


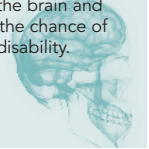


By JANET RAE BROOKS
Photos by SEAN GRAFF

Real-Time DRAMA

New Treatments for Old Diseases at the Clinical Neurosciences Center

12:00 p.m.	12:05 p.m.	12:35 p.m.	12:55 p.m.	1:15 p.m.	1:30 p.m.
<p>Eating lunch at his kitchen table, a farmer in southern Utah suddenly finds his speech slurred and his left arm numb.</p> 	<p>His wife insists on driving him into town to the Beaver Valley Hospital.</p> 	<p>The doctor on duty examines him, then immediately requests a telemedicine consultation with a stroke specialist at the University of Utah's Clinical Neurosciences Center in Salt Lake City.</p>	<p>Using a two-way video and audio link, a U of U neurologist examines the patient, reviews his brain scan, and confirms the stroke diagnosis.</p> 	<p>The patient is started on an intravenous clot-busting drug—it must be given within three hours of the first stroke—to restore blood flow in the brain and reduce the chance of lasting disability.</p> 	<p>AirMed is dispatched to Beaver. The patient is flown to University Hospital's Stroke Center, where he's met by a specially trained "brain-attack" team: emergency physicians, neurologists, neurosurgeons, and radiologists ready 24/7 to provide further treatment.</p>

It's a dramatic scene—the kind played out with precision and compassion at the new University of Utah Clinical Neurosciences Center (CNC). Unparalleled advances in our understanding of the brain and its diseases have transformed clinical care not only for stroke, but other conditions, such as brain tumors and Parkinson's disease, as well. "We can do so much for stroke patients in the first 24 hours," said Stefan-M. Pulst, M.D., Dr. Med., professor and chair of the Department of Neurology at the University of Utah School of Medicine. "Fifty years ago, we could do very little. That we can—and have to—respond quickly has changed the face of neurology."

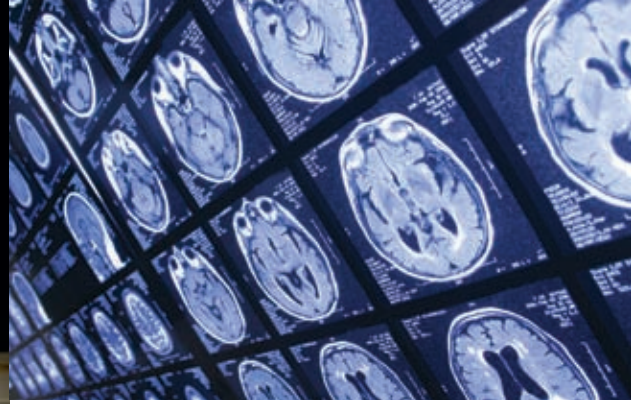
At the forefront of new treatments for old diseases in the Intermountain West is the University's CNC, which for the first time unites the School of Medicine's departments of Neurology and Neurosurgery, and Division of Neuroradiology. The five-story building—which houses collaborative outpatient clinics, 42 exam rooms, four neurosurgical operating rooms and recovery room, research laboratories, Stroke Center, and telehealth unit—is connected by walkways to University of Utah Hospital and Huntsman Cancer Hospital. Also affiliated with the CNC are the largest pediatric neurosurgery service in North America, which operates at nearby Primary Children's Medical Center, and additional imaging facilities and clinics on the U campus and in the community.

Since opening in May 2008, the CNC already has earned national kudos. The Stroke Center and University Hospital recently received the top designation in the American Stroke Association's "Get with the Guidelines" program: one of only two hospitals in the western United States to earn the award. In February, the CNC was named a national Neurosciences Center of Excellence by health-care organizations NeuroSource and HealthTech. The designation recognizes the center's "commitment to technology and early adoption of treatment techniques," and its success in translating research into new treatments.

Soon the U of U center, which draws patients from throughout Utah and five surrounding states, will become one of a dozen hospitals in the world with an intra-operative magnetic resonance imaging machine (MRI) that can be rolled into the operating room on tracks for mid-surgery imaging.



Stefan-M. Pulst, M.D., Dr. Med.



“We can do so much for stroke patients in the first 24 hours.”

