

Heart attack—NASA research on cardiac resynchronization therapy and defibrillators (CRT-D)

ABSTRACT—ISSO Annual Report Editor Irving Rothman has become the beneficiary of NASA research after suffering a heart attack earlier this year. While hospitalized, Rothman wore a pulsating device around his calves that was developed through NASA research on muscle atrophy. Once discharged, he was fitted with a defibrillator vest designed to deliver electric shock if he experienced another cardiac event. The defibrillator and the subsequent bi-ventricular implant Rothman received also typify NASA's relationship with the private sector. Through its Commercial Technology Program, the agency continues to support advances in private research that, in turn, benefit the space program. Sustained cooperation in the areas of telemedicine and medical informatics remains a NASA priority.¹

COUNTERMEASURE TO MUSCLE ATROPHY

After suffering a heart attack on January 16, 2008, UH professor Irving Rothman, editor of the ISSO *Annual Report* since 1992, awoke in the intensive care unit of a local hospital with his calves encased in cloth sheaths that inflated and pulsated every 60 seconds. He soon realized that he had displaced the white rat in the laboratory as the beneficiary of NASA research conducted at the University of Houston. The device wrapped around each of his calves was intended to prevent muscle atrophy and life-threatening blood clots from forming in Rothman's legs while he was bedridden. It is now widely used in hospitals and nursing homes on immobilized patients and diabetics at risk of losing limbs.

In 2001, the University of Houston Institute for Space Systems Operations (ISSO) published the findings of a research team led by UH professor Charles S. Layne and NASA co-PI Daniel L. Feedback, who had conducted studies utilizing dynamic foot pressure to mitigate and reverse muscle atrophy.² The Layne-Feedback research team sought to solve a problem that had been recognized in the planning and implementation of the International Space Station. Long-term missions and extended stay in space meant that astronauts could suffer loss of muscle mass and strength without passive exercise in the resistant forces of gravity. Astronauts must maintain their physical fitness and health, "particularly if the exploration of Mars is to be pursued," the researchers wrote. "Weightlessness," they explained, "has been shown to cause a decrease in muscle volume, mass and strength, alterations in fiber type and myosin heavy chain (MHC) expression as well as a decrease in neuromuscular function and muscle capillarity."³ In fact, after long space missions, astronauts experienced difficulty walking when they departed from their landing craft. Thus, investigators sought to resolve the problem of micro-



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gravity-induced atrophy particularly affecting the specific anti-gravity muscles of the lower limbs.⁴

Photographs of their research show experiments upon white rats with their legs held in hindlimb suspension (HLS). This methodology employed a "widely used model of microgravity-induced skeletal-muscle (SKM) atrophy," the researchers wrote. Investigators would suspend a rat's legs, which were outfitted with inflatable latex bladders, at a 25-degree angle. They then stimulated the suspended limbs by inflating and deflating the bladders over a 14-day period.⁵ The rat's musculature sustained form and strength while the limbs remained immobile. This inflatable bladder device was the precursor of the

apparatus now used on bedridden hospital patients, including Rothman during his inpatient cardiac care in the Intensive Care Unit (ICU) at Methodist Hospital in Houston. Houston orthopedic surgeon Howard Z. Finkel reminds that an extremely important purpose of inflatable bladders is the prevention of blood clots in the legs which can flow to the heart resulting in pulmonary embolisms.

WEARABLE DEFIBRILLATOR

When Rothman was discharged from the hospital, he was outfitted with a LifeVest System[®], Model WCB 3100, cited by its manufacturers as "the first wearable defibrillator." The device is registered, with patents owned by the ZOLL Lifecor Corp. of Pittsburgh, Pennsylvania.⁶ The LifeVest was designed to monitor the heartbeat of the wearer and to deliver electric shock in the case of life-threatening arrhythmia. If conscious, the wearer could prevent the shock by manually disarming the LifeVest. If unconscious, targeted shock would restore normal heart rhythm.

