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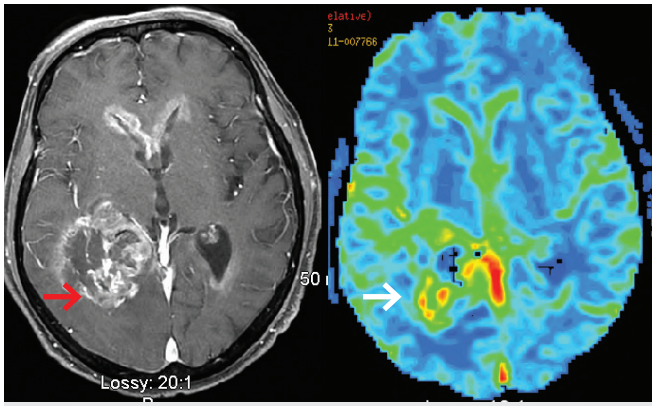
MRI Perfusion: Adding Physiologic Assessment to Tumor Imaging

John Winn, MD

Magnetic resonance imaging (MRI) plays an ever-expanding role in the evaluation of intracranial tumors. It is essential for diagnosis, characterization, treatment planning and post-treatment surveillance. Recent advancements in MRI neuroimaging allow assessment of not only anatomic detail but also physiologic alterations of a tumor and its surroundings. This combined structural and biological assessment permits a more complete assessment of a tumor and subsequent post-treatment monitoring.



Large heterogeneously enhancing right temporo-occipital mass with subependymal spread (left). Focal area of increased CBV (white arrow) on MR perfusion image (right) suggests an area of the mass with tumor hypervascularity. The corresponding enhancing portion of the mass (red arrow) can be targeted for stereotactic biopsy.

One such advance is MRI perfusion imaging, which shows the amount of blood that passes through the vascular network of a portion of the brain. Tumors, just like normal brain tissue, require blood flow to deliver oxygen and nutrients to grow. More aggressive tumors outgrow the native blood supply leading to tissue hypoxia. This in turn stimulates mediators of angiogenesis, such as vascular endothelial growth factor (VEGF), to induce formation of new blood vessels which are abnormally tortuous, immature and leaky. Thus, tumor blood vessels demonstrate abnormal blood flow characteristics, including an increase in cerebral blood volume (CBV), which is depicted by perfusion imaging. Because more aggressive, higher-grade tumors demonstrate a greater elevation of CBV on perfusion images when compared to less aggressive lower-grade tumors, the degree of malignancy can be determined.

This grading of primary brain tumors guides therapy and assesses overall prognosis in patients with brain tumors. The degree of malignancy may vary within different areas of a tumor. Tumor grading is based on the region of highest grade anywhere in the tumor. Surgical biopsy is prone to sampling error since the area biopsied may not demonstrate the area of highest grade. Perfusion images, in contrast, provide an assessment of overall degree of malignancy. High-grade gliomas are usually treated with adjuvant radiation therapy or chemotherapy after resection, whereas low-grade gliomas are usually not. Thus, inaccurate assessment can lead to errors in treatment. With conventional MR imaging, the target for biopsy is usually the area of greatest

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John Winn, MD

Back from the Brink

On a warm June afternoon, Michael Hermes, 47, was dropping off umbrellas for a graduation party at his niece's home in Napa when the first wave of dizziness hit him.

He asked his wife Michelle to drive him home to Vacaville, hoping that the dizziness would clear quickly.

But it didn't. After the drive home, not only was he still feeling dizzy, but one side of his body felt numb. When his vision started to blur, he knew something was really wrong.

He and his wife headed for NorthBay VacaValley Hospital, where he was quickly assessed by the emergency department staff for a possible stroke.

Soon, he was being introduced to Alan Shatzel, DO, via a teleconferencing robot. Dr. Shatzel, Medical Director of Neurology Services for the Mercy Neurological Institute, asked Hermes a number of questions and examined him

through the camera eyes of the robot. CT scans were ordered and medication begun.

