



VA Research Currents

New limb-loss center to incorporate robotics, tissue engineering

VA's Rehabilitation Research and Development Service has awarded \$4.7 million over five years to researchers at the VA medical center in Providence, R.I., to develop state-of-the-art care for veteran amputees, in collaboration with Brown Medical School and the Massachusetts Institute of Technology.

The new "Center for Rebuilding, Regenerating and Restoring Function After Limb Loss" will provide patient care and conduct research in tissue engineering, neurotechnology, materials science, robotics, and advanced surgical techniques. VA expects the center to significantly improve outcomes for recent combat-injured veterans and other VA patients who have lost limbs.

The initiative comes as the U.S. military has seen a sharp increase in the number of combat-related amputees. Due to advances in body armor and battlefield first aid, many soldiers who would otherwise have been killed in action are surviving, albeit with severe injury to their extremities.

Researchers at the center, led by orthopedic surgeon Roy Aaron, MD, will advance the concept of a "biohybrid" limb: an intricate meshing of restored and enhanced biological tissues—skin, bone, nerves, cartilage—with high-tech prosthetic components. The goal is to provide the amputee with a limb that functions as naturally as possible. Scientists with the program

are even working on harnessing brain signals to directly control robotic limbs.

Much of the early work at the center will apply mainly to traumatic amputees. Veterans from around the country who are medically eligible will be accepted for treatment. But

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Update from Biomedical Laboratory Research and Development

BLR&D—the old and the new

By Timothy O'Leary, MD, PhD, director

Biomedical laboratory research is the cornerstone on which virtually all significant advances in medical practice are based. New surgical procedures are developed in animal models and, increasingly, in virtual reality simulation systems.

The pace at which fundamental understanding of disease pathogenesis leads to more effective treatment can be very fast indeed. Effective treatments for chronic myeloid leukemia and gastrointestinal stromal tumor (GIST) have quickly resulted from understanding BCR/ABL gene fusion and the importance of KIT mutations respectively. The first paper describing the importance of KIT mutation in GIST was published on Jan. 23, 1998. Just four years later, on Feb. 1, 2002, the Food and Drug Administration approved Gleevec®, a drug that inhibits the tyrosine kinase activity of the KIT protein, as treatment for this frequently unresectable and often fatal tumor. The

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First FRAC meeting held

VA's Field Research Advisory Committee (FRAC) held its inaugural meeting July 9 in Washington, DC. The nine-member group, elected by their VA peers, received updates from Office of Research and Development (ORD) leaders and offered input on a wide range of issues affecting investigators and research administrators.

Stephan Fihn, MD, MPH, acting chief research and development officer (CRADO), opened the meeting by outlining his goals for the months ahead. He said he would work to resolve pending issues and problems within ORD, complete the reorganization begun last fall, and help make the job of CRADO attractive to high-caliber candidates. Fihn cited the high level of collegiality and cooperation among the service directors.

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package insert for Gleevec® emphasizes the importance of a tissue-based laboratory test in achieving accurate diagnosis of the tumor itself.

The pace at which understanding led to new treatment was in this case very fast. Nevertheless, it serves as an important example of the fact that developing fundamental understandings of disease pathogenesis may be expected to lead to new diagnostic tests, less toxic treatments, and better lives for our patients. Laboratory research is as much the bedrock for VA research as it is for the international medical research enterprise.

We are challenged, however, to find more reliable ways to assure that the results of our pre-clinical research programs are effectively translated into better care for our veterans. There is no simple “roadmap” to assure that each investigation we undertake will have an identifiable clinical impact.

Just as winning the Tour de France requires support from a team of exceptional cyclists, developing a new drug or laboratory diagnostic requires support from teams of researchers that have investigated related problems and shared their insights through meetings and publications. It usually requires partnering (with appropriate attention to ethical issues) with scientists and

engineers from the drug and diagnostics communities, who are better organized to bring a product to clinical use than are government and academia. It often requires patenting an important idea to provide the market incentives necessary to justify the risk of product development. Within the VA, it also requires effectively informing both the scientific community and the public at large of why and how our laboratory research can help the veteran population we are called on to serve.