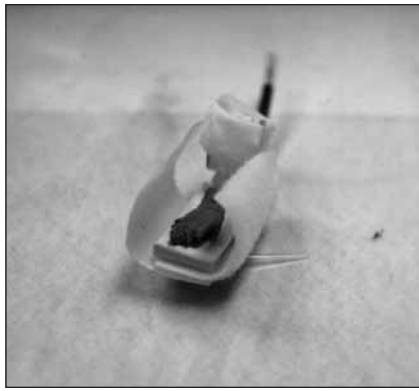
Paul Zoll, Harvard Medical School, introduced the first commercial, external, AC-powered cardiac pacemaker in

1956. It was manufactured by the Electrodyne Corp. (U.S. Patent 100800-33495) and described as “an external defibrillator having a battery; a capacitor electrically communicable with the battery; at least two electrodes electrically communicable with the capacitor and with the skin of a patient; a controller configured to charge the capacitor from the battery and to discharge the capacitor through the electrodes; and a belt supporting the battery, capacitor, electrodes and controller in a deployment configuration, the defibrillator having a maximum weight per unit area in the deployment configuration of 0.1 lb/in² and/or a maximum thickness of 1 inch. The support may be a waterproof housing.”⁷

In fact, the device worn by Rothman had four electrodes to monitor heart rhythm and three therapy pads. Were he to have suffered an arrhythmia, the system would have first laid a gel to protect the skin and then administered the shock. And while Rothman experienced no alarms indicating a cardiac event during the 53 days that he wore the vest, the displacement of the electrodes caused by normal body movement did sound low-level alarms. As it happened, Rothman never lost consciousness during this period and would have been able to prevent any shock simply by pressing buttons on the battery-powered monitor.

These procedures had been investigated by NASA researchers five years earlier. Jonathan B. Clark and James S. Logan, both M.D.s, engaged in a NASA physiologic monitor experiment in 2003 designed “to test wireless medical monitoring devices and their accompanying procedures in a metal-walled habitat similar to the International Space Station (ISS).”⁸ Their testing methodology was routine: “During the experiment, crewmembers wore devices, which consisted of electrode leads attached to wireless transmitting devices, to record activity and respiration while inside the habitat.” Furthermore, Clark and Logan summarized, “these devices were tested in two different scenarios: exercise and simulated injured crewmember.” NASA investigators sought to match conventional scales on traditional EKG machines. The final unpublished conclusions were that the device did not work as effectively as it might have because the sensors were attached to “the same plastic strip.”⁹

It is significant that the ZOLL LifeCor vest had each of the electrodes separately affixed to the vest with individual Velcro patches, though linked with a single electric wire attached to the sensors. There seemed to be no way prevent individual



INFLATABLE RAT BOOT—Charles Layne and Daniel Feeback measured pressure exerted on the muscles in a rat’s foot by inserting the foot in an inflatable boot. The inflatable boot consisted of a thin base made from an extremely light yet durable metal sheer with an inflatable/deflatable latex bladder adjusted on it. Velcro restraint straps secured the boot to the sole of the foot of the dominant leg during rat hindlimb suspension. The bladder was connected to an air pump by a single air/vacuum line. Pump cycling time and duration were controlled by a microprocessor.



LIFEVEST SYSTEM—The LifeVest is the first personal defibrillator worn outside the body rather than implanted in the chest. The non-invasive device continuously monitors the patient’s heart to detect life-threatening abnormal heart rhythms. If a life-threatening rhythm is detected and the patient is unconscious, the device delivers an electrical shock to restore normal rhythm.

sensors from turning from the chest as a consequence of bodily movement; the problem in each instance was immediately acknowledged by low bell tones sounded from the monitor worn at the side of the vest. Electrodes were easily repositioned after a low tone had sounded, but the problem noted by Clark and Logan remains an issue of ergonomic design.