“Time Is Brain”

If administered within hours of a stroke, new thrombolytic drugs can dissolve clots and reopen blocked blood vessels in the brain. “We’ve had some dramatic recoveries,” said William Couldwell, M.D., Ph.D., chair of the Department of Neurosurgery, who likened the new drugs to “Draino.” For patients whose blockages persist, the Stroke Center’s brain-attack team can turn to other options. Interventional radiologists, guided by computed tomography (CT) or MRI scans, can insert a tiny catheter into blocked arteries to infuse the clot-busting drug directly at the clot site. Up to eight hours post-stroke, they also can extract clots intra-arterially with special mechanical devices. A catheter retriever, or MERCI (mechanical embolus removal in cerebral ischemia), is inserted just beyond the blockage; the clot is then ensnared with the coiled tip and withdrawn. Penumbra, another new device in use just a few months, pulls the clot

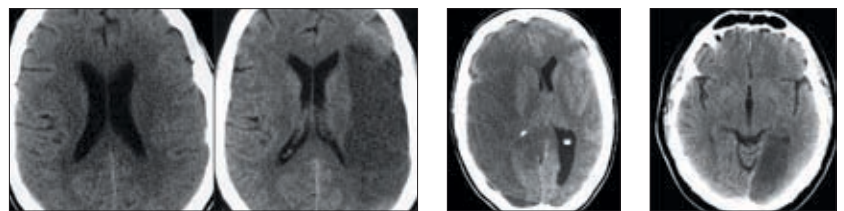
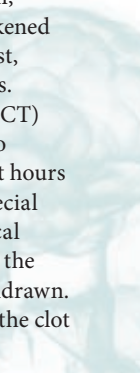
back with suction pressure. If either device is ineffective by itself, they can be used together.

“I’m amazed at what we can do with this new technology,” said Edwin A. “Steve” Stevens, M.D., professor and chair of the Department of Radiology. “Thirty years ago, we didn’t have any digital high-resolution imaging capabilities, roadmapping technique, or microcatheters. And the use of mechanical blood clot extraction devices has only recently been possible. Most of the time, we can open the blood vessel.”

Stroke Center director Elaine Skalabrin, M.D., was drawn to the U in 2000 by the opportunity to build a comprehensive stroke care program. “I saw it was a new era,” said Skalabrin, assistant professor of neurology and director of Neurosciences Critical Care.

Her first year, Skalabrin, along with her colleagues, established evidence-based treatment protocols, created quality assurance systems, and developed partners, within and outside the medical school, including the American Stroke Association. Her next step was education. “I think the second year I was here, I did 40-some lectures,” said the neurologist who has worked tirelessly to educate Utahns and local first-responders to treat stroke as an emergency. “Time is brain” is her mantra: speedy restoration of blood flow to the brain means fewer dead brain cells. In 2004, she launched the annual Utah State Stroke Symposium, bringing together doctors, nurses, hospital administrators, and others involved with stroke care. Her dedication has paid off: more stroke victims in the Intermountain West are reaching hospitals in time to take thrombolytics.

Skalabrin also has championed the accessibility of stroke specialists to rural residents, teaming with the Utah Telehealth Network in 2004 to set up the Telestroke Program. The U’s stroke specialists serve six hospitals throughout the region. Along with



Stroke at 2 hours and at 48 hours in the left MCA

CT Acute Stroke

CT Subacute Stroke

Elaine Skalabrin, M.D.



William Couldwell, M.D., Ph.D.

other neurologists on the brain-attack team, Skalabrin has installed a telestroke camera in her home. “It saves time. I live 35 minutes from the hospital. Brain tissue dies quickly,” she added.

The Stroke Center is participating in two large multi-center stroke trials: one examining genetic predisposition by analyzing the blood of siblings with stroke; the other looking at insulin resistance in stroke, now recognized as a cause of atherosclerosis. Also under investigation is a promising new neuroprotective drug that might help prevent damage or death of brain cells until blood flow is restored.

Better Resection, Better Survival

Brain tumors are another old neurological disease with compelling new treatments. Non-invasive CT scanning and MRI play a central role in the initial diagnosis. Most tumors are removed with

intra-operative computer navigational systems, which allow for minimally invasive surgery. Tumor coordinates are input into the navigational system like GPS coordinates. This new precision allows neurosurgeons to make small linear incisions, instead of the large U-shaped cuts formerly used. “We know the tumor isn’t going to be off more than a millimeter or two in either direction,” said Randy Jensen, M.D., Ph.D., associate professor of neurosurgery and member of the brain tumor research team at the University’s Huntsman Cancer Institute.