"I remember that I had one idea of the timeline and my wife had another. Now I know why they were so persistent about what time we left Napa. They wanted to make sure I was in the time range to qualify for the medication," Hermes said, referring to IV tPA.

All he remembers is receiving the medication they called IV tPA, and then an ambulance ride to Mercy, with his son at his side.

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Mercy Foundation Donor Behind Telehealth Network to be Honored

In 2008, a $500,000 gift to Mercy Foundation by the Elliott Family Foundation, the philanthropic entity of local developer Elliott Homes, Inc., helped to launch the Mercy Telehealth Network. The Telehealth Network connects Mercy stroke specialists via robotic technology to stroke patients in emergency departments at community hospitals.

Elliott Family Foundation President Roxanne Elliott will be accepting the Outstanding Philanthropic Organization award on behalf of her family on Nov. 10 at the National Philanthropy Day luncheon.

After family matriarch Margaret Elliott passed away from complications of stroke, the Elliott family was inspired

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Surgical Management of Epilepsy

Cully A. Cobb III, MD, FACS

Most patients with epilepsy can be managed with medications. Patients whose seizures persist despite medications are at risk for sudden death, injury during seizures, impaired quality of life and gradual deterioration in memory and cognitive function. When medical management does not provide adequate control of seizures, or when side effects of medications are intolerable, surgical treatment is sometimes an option.

The simplest surgical intervention for epilepsy is placement of a vagal nerve stimulator. Vagal nerve stimulation may not be a surgical solution for everyone but it does improve seizure control in 30–50% of patients—and the risks are low and side effects usually minor.

Sometimes control of seizures requires removal of the portion of brain causing the seizures or its disconnection from the remainder of the brain. This approach demands very precise identification of the seizure focus and careful weighing of risks and benefits. Video EEG monitoring with scalp or intracranial electrodes, Wada testing to assess memory and language localization, MRI, PET and SPECT scanning, and neurpsychological assessment are tools which are used to select the best candidates and the best surgical approaches. Surgical decisions require input from a neurologist specializing in epilepsy and a neurosurgeon as well as from specialists in medical imaging, neurophysiology and neuropsychology and from counselors and social workers as well.

"These patients often still need to take antiepileptic drugs but usually at doses which cause minimal side effects."

The most common site of onset for focal epilepsy is the temporal lobe. When seizures are confined to a single temporal lobe, removal of the epileptic focus results in a seizure-free outcome in approximately 70% of patients. These patients often still need to take antiepileptic drugs but usually at doses which cause minimal side effects.

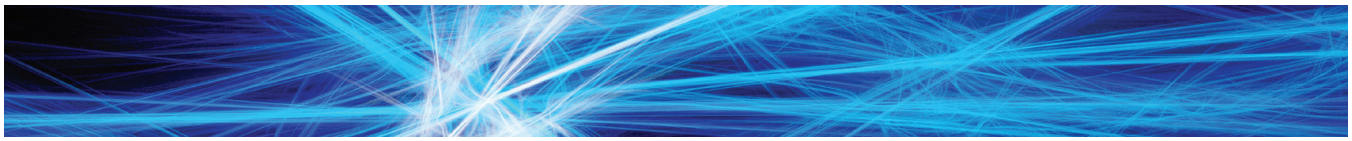
The success rate for resection of seizure foci outside the temporal lobe is less than for temporal foci, but when a focus can be clearly defined, surgery may still be worthwhile. If the seizure focus is at the interface between surrounding brain and a lesion (such as a tumor, developmental anomaly or vascular malformation), a decision must be made about whether the seizure focus is in the lesion itself or in the surrounding brain. Removal of the lesion without looking for an adjacent seizure focus may not give seizure relief. Electrodes can be placed adjacent to the tumor at the time of resection or as part of a separate procedure to localize the seizure focus. When seizures spread into areas of the brain that are too critical for resection it is possible to interrupt the pathways that spread seizures from one area of a gyrus to an adjacent portion of the same gyrus without interfering with the overall function of that area. This is a less effective but sometimes helpful procedure.