IMPLANTABLE DEFIBRILLATOR (ICD)

Interventional cardiologist Frank Rickman of Houston Cardiovascular Associates treated Rothman following his heart attack, which caused damage to the left anterior descending artery (LAD), by clearing the aorta and inserting two stents. The procedure was a success, and Rothman returned home, but Rickman and his associate, electrophysiologist Thomas Hong, continued to monitor their patient through reports transmitted by the LifeVest. Rickman and Hong concluded that Rothman’s heart was pumping blood at an ejection rate of only 33 percent, compared to a normal rate of 55 percent. Consequently, they adjudged the need for cardiac resynchronization therapy (CRT).

This methodology allows for a device implanted in the chest to resynchronize the contractions of the ventricles of the heart by transmitting “tiny electrical impulses to the heart muscle.” This helps the heart pump blood and provide oxygen throughout the body. According to Medtronic, Inc., “CRT defibrillators (CRT-D) also incorporate additional lifesaving therapy to quickly terminate an abnormally fast, life threatening heart rhythm.”¹⁰ Rickman, who had inserted two stents in Rothman’s aorta after his initial attack and cleared other vessels of blockage, consulted with Hong on the viability of an internal monitoring system. Some people with too severe heart damage cannot be candidates for the defibrillator. Rothman was, fortunately, determined to be at a stage where the implant was advisable. Far beyond the capacity of the early pacemaker, the biventricular implant is the latest technology to restore health and normal routine to the life of a cardiac patient. The viability and advantages of the defibrillator and implant procedure have been supported by Robert C. Stoler, interventional cardiologist, Cardiology Consultants of Texas, Dallas, Texas.

The CRT-D has been available to implant patients since March 20, 2007, when Medtronic, Inc. announced “the first clinical implants in the United States of the Medtronic Attain Ability™ over-the-wire lead (Model 4196), a dual-electrode left ventricular (LV) lead for use in heart failure patients with

cardiac resynchronization therapy devices.”¹¹ What is noteworthy for this report is the fact that Medtronic licensed “a unique insulation material” for its Attain Ability lead from NASA. The dual-electrode lead is inserted into the left ventricle—a challenging anatomic task for the electrophysiologist who has to “deliver the left heart lead in difficult to access veins.”¹² The design of the lead enables the device to stimulate the left ventricle when needed.

A key NASA study in 2007, NASA NCC 9-58, focused upon cardiac resynchronization therapy, proving that implantation of the CRT defibrillator as “a point-merge approach...is reliable, accurate and fast.”¹³ NASA methodology added a tool of measurement “not currently available in cardiac imaging modalities...useful to enable positioning a pacing lead to the optimal implantation site.”¹⁴ The technology involved more accurate positioning of the LV lead through coronary vein multiple-slice tomography (MST) and tissue synchronization imaging (TSI).

Indeed, the NASA technology has proved “very effective for visual assessment of left ventricular mechanical dyssynchrony.”¹⁵ Researchers tell us that “dyssynchronous myocardial contraction is a chronic condition of the heart that is a predictor of adverse cardiac events...associated with a poor prognosis.”¹⁶ Resynchronization, therefore, is the critical therapy, requiring that the CRT-D implant, as well as the additional lead, intravenously be placed within the left ventricle, a procedure demanding the impeccable precision enabled by advanced technology.

Advanced implantable pacemakers and defibrillators have been a NASA priority since 1970, when the agency began development of an automatic implantable cardioverter defibrillator (AICD) to combat sudden cardiac death. Over the course of two decades, the Goddard Space Flight Center has led in the development of the device, which received FDA approval and was subsequently manufactured by Cardiac Pacemakers, Inc., a subsidiary of Eli Lilly and Company.