Patients with brain tumors undergo functional MRIs before surgery. “By doing that, we can identify and stay away from areas of the brain that control critical functions, such as language or movement, which could have a significant impact on patients,” explained radiologist Stevens, who holds an H.A. and Edna Benning Presidential Endowed Chair in the medical school.

Soon U neurosurgeons will be using a \$6 million MRI machine in the operating room. “With the intra-operative MRI, we can literally just snap a picture, put it into the intra-operative computer guidance system, and use that to precisely remove the residual tumor, while sparing other tissue,” said Jensen. When tumors are excised, the brain tends to relax into the cavity created, sometimes making it difficult for surgeons to identify tumor margins.

Richard Lemons, M.D., Ph.D., chief of pediatric oncology at the School of Medicine and medical director for Pediatric Hematology-Oncology-Bone Marrow Transplant at nearby Primary Children’s Medical Center, summed up the advantage: “The better the resection, the better the survival, in general.”

An important alternative to surgery, especially for tumors located in deep recesses of the brain or close to vital areas, is stereotactic radiosurgery. The tumor’s location is pinpointed three-dimensionally with imaging, and a computer-aided treatment plan is drawn up to match the tumor. Then, with the patient’s head locked in a helmet-like frame, a linear accelerator delivers radiation to the tumor from different angles as its robotic arm rotates around the patient. Not only does stereotactic radiosurgery spare surrounding healthy tissue, but the outpatient procedure also can be repeated, unlike conventional brain tumor radiation.

Neuro Nursing’s Specialty Care

In the room where a 63-year-old woman recovers from a debilitating stroke, the lights are dimmed and the blinds closed, and everyone speaks in a gentle, soothing tone, per her nurse’s instructions.

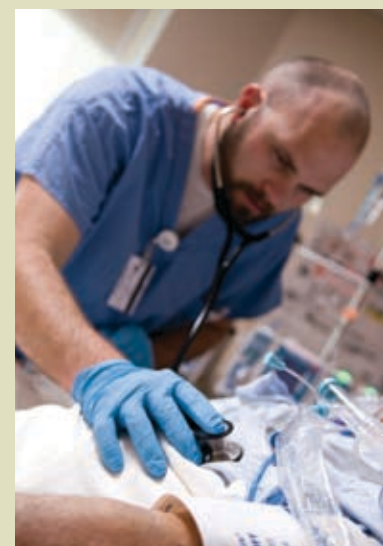
Diana Arensman, R.N., a Neuro Critical Care (NCC) nurse at University of Utah Hospital, always keeps her patients’ unique needs at the top of mind. Some patients are recuperating from strokes; others, from brain injuries, and a few, from surgery for brain tumors. “It’s a lot of pressure,” she said of working in the NCC unit, “but this is a specialty that gets to your heart. Through intense training and experience, the challenges eventually become rewarding, and that’s something that stays with you.”

Before neuro critical care nurses begin work on the U Hospital unit, they complete six to eight weeks of specialized training beyond their basic education. They also are required to have neuro experience before joining the critical care team. If asked how to define their profession, however, NCC nurses are likely to say it’s the care and attentiveness they provide to each individual: learning to understand emotional cues and facial expressions, and creatively communicating with patients who may not be able to speak.

“Sometimes a neuro critical care nurse will spend six or more hours at a time in one room,” said Bruce Garrett, R.N., B.S.N., a veteran NCC nurse. “It’s a whole different level of care. It takes a great deal of knowledge and a lot of critical thinking.”

That knowledge can include the proper way to move patients with spinal or brain injuries—or, in some cases, knowing when not to move them. The nurses often double as teachers, educating patients and their loved ones on the complexity of a severe head trauma or neurological disorder. They also are highly skilled at comfort care: phrases such as “You can trust me” and “We’re in this together” are heard frequently throughout the unit.