When seizures are generalized but begin on one side or the other, cutting the corpus callosum (a corpus callosotomy) can separate the side of the brain having frequent seizures from the uninvolved side. This can convert generalized seizures to focal ones, which can dramatically improve quality of life.

Epilepsy surgery has extended satisfactory control of seizures to a larger number of patients, but both medical and surgical treatments have become complicated. Choosing the best treatment requires the expertise of a multidisciplinary team. Decisions regarding localization, chance of benefit from surgery and choice of surgical approach are made in a multidisciplinary epilepsy conference. This team approach is available through the epilepsy service at the Mercy Neurological Institute.

If you have comments or questions for Dr. Cobb, please e-mail him at mercyneuro@chw.edu.

Cully A. Cobb III, MD, FACS



Brain Waves: Updates from the Mercy Neurological Institute

ASA RECOGNIZES MERCY HOSPITALS

The American Stroke Association (ASA) has recognized three of the Mercy Neurological Institute's Sacramento-area hospitals for their success in using Get With The Guidelines to improve quality of care for stroke patients.

Woodland Memorial Hospital, Mercy General Hospital and Mercy San Juan Medical Center each were honored by ASA and appeared in advertisements that ran in the *U.S. News & World Report*.

Woodland received a Gold Plus rating and Mercy General and Mercy San Juan both received Silver ratings for their stroke care. Get With The Guidelines is a program that helps ensure consistent application of the most recent ASA scientific guidelines for patient treatment. The program includes in-hospital modules for heart failure, stroke and resuscitation as well as a program for outpatient practices.

To achieve the Gold rating, Woodland followed treatment guidelines in certain key measures at least 85 percent of the time and maintained the performance level for two one-year periods. To achieve silver, Mercy General and Mercy San Juan maintained this performance for at least one year.

SPINE CERTIFICATION AT MERCY GENERAL

Earlier this year, Mercy General Hospital (MGH) received The Joint Commission Gold Seal of Approval™ for spine care. MGH achieved this honor by successfully demonstrating compliance with The Joint Commission's national standards for healthcare quality and safety in rigorous, on-site program reviews.

Two spine surgery programs—laminectomy and spinal fusion—received The Joint Commission certifications. MGH is the only hospital in California with these certifications.

Neurosurgeon Brings His Talents Back to California

The expertise offered by Mercy Neurological Institute to the Greater Sacramento area has expanded with the addition of neurosurgeon Michael Chan, MD. Dr. Chan, a native of Northern California, comes to Sacramento from Chicago, where he completed his neurosurgical residency at the University of Illinois, Chicago Medical Center.

Dr. Chan, who will operate at Mercy General Hospital, performs the latest techniques in spine and brain procedures, including minimally invasive endoscopic techniques to treat pituitary tumors. He has special interests in minimally invasive spinal surgery as well as complex surgery of the cervical, thoracic and lumbar spine and spinal fusions.

Dr. Chan earned his undergraduate degree in molecular and cell biology with an emphasis on neurobiology from the University of California, Berkeley, and a Master's in Biomedical Sciences from Barry University, Florida. He received his medical degree from the Medical College of Ohio. In addition to completing his residency in Chicago this year, Dr. Chan was also Instructor of Neuroanatomy for medical students at the University of Illinois. He served as a mentor for the university's College of Medicine Tomorrow's Physician Program, where he was awarded the Alpha Omega Alpha Faculty Teaching Award in 2010.

Dr. Chan believes that educating his patients and their families on their conditions helps them make the best choices in the management of their health.

To reach Dr. Chan, please send an e-mail to mercyneuro@chw.edu.

Exercise and Brain Health

Andres Peña, MD

Modern medicine has found that one of the most effective means of treatment for several of the most frequent and disabling conditions we face in our lifetime lies in a tool that has been available since the beginning of time. Exercise has been proven to be an essential component of the treatment of several of the most frequent causes of mortality, morbidity and disability.