Two private companies, Intec Systems and Medrad, Inc., both of Pittsburgh, Pennsylvania, received NASA funding through researchers at Baltimore’s Sinai Hospital to produce the early defibrillators. In 1976, the first AICD was tested on a dog. By 1980, cardiologists at Johns Hopkins University had successfully performed the first implant in a human, and in 1985 Intec Systems was purchased by Eli Lilly.

The AICD is but one example of the interplay between the public and private sector characteristic of NASA research. The device developed by Intec Systems and Medrad and marketed by Cardiac Pacemakers benefited from NASA’s need for miniaturized components and medical equipment to serve astronauts in space. Indeed, the defibrillator proved capable of detecting and resolving arrhythmias in astronauts.¹⁷ But the medical community—and the patients it serves—also benefited from advancements in implantable wireless devices capable of saving lives and improving quality of life.

It has been estimated that, at one time, 80 percent of those suffering cardiac arrest died before help could arrive, and those who recovered initially faced mortality within two years. The AICD predictably reduced the incidence of mortality in that time frame to less than 3 percent.¹⁸ “The implantable car-

diac defibrillator is like having an emergency room implanted in your chest,” says Douglas Zipes, chief of cardiology at Indiana University School of Medicine.¹⁹ Zipes was responsible for the scientific conduct of a NASA-funded study comparing anti-arrhythmic drug treatment to cardiac therapy using the AICD. In that study, the defibrillator saved so many more lives that testing was halted, citing needless risk to patients in the drug treatment portion of the research.²⁰

PATIENT MANAGEMENT SYSTEM

In the past, cardiology patients were required to visit their physician’s office periodically to have their pacemakers checked by an electrophysiologist. Today, the patient may sit at home while records of his or her physiological performance and heart activity are transmitted to the physician in the medical center. This remote data delivery system was developed by Boston Scientific Corp. and approved by the FDA in November 2006.

The LATITUDE[®] Patient Management System was at the time the singular remote patient monitoring system capable of providing clinicians with direct device data integration into GE Healthcare’s Centricity Electronic Medical Record (EMR).²¹ The Latitude system, designed and manufactured by Guidant Corp., includes a digital blood pressure monitor (A&D Medical UA-767 Plus BT) and a precision weight scale (A&D UC321 PB2), which transmit data along with the implanted pacemaker and defibrillator to a communicator, i.e., a monitor. The communicator is programmed to allow the physician’s office to receive data from the patient’s home at scheduled intervals. Thus, the patient’s blood pressure and pulse rate, weight, pacemaker, and defibrillator activity are under regular surveillance.

NASA’s need to monitor the human body in space has been an important factor in the development of exterior and distance monitoring devices. As recently as 2004, NASA sought SBIR proposals for development of compact, wireless biometric monitoring devices and a real-time processing system for future flight crews. The Request for Proposals also sought research and development of non-invasive, unobtrusive medical devices. In 2005, research teams at the NASA Glenn Research Center engaged with researchers from Case Western University and the University of Akron (Ohio) in the development of an arrhythmia monitoring system designed to collect real-time electrocardiogram signals from a homebound patient or a patient in transit. Signals are relayed via GPS to a remote station, where they can be displayed on a computer screen and analyzed by electrophysiologists.²²

CONCLUSION

That NASA research is of great benefit to modern medical technology is readily demonstrable. But more is true. Indeed, a genuine symbiosis exists between the space agency and the private sector. In 2005, for example, three members of Guidant’s Design for Reliability Team served as system safety experts examining the space shuttle program. Considered a “pioneer” in life-saving cardiac and vascular technology,²³

Guidant was purchased in April 2006 by Boston Scientific.

The beneficiary of decades of medical research and development, ISSO's Rothman received his biventricular implant on March 12, 2008. The implant device, a CRT-D, was manufactured by Boston Scientific. Shortly thereafter, Rothman entered and successfully completed a strengthening program for cardiac patients at the Cardiovascular Rehabilitation Center of Methodist Hospital under the supervision of Ala Pourmahram. He is expected to return to university teaching and normal life.

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