Linking lab, clinical research

Translating our research into practice is not a new mission, but rather an old mission to which we need to pay increasing attention. The Merit Review program, and thus the creativity and efforts of the broad VA research community, remains the basis on which the VA’s biomedical research program will be built. In an era of diminishing resources, however, we must recognize that effective competition for NIH grants and effective cooperation with industry are also required for a robust research program.

As the new person on the block (and as a clinician scientist), I am committed to working with the both the VA research community and the broader clinical community to help strengthen this already impressive program of veteran-centered research. Dr. Brian Schuster, the new director of Clinical Science Research and Development, shares my commitment to laboratory research as I share his commitment to clinical research. We believe that working together with the Field Research Advisory Committee, Veterans Health Administration leadership and patient care services, and the research community we can help create an environment in which the glory days for VA research are in our future. ■

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research at the center could eventually benefit a much wider population of veterans and other Americans with both upper- and lower-limb loss.

In one program at the center, VA and Brown orthopedic surgeons will perform a procedure known as the Ilizarov technique to lengthen the residual limb of above-knee or above-elbow amputees. The method so far has been used mostly on children with deformed limbs. It involves slightly separating the bone in the residual limb and implanting wires through the bone. The wires are connected to a rigid external frame. The separated bone begins to naturally fuse together. However, at home the patient adjusts the frame at prescribed intervals to move the wires and separate the bone anew. Over time, this cycle of separation and healing lengthens the bone. Along with this, the VA-Brown team will explore ways to implant an “endoprosthesis”—similar to a joint replacement—to restore the knee or elbow’s function.

Researchers believe these surgical methods, combined with other therapies, may eventually enable doctors to transform an above-knee amputee into a below-knee amputee, or an above-elbow amputee into a below-elbow amputee, reducing complications and enabling greater mobility and control once a prosthesis is fitted.

Other teams at the center will explore tissue-engineering techniques to further restore the residual limb—such as cell transfer, encapsulated drug delivery and gene therapy. Another group will study osseointegration, a technique developed in Sweden wherein prosthetic components are affixed to specially implanted titanium bolts that integrate with the bone of the residual limb.

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Study: VA tops managed health plans for recommended diabetes care

Nearly a decade after VA instituted broad improvements in how it care for patients with chronic illnesses, a study published in the Aug. 17 *Annals of Internal Medicine* shows that VA patients with diabetes are more likely to receive recommended tests and have better outcomes than managed care patients.

The study included 1,285 patients with diabetes from five VA medical centers nationwide and 6,920 patients in eight commercial managed-care health plans, ranked among the nation's best in diabetes care by the National Committee on Quality Assurance. The researchers checked whether patients received seven standard recommended tests or services: eye exam, hemoglobin A1c test (a measure of glucose control), cholesterol screening, foot exam, urine analysis, counseling on aspirin use, and flu vaccine. They also looked at patients' blood pressure, cholesterol and blood sugar, or hemoglobin A1c. The information had been collected as part of the Translating Research into Action for Diabetes initiative of VA and the Centers of Disease Control and Prevention (CDCP).

The VA patients were more likely to receive each of the screening measures or preventive services. For example:

- 93 percent of VA patients had an annual hemoglobin A1c test, compared to 83 percent of managed care patients.
- 91 percent of VA patients had an annual eye exam, versus 75 percent of managed care patients.
- 98 percent of VA patients had an annual foot exam, versus 84 percent of managed care patients.

VA patients also had their hemoglobin A1c and LDL cholesterol levels in better check. Blood pressure control was comparable for both sets of patients.

“A nationally funded health care system can provide excellent quality of care,” said lead author Eve Kerr, MD, MPH, a research scientist at the VA Ann Arbor Healthcare System and assistant professor of internal medicine at the University of Michigan Medical School. “The VA has instituted system-wide standards, integrated care, and a way to track and monitor how their

patients are doing. Other organizations can learn from the VA and how they achieved their quality improvements over the last 10 years.”

Beginning in 1995, VA instituted a series of quality improvements focused on managing chronic diseases, including diabetes. The changes included performance monitoring, computerization of medical records, disease management programs, patient reminders, and automated feedback to doctors on quality of care. The study authors suggest that VA's national system makes it easier to implement sweeping changes and track the results.