The question is how to design the right exercise program for each individual. The exercise program for a person recovering from a stroke when obesity and other co-morbidities are present is not the same as a program for a person training for an ultra marathon or an ironman triathlon. Knowledge of the pathological disorder and of rehabilitation options is indispensable in arriving at an adequate level of reintegration that fits the individual needs of each patient.

It has been proven that protocols that combine aerobic exercise with resistance training in elderly patients benefit cognitive functions, including executive function, selective attention and conflict resolution. Other studies have found a clear relationship between the incidence of mild cognitive impairment (a precursor of dementia) and physical frailty, and physical deconditioning. Greater levels of physical frailty correlate with more rapid decline in cognitive function observed. Some studies have shown clear improvements in balance and reductions in fall risk in seniors participating in an exercise program such as Tai Chi.

Within the frame of the neurological disorders such as stroke, it is very well established that exercise improves the lipid profile, blood pressure, excessive weight and insulin sensitivity, which are among the most important risk factors for stroke. After a stroke has occurred, a proper exercise prescription helps to improve mobility, independence, fall risk and secondary injuries, while at the same time reducing the risk of a second stroke. Also, the recovery process of a person who has presented with a stroke is much easier if there is a baseline of fitness as compared to a person who is severely deconditioned. Pre-stroke fitness is an independent factor in the prognosis of future independence after a stroke.

In Multiple Sclerosis, the most disabling feature of the illness is often not even a specific neurological deficit but the severe fatigue that limits participation in activities of daily living, recreation or work. There is a delicate balance between allowing deconditioning to settle in because there is no left-over energy to be able to participate in therapeutic exercise and overdoing the physical activity, leaving no energy for the other activities that provide enjoyment of life. In this case, an individual program tailored to the specific needs and capacities of the person makes more sense than just going to the gym and working with the trainer who probably is very effective on treating young healthy customers but not experienced in working with patients with neurological impairment.

Unrealistic expectations and poor planning are common problems in beginning an exercise program. Often the person gets motivated one day, (New Year's resolution anyone?) goes to the gym and does as much exercise as he/she would have been able to do at age 20 and the next day is in profound pain, or even injured, and questioning if he/she should exercise at all. Instead of improving anything, this approach worsens the condition and promotes deconditioning in the long run.

A proper exercise prescription requires a detailed evaluation not only of the medical diagnosis and treatment, including what medications the person is taking, but also the social component and the personal views of each patient. There is no single formula but rather different options for different ages, pathological processes and objectives. The intervention of a physical medicine and rehabilitation doctor can make a substantial difference in the well being of our patients, especially those suffering from debilitating and disabling conditions. Here in the Mercy Neurological Institute, we are applying these principles on ourselves as we train on a progressive basis for the National MS Society bike ride with the goal of increasing awareness to MS and of the benefits of exercise when properly planned.

If you have comments or questions for Dr. Peña, please e-mail him at mercyneuro@chw.edu.

Andres Peña, MD

MRI Perfusion: Adding Physiologic Assessment to Tumor Imaging, continued from page 1

contrast enhancement. Enhancement is a product of an area of destruction of the capillary endothelium (breakdown of the bloodbrain barrier) by the tumor. However, this is not necessarily the most malignant or vascular portion of the tumor. Perfusion imaging, therefore, can be a supplementary tool in identifying the area of greatest tumor vascularity and tumor grade and can aid targeting of the biopsy and thereby optimize diagnostic accuracy. It may also show an area of increased blood volume to target for biopsy in a tumor that does not enhance at all.

MR perfusion can also be contributory in the postoperative/post-treatment surveillance of brain tumors. Conventional MR imaging depicts treatment response by changes in size, enhancement and surrounding tissue signal. Early changes in tumor hypervascularity, detected by increased CBV on MR perfusion studies can be seen prior to any changes in traditional MR characteristics, leading to earlier diagnosis of tumor recurrence or conversion from a low-grade to a higher-grade tumor. In addition, newer anti-angiogenic drugs for treatment of high-grade gliomas target actively dividing tumor vasculature without damage to the normal brain vasculature. Perfusion imaging, which demonstrates areas of tumor revascularization, can potentially provide a more accurate assessment of treatment response to these agents.