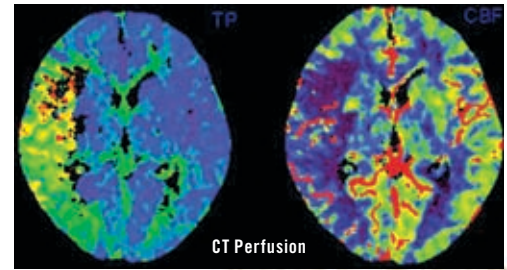
After serving 19 years in various capacities at University Hospital, Arensman believes critical neuro nursing at the bedside is where she belongs. “Every day is different, and I always have to be alert and aware of each patient and how their condition can change so quickly,” she noted. “But of all the things I’ve done professionally in my life, this is by far the best...” —*Ryann Rasmussen*



Luke Hemphill, R.N.



Edwin A. "Steve" Stevens, M.D.



During a stroke when one or more blood vessels supplying the brain are occluded, contrast material injected through an IV does not arrive in the brain in a timely manner. The scan at left shows increased transit time of blood flow until the peak effect of contrast is reached. At right, the scan shows decreased flow through an area of the brain supplied by the right middle cerebral artery, which causes paralysis of the left half of the body.

“Now we can reach virtually any blood vessel in the brain. Most of the time, we can open the blood vessel.”

New methods to directly deliver chemotherapy, including mini-pumps implanted in and around tumors, are being evaluated in trials. Pumps also could be used for other conditions, such as stroke and Parkinson's, to deliver drugs too toxic to take orally. Pumps could even be implanted under the scalp and left in for days or weeks. “Theoretically, they could be permanent,” said Couldwell.

At the CNC, Jensen offers patients a number of novel clinical trials for treatment of malignant brain tumors, including an immune vaccine, given weekly while patients are receiving radiation and chemotherapy. His lab is investigating how tumor cells are affected by hypoxia and how they communicate to create their own blood vessels, which might lead to the development of interventions to stunt their growth. The genetic pathways leading to brain tumors is another area of investigation. Eventually, a drug could be designed to suppress functioning of the pathway.

Stimulating Alternative

For Parkinson's patients who can't rely on medication to control their symptoms, a new surgical technique—deep brain stimulation—has emerged as an effective option. Previously, lesional surgeries in deep parts of the brain were the mainstay of treatment for Parkinson's. In the late 1960s, levodopa, the precursor of the neurotransmitter dopamine, was introduced as a replacement transmitter. Since 1997, some 30,000 stimulators have been implanted into 5-10 percent of Parkinson's patients in the United States.

“The minority of patients who can't be controlled with medication, or can't handle the side effects, are candidates for deep brain stimulation,” said Couldwell, who noted that “medication can become less effective over time.”

Approved by the U.S. Food and Drug Administration (FDA) in 2002, deep brain stimulators emit high-frequency electrical pulses that physiologically jam the abnormal electrical signals causing Parkinson's symptoms. Stimulator output can be adjusted

to produce remarkable results in some patients: tremors are reduced, motor function improves, and dyskinesia—drug-induced, involuntary writhing and twisting—is reduced. Not only do patients increase their function, they also can dramatically decrease, perhaps even stop, their medication, said Paul House, M.D., assistant professor of neurosurgery. And deep brain stimulation offers another advantage: unlike lesional surgeries, the new procedure is reversible, since it does not damage tissue or destroy nerve cells.

The CNC team performs about one procedure per week. Having a team of experts to assess patients, perform the surgery, and fine-tune the stimulators is critical, said House. “We have a nurse practitioner, three neurologists, myself, a neuro-psychologist, and a physiotherapist just to evaluate the patients. And of course you have to have some specialized imaging.”

A scan allows the neurosurgeon to pinpoint the exact placement of the stimulator system. An electrode, or insulated wire, is implanted deep in the brain through a small hole drilled in the skull. The tip of the electrode touches the target site; the other end is anchored near the surface of the skull. Patients with symptoms on both sides of the body need two electrodes. A connecting wire runs from the scalp underneath the skin behind the ear and down the neck to just below the collarbone, where it is attached to the implanted battery or neurostimulator.

After surgery, as patients begin reducing their medications, frequency, voltage, and amplitude settings are customized to reduce symptoms. Eventually, stimulators may be self-correcting to maintain the brain patterns of well-controlled Parkinson's. U researchers are examining brain-firing patterns with stimulation and without it; with and without medication.