Collaborating on the study were researchers from Northern California Kaiser Permanente, Pacific Health Research Institute, Indiana University School of Medicine, University of Medicine and Dentistry of New Jersey, and the CDCP. Funding was provided by VA, the CDCP, and the National Institute on Diabetes, Digestive and Kidney Diseases. ■

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Some amputee patients at the center will be fitted with myoelectric component developed by bioengineer Hugh Herr, PhD, at MIT. These knee and ankle systems will rely on tiny sensors called BIONs (bionic neurons), developed by the Alfred Mann Foundation in California. These sensors, implanted in the residual limb, will read electrical signals from the patient's muscle and feed the information to an “onboard” microprocessor in the prosthetic device. As a result, the device will respond to the amputee's intent.

Further developing the concept of linking prosthesis and nervous system, a Brown-VA group led by neuroscientist John Donoghue, PhD, will seek to use mathematical algorithms to translate the brain's complex electrical impulses into signals that can control prosthetic limbs. In earlier studies with monkeys, Donoghue has shown that output from the brain can be used to control computer cursors almost as effectively as a natural hand. The work promises to benefit amputees as well as those with spinal cord injury or other conditions involving paralysis. ■

Diabetes Care supplement

VA diabetes researchers documented VA's successes—and areas needing improvement—in a supplement to the May 2004 issue of *Diabetes Care*. The Seattle VA Epidemiologic Research and Information Center (ERIC) edited the supplement, which includes 16 articles. One study, for example, found that VA patients received an equal or higher level of preventive care compared to non-veterans or veterans receiving non-VA care.

The supplement is online at http://care.diabetesjournals.org/content/vol27/suppl_2/.

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Next was an update from acting Undersecretary for Health Jonathan Perlin, MD, PhD, MSHA, who sketched a timeline for the recruitment of a new CRADO—not likely to begin until late 2004—and emphasized that all branches of VA research must mesh their efforts to support VA health care and “improve the health and welfare of veterans.”

In reviewing some of its operating procedures, the FRAC voted to change the minimum initial term of members from one to two years. Members then discussed the appropriateness of having the CRADO—a representative of Central Office—chair the FRAC, a field-based group. The group agreed that the CRADO brings to the role a unique and much-needed overview of timely and critical issues affecting VA research. The members also acknowledged that ORD now appears considerably more open to field input than in the past.

John Bradley, ORD’s director of finance, updated the group on key budget and finance issues. He was

followed by Timothy O’Leary, MD, PhD, and Brian Schuster, MD, directors of Biomedical Laboratory R&D and Clinical Science R&D, respectively, who offered a joint overview of their services, in keeping with their collaborative approach to managing the programs. They stressed that biomedical and clinical research are linked on the continuum of medical research, and said any research funded by their services must be strongly relevant to veterans’ health care. They said plans are being considered to conduct an overall assessment of clinical and biomedical research in VA—with input from the FRAC and experts outside VA, among other sources—to determine if resources can be used more effectively. Questions and comments from FRAC members centered on issues such as Merit Review and the Career Development program.

Robert Ruff, MD, acting director of Rehabilitation R&D, and Shirley Meehan, PhD, acting director of Health Services R&D, covered new initiatives, past accomplishments and current trends in their respective services. Their presentations were followed by

an overview of key issues in peer review by Joe Gough, acting director of administration, and Leroy Frey, MD, director of Program Review. Among other points, they informed the FRAC that productivity scoring—assigning separate scores to proposals based on investigators’ publishing track record—has been discontinued.

FRAC members discussed several points relating to peer review. Fihn said he expects the continuing reorganization in ORD to help make the process more efficient and responsive.

Regarding communication between ORD and the field, FRAC members suggested that the various websites associated with VA research be more effectively consolidated, and that Central Office take better advantage of e-mail to convey important information to the field.

The next FRAC meeting is set for Sept. 2004.

For a complete listing of FRAC members, see the June 2004 VA *Research Currents* in the Publications section of the VA research website: www.va.gov/resdev. ■

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