One of the biggest pitfalls of post-treatment imaging of tumors is difficulty distinguishing recurrent tumor from radiation necrosis. Recurrent tumor and radiation necrosis can have identical imaging characteristics of an enhancing mass with surrounding edema. The two entities can also be clinically indistinguishable with focal neurologic deficits and even signs of increased intracranial pressure. However, they are pathologically different with tumor necrosis revealing extensive vascular injury and tissue hypoxia as opposed to revascularization, which is seen in recurrent tumor. Currently, biopsy or resection of the lesion is the definitive means of differentiating the two. By identifying absence of increased CBV in a postoperative "mass," radiation necrosis may be diagnosed and managed without the necessity of surgical biopsy, which can lead to more damage to adjacent brain tissue. Alternatively, when areas of increased CBV suggest neovascularization associated with recurrent tumor, treatment with repeat surgery with adjuvant chemotherapy or high-dose radiation is appropriate.

MR imaging is no longer merely an anatomic picture. With the advent of advanced techniques available at some of the Mercy Imaging Centers such as MR perfusion imaging, detection of physiologic alterations in hemodynamics can now supplement anatomy in providing the most accurate information in preoperative and postoperative assessment of brain tumors.

If you have comments or questions for Dr. Winn, please e-mail him at mercyneuro@chw.edu.

Mercy Foundation Donor to be Honored, continued from page 2

to provide a generous donation to Mercy. The Network quickly became a model for comprehensive stroke care and has grown to seven network sites from Sacramento to Bakersfield.

In recognition of its community support, the Elliott Family Foundation will be recognized this November with the Association of Fundraising Professionals Outstanding Philanthropic Organization award, which honors organizations that demonstrate excellent financial and in-kind commitment for the local community.

"The Elliott Family Foundation's philanthropy has expanded our ability to reach out to suburban and rural hospitals so patients can be evaluated by the best physicians and most experienced stroke team available," said Alan Shatzel, DO, Medical Director of Neurology Services for the Mercy Neurological Institute and Mercy Foundation board of trustee member. "Lives will be saved and disability avoided because of the Elliott family's generosity."

Back from the Brink, continued from page 2

NorthBay launched its stroke program in 2010 in partnership with the Mercy Neurological Institute, which provides neurologists around the clock who consult with NorthBay medical staff by means of the telehealth robot.

"The partnership has been a dynamic and thoroughly enjoyable experience," says Kathy Richerson, Vice President and Chief Operation Officer for NorthBay Healthcare. "Mercy's responsiveness to our questions, concerns and requests for information has been tremendous. The program was a first for NorthBay, introducing telemedicine and remote assessment and care for patients. There was skepticism at first, but as the plan unfolded, the excitement grew and now there is comfort and reliance on the expert consultation Mercy provides." In some cases, NorthBay Hospital is able to provide all the treatment necessary, but in cases such as Hermes' where advanced interventional procedures or surgery are required, patients are transferred emergently to Sacramento to Mercy General Hospital or Mercy San Juan Medical Center.

For Hermes, stroke intervention was not only essential but was emergent. By the time he arrived at Mercy General, the numbness had spread to his left side. "They told my wife to say goodbye and that if they didn't do the interventional procedure that minute, I might not make it. I was praying like you wouldn't believe," he recalls. In Mercy General's advanced neurointerventional bi-plane angiography suite, neurointerventionalist Lotfi Hacein-Bey, MD, removed a clot from the artery supplying the intracranial right vertebral artery. Ironically, it was the unusual narrowing of his artery that probably saved Hermes' life. That narrowing prevented the clot from traveling far out into the basilar artery, said Dr. Hacein-Bey. "We got to him just about the time he was starting to deteriorate, with rapidly worsening paralysis on his left side and loss of consciousness. After removal of the clot which blocked the artery, preventing flow to the brainstem, we found the underlying vessel narrowing, and we dilated it with a balloon. We dilated it, thinking it would get better in time, but it didn't," explained Dr. Hacein-Bey. "And because it was the only vessel supplying the brain stem, we offered him a stenting procedure a month after the initial procedure to prevent re-narrowing and fatal closure of the artery."

