeletal muscle "blankets." A pacemaker stimulates these living blankets to contract in unison with the heart, taking some of the workload off the tired organ.

"The advantages of using [a patient's] skeletal muscle are obvious," says Badylak, a research physician at Purdue's Hillenbrand Biomedical Engineering Center, which last month hosted a conference on cardiac assistance with skeletal muscle. "It's readily available, and in most cases you have a very willing donor; you don't have to worry about immunosuppression [necessary with transplants] and its attendant infection problems; and there are no tubes going into the body to increase the chances of infection."

But problems do occur, he and others note. For one thing, Badylak says, "skeletal muscle is not like heart muscle that beats every day and night all the time without stopping. Skeletal muscle gets tired and needs a rest."

Experiments have been performed on dogs with drug-induced heart failure for more than 30 years, says John D. Mannion of the Thomas Jefferson University in Philadelphia. However, he says, until the 1980s — and sometimes still today — skeletal muscle "used to last five minutes, then fizzle out."

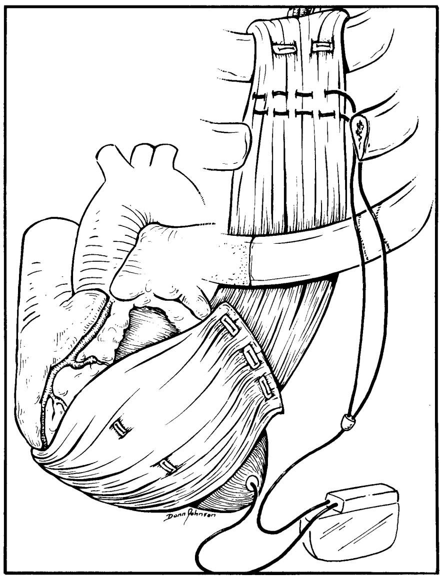
In part, says Mannion, this muscle failure has been due to the extreme rigors of the experimental surgery. "Part of the problem is that we expect skeletal muscle to do things that we'd never expect cardiac muscle to do. We cut off the blood supply, let it dry out and expect it to function well."

But there are fundamental differences between the muscle types, too. Skeletal "fast-twitch" muscle contracts quickly in response to an electrical stimulus, but tends to tire quickly as well. Cardiac muscle responds with slower, stronger contractions, but does so repeatedly without fatigue — in part because it derives its energy from a different metabolic pathway.

This metabolic bottleneck seemed impassable until researchers found, in the past decade, that muscle types are far more "plastic" than they imagined. When skeletal muscle is stimulated with a steady, rhythmic train of low-voltage bursts for several weeks, it undergoes a dramatic structural and biochemical transformation that leaves it remarkably similar to cardiac muscle.

Although "conditioned" skeletal muscle still tires more easily than its cardiac equivalent, scientists no longer see fatigue as the primary roadblock to widespread clinical application of skeletal-muscle heart assists. They've turned their efforts instead toward finding the best muscle-wrap techniques and ideal patterns of electrical stimulation. Other researchers, working exclusively with animals, are testing a variety of implantable, muscle-wrapped balloons — so-called skeletal-muscle ventricles — that they splice into the circulatory system to act as auxiliary pumps.

Researchers have performed the heart-wrap technique on approximately 30 patients in five countries, according to Juan Carlos Chachques of the University of Paris' Hôpital Broussais, where about half the operations have been done. The most common approach involves freeing a large portion of the latissimus dorsi — a muscle that normally stretches from under the arm to the middle-lower back — while leaving intact most of its blood supply and motor-nerve connections. After removing one rib, surgeons pull the muscle flap into the chest cavity, where they suture it around the heart in a spiral pattern.



Donn Johnson

Researchers can reroute the latissimus dorsi over a rib, then wrap it around a weakened heart. An implantable pacemaker triggers muscle contraction.

Surgeons can further stabilize the muscle by stapling part of it to a remaining rib. Then they wire a pacemaker-like electrical stimulator between the heart and the muscle. This pacemaker, sensing the heart's natural electrical pulses, delivers carefully timed bursts of electricity to the latissimus dorsi, causing it to contract in synchrony with the heart's left ventricle.

It is difficult to know how much cardiac improvement results from the technique, say Chachques and Magovern, in part because surgeons often treat other cardiac problems in the same operation. Moreover, since the procedure is offered only to the most severely ill patients, the short-term mortality rate of about 50 percent does not necessarily indicate its potential value in healthier patients. But as measured by such indicators as total cardiac output and hospitalization rate before and after surgery, the procedure seems promising, researchers say.

"On average, I'd say we're seeing about a 20 percent improvement in the cardiac output," Magovern says. "And 20 percent can mean the difference between being almost an invalid and resuming a fairly normal life."

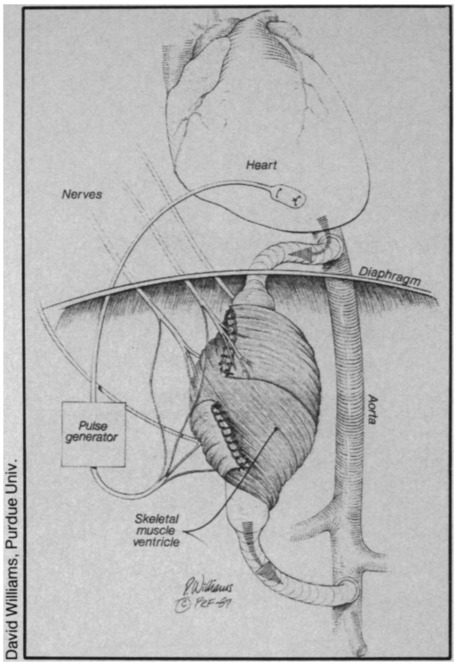
Those figures may improve. he adds, with an advanced pacemaker available in France but still awaiting U.S. approval by the Food and Drug Administration (FDA). Magovern, chairman of surgery at Allegheny General Hospital in Pittsburgh, has asked the FDA for permission to use the experimental device on 10 patients and expects a reply "momentarily."