The CNC also is pushing forward understanding of Parkinson's on the research front. In the Department of Neurology, Duong Huynh, Ph.D., research associate professor of neurology, is investigating the molecular pathways leading to Parkinson's. Pulst, who also is a member of the Utah



Neuro Critical Care nurses provide specialized care for University of Utah Hospital patients: Monique Kirk, R.N., at right; Laura Clinger, R.N., opposite page, lower left; and Megan Kelly, R.N., top right.



Brain Institute, with colleagues in his lab has identified several genes responsible for neurological disorders. Using experiments at the bench and real-life data from the Utah Population Database, his lab is defining the interactions of genetic and environmental factors that cause neurodegenerative diseases.

Community Outreach

At the CNC, collaboration doesn't end in the clinic or the research lab. Last fall, the CNC opened the Brain Health Learning Center in the University's Research Park. The centralized location provides patients with multiple sclerosis (MS), movement disorders, Parkinson's disease, Alzheimer's, and dementia access to a library with printed literature and audio-visual materials, computer stations, and meeting space. The center organizes educational seminars, provides referrals to neurologists, and oversees support groups in seven locations throughout the state. Space also is provided to house the Utah chapters of the American Parkinson Disease Association and the MS Society, in addition to the U Center for Alzheimer's Care, Imaging, and Research.

"The community has an important voice in our development," said Candice Gourley, M.S.H.A., M.B.A., who serves as CNC administrative director. She helped create a Neurosciences Community Advisory Board last fall as another new way to help patients deal with old diseases. "We're working with community physicians to streamline referral systems and increase access to our specialty services, and we're asking for feedback to help us identify areas where we can best serve the region." ▣



Taking an Active Role with Parkinson's

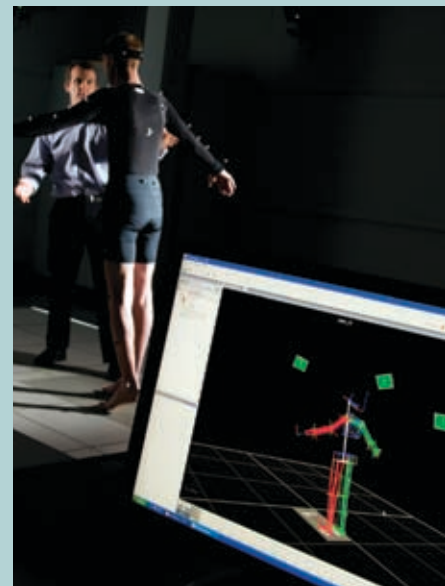
When Lee Dibble, Ph.D., P.T., was doing his doctoral research in Parkinson's disease (PD), he noticed that, with their diagnosis, patients were handed a prognosis that seemed to them more like "a time bomb": the degenerative neurologic condition would cause slowness of movement, increased tremors, and loss of balance control that eventually would result in significant disability. With no known cause or cure for the disease, their initial treatment included a prescription for medication and a warning that they were at risk for falling.

Dibble wanted to help these individuals take an active role in managing the chronic disease and ideally improve their quality of life. He switched his research focus from the effects of surgical treatments to studying the mechanisms underlying the therapeutic effects of physical activity and exercise for persons with PD.

Two years ago, Dibble, U of U assistant professor of physical therapy in the College of Health, received a three-year, \$250,000 grant from the National Institutes of Health to determine if high-force resistance training would improve muscle structure, muscle force output, and the speed and amplitude of balance responses. He also is comparing the effects of exercise with therapeutic response to medication.

Now more than halfway through the clinical study, Dibble—who is collaborating with colleagues in the College of Health, School of Medicine, U mechanical engineering department, and Brigham Young University—reports substantial gains in persons with PD immediately after participating in the 12-week study, in addition to preservation of the gains six months later. But questions remain: Does exercise protect the brain from further deterioration? Are the observable changes occurring only in the musculoskeletal system, or do they indicate alterations in the central nervous system?

Dibble hopes that his research will contribute to improved treatment. If he has his way, people with PD someday may be handed a prescription for exercise, recommendations for eating, and resources for psychological and emotional support, along with their diagnosis and medication. —Amy Albo



Physical therapist Lee Dibble, Ph.D., P.T., helps steady a patient with Parkinson's in the College of Health's Motion Analysis Core Facility.