Three weeks later, Hermes was a "walking miracle."

Hermes, a produce manager for Food 4 Less in Woodland, received further care in Mercy General's Acute Care Rehabilitation program. Balance and coordination are still impaired, but speech, swallowing and cognitive functions are intact. "I really think it was a matter of everything lining up," Hermes says. "That's why I believe in a higher power. I'm not done yet."

Looking back, Hermes realizes he could have made some healthier choices. He worked long hours, ate fast food on the fly and stopped taking his cholesterol medicine, even though his family had a history of high cholesterol and cardiovascular issues.

"I thought I was in fairly decent shape, that I was strong, and that it couldn't happen to me. I thought I'd save $40 a month, but now I'm religious about taking my medicine."

His message to anyone on cholesterol medication is to take it seriously and not to skip a dose. And if you do have any problems, get in to the emergency department right away. Call 9-1-1 and give the team time to assemble, because when it comes to a stroke, every minute counts.

Dr. Shatzel agrees.

"Patients who come to the Emergency Department immediately when symptoms occur have a better opportunity to have full and complete recovery," says Dr. Shatzel. "Patients who have access to experienced stroke teams and comprehensive stroke centers like Northbay's and Mercy's have the best chance of survival and recovery."

"Had he not received IV tPA and subsequent transfer to our interventional center for definitive clot removal and vessel repair, Hermes would likely have been left more severely disabled," explains Dr. Shatzel.

If you have comments or questions, please e-mail us at mercyneuro@chw.edu.

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Continuing Medical Education 2011

Month	Date	CME	Time	Location
October	Thu 10/6	Neuro Grand Rounds	12:30 p.m.	MGH Greenhouse A&B
	Fri 10/7	Neuro Grand Rounds	12:30 p.m.	MSJ Conference rooms 2,3,4
	Tue 10/18	Neuroscience tPA	6 p.m.	MGH North Auditorium
	Tue 10/18	Neurocritical Care	7 p.m.	MGH North Auditorium
	Tue 10/25	Epilepsy Case Conference	6 p.m.	MGH North Auditorium
November	Wed 11/2	Insights & Innovations: The Spine	5:30 p.m.	Sheraton Grand Sacramento
	Thu 11/3	Neuro Grand Rounds	12:30 p.m.	MGH Greenhouse A&B
	Fri 11/4	Neuro Grand Rounds	12:30 p.m.	MSJ Conference rooms 2,3,4
	Tue 11/15	Neuroscience tPA	6 p.m.	MSJ Suite 145
	Tue 11/15	Neurocritical Care	7 p.m.	MSJ Suite 145
December	Thu 12/1	Neuro Grand Rounds	12:30 p.m.	MGH Greenhouse A&B
	Fri 12/2	Neuro Grand Rounds	12:30 p.m.	MSJ Conference rooms 2,3,4

Neuro Grand Rounds. Offered the first week of every month starting after summer hiatus in September at 12:30 p.m. The first Thursday is held at Mercy General—Greenhouse A&B. The first Friday is held at Mercy San Juan—Conference rooms 2, 3, 4

TPA and Neurocritical Care Conferences. Join us for case presentation and discussion related to IV/IA tPA administration for acute stroke moderated by Karsten Dengel, MD. Followed by case presentation and discussion of Neurocritical Care techniques and advanced therapy moderated by Alex Nee, MD. Held the third Tuesday each month alternating Mercy General and Mercy San Juan starting at 6 p.m.

Epilepsy Case Conference. Join us for didactic session, case presentation and discussion of epilepsy cases being considered for surgical cure. Epilepsy Conference is moderated by Edwin Cruz, MD. Held the fourth Tuesday mostly bi-monthly odd months starting at 6 p.m.

Contact Ann.Engwer@chw.edu or 916.962.8751 with any questions