Researchers experimenting with skeletal-muscle ventricles, or SMVs, face many of the same problems their heart-wrap colleagues do, and a few more. Their approach to cardiac assistance is to add to the body's circulatory system some biocompatible tubing and one or two synthetic balloons. They generally splice this extra bit of plumbing into the aorta – the large artery through which oxygenated blood leaves the left ventricle on its way to the rest of the body. They wrap skeletal muscle around the balloon(s) and wire the muscle to contract in synchrony with the heart.

In these systems, depending on the specific design, it's often more helpful for the balloon pump to contract while the heart is "resting" between beats. And in one experimental version of this "extra-aortic balloon," described at the conference by Garrett Walsh of the Montreal General Hospital, surgeons place the balloon under the intact latissimus dorsi, bringing the balloon to the muscle instead of vice versa.

In most SMVs, however, scientists have trouble preventing clot formation. Blood pooling within the oddly routed system – and contact between the artificial materials and the blood – often results in multiple clots that can block crucial vessels and lead to death.

So, while researchers express pleasure about the blood pressures that balloon pumps can generate in dogs and other animals, "we don't believe at this point that a skeletal-muscle ventricle is anywhere near clinical application," Magovern says. Adds Walsh: "In some respects it's the Wright Brothers stage."



David Williams, Purdue Univ.

One experimental configuration of a skeletal-muscle ventricle that physicians may someday implant as a heart assist.

Whichever way skeletal muscle eventually supports cardiac function, pacemaker technology will prove critical to its success. New research demonstrates that single bursts of electricity – those typically delivered by FDA-approved pacemakers – do a poor job of getting skeletal muscle to contract. A burst of about eight jolts in extremely rapid succession seems to get the best contraction. The device used by Chachques and sought by Magovern delivers such a burst, but even better technology is on the horizon.

A new stimulator, expected to be available in Europe soon, is totally programmable, say researchers. By manipulating voltage levels, burst frequencies and other parameters, the device should help researchers determine the ideal "training schedule" for getting skeletal muscle to behave more like cardiac muscle. Today, concedes Badylak, "I don't think we're anywhere near knowing what the optimum stimulation parameters are."

But with improved knowledge about how to condition skeletal muscle for cardiac duty, and with a programmed pacemaker capable of handling a large number of contingencies, the future of cardiac assistance with skeletal muscle looks bright, concludes Ray Chu-Jeng Chiu of Montreal General Hospital. Ideally, he says, a stimulator would fire just frequently enough to keep the muscle conditioned, and would kick in fully only when blood pressure drops, indicating the heart's inability to handle its workload. The upcoming model should stop firing if it senses very unusual cardiac rhythms, to ensure it doesn't exacerbate the arrhythmia. And perhaps someday, Chiu says, a stimulator will deliver strong, defibrillating shocks when necessary to restore a normal rhythm.

"If we get that," he says, "it'll be like having a little cardiologist sitting inside the patient." ☐

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government and industrial radiation-safety standards. This statement, although impressive and a very useful shield behind which industry may hide, is irrelevant to the case because all existing safety standards have been based on the field intensities at which *cell damage occurs.* In developing these "standards," no consideration has yet been given to those far lower intensities that cannot damage cells but merely shift their energy level and metabolic cycle.

It is my observation that VDT manufacturers are quietly beginning to clean up their act, and eventually harmless plasma displays will probably replace cathode ray tubes. But what about the tens of millions of radiating VDTs that are out there and will continue to be used for many years to come?

Charles Wallach
President, Behavioral Research Associates
Canoga Park, Calif.

For a couple years now, I've been reading articles on VDT hazards looking for reports on two forms of radiation that I've never seen discussed. Your article got close to one. It mentioned a "sawtooth-shaped wave," presumably from the magnetic coils that deflect the electron beam that paints the screen. While I can find that on my terminal with an oscilloscope probe, I can find a much stronger spike waveform near the flyback transformer in the high-voltage section. By placing a bare oscilloscope probe by my terminal's side near the flyback transformer, I measure a 0.4-volt spike. This the most conservative measurement I can do; if I use my hand as the antenna and touch the probe tip with my other, I get more than 4 volts. Another display I own radiates so much I can't put it on top of data cables because the signal couples into the wires and causes data errors.

The flyback transformer is also the source of a form of radiation I've never read about in the press, audible radiation. Each pulse in the transformer makes its shape pulse slightly, causing a sound wave. The frequency is generally 15 to 20 kilohertz, a range that many people can hear. One VDT I had in my office was so loud I would get a headache if I used it for 15 minutes. Since researchers can't confidently blame electromagnetic radiation for problems, I think they need to study every possibility.

Finally, I've noticed that the studies seem to focus on people who use VDTs for all their work. Within the software engineering community, I've heard very few complaints about VDTs. While we can spend 50 to 75 percent of our workday using them, we also move around, go to meetings and read SCIENCE NEWS. Therefore, I am pleased to see that researchers are becoming less concerned about the electromagnetic radiation and more concerned about job requirements and ergonomics.

Eric Werme
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