



A physician's newsletter from the Departments of Neurology and Neurological Surgery at The University of Miami

## Remarkable Academic Contributions by our Endovascular Group

By Roberto C. Heros, M.D., F.A.C.S.

**W**e have commented on a couple of occasions in this publication on the groundbreaking clinical advances brought about by our excellent endovascular group. It is remarkable that in spite of the extraordinary busy activities of this group, they have been extremely productive academically. The Director of Endovascular Neurosurgery, Dr. Ali Sultan, has led a group of our neurosurgical residents and fellows in the development of 18 publications in peer reviewed journals over the last four years.

These publications have described new developments in a variety of areas such as the treatment of retinoblastomas by direct endovascular injection of chemotherapeutic agents, an accelerated technique for embolization with Onyx 500, a comparison of open versus endovascular carotid sacrifice, the description of several unique types of endovascular complications and how to avoid them, the direct percutaneous embolization of head and neck tumors to facilitate their surgical excision, a safe and effective technique for inserting spinal fluid drainage catheters and rescue of ischemic brain regions by retrieval of coil/clot masses.

In addition, they have described their experience with the embolization of pediatric tumors and arteriovenous malformations with Onyx and embolization of orbital hemangiomas in children. They have also developed in the laboratory percutaneous models of embolization in rabbit spleen, a mathematical model of coil compaction, embolization in a mouse model of retinoblastoma and the ability to measure venous pressure in a pig model of arteriovenous malformation. The residents and fellows that have participated in this remarkably prolific academic activity include Drs. Stacey Quintero-Wolfe, Samy Elhammady, Roham Moftakhar, Hamad Farhat, Eric Peterson, Jeremiah Johnson, Ramu Tummala, Asterios Tsimpas, Ramsey R. Ashour and Koji C. Ebersole.

Dr. Dileep Yavagal, Director of Endovascular Neurology, has also been extremely active in the laboratory and has participated in the development of several clinical studies. He has focused his research on novel catheter-based endovascular therapies for the treatment of acute ischemic stroke including intra-arterial catheter based endovascular delivery of adult mesenchymal stem cells in rodent and canine stroke models. He is the recipient of a competitive interdepartmental research development initiative grant from the University of Miami to study the safety and efficacy on intra-arterial delivery of stem cells in a large animal stroke model as well as in rodents. He and his colleagues were able to find for the first time the safe maximal tolerated dose of intra-arterial stem cells delivery. This work was selected for oral presentation at the 62nd annual meeting of the American Academy of Neurology this year. Efficacy studies of intra-arterial delivery of mesenchymal stem cells in large rodents have found significantly superior outcome in treated animals as compared to controls.

Dr. Yavagal also leads a single center cohort study through UM of "Acute Management of Ischemic Stroke" to evaluate the impact of advanced neuro-imaging to select patients for endovascular therapies after an acute stroke. This study has already led to two national platform presentations. He has also completed a multi-center retrospective study of the safety and midterm outcomes of simultaneous endovascular therapy to embolize ruptured aneurysms and treat associated vasospasm. Dr. Yavagal is also the principal local investigator for two NIH sponsored and one industry sponsored randomized control trials of



Jeremiah Johnson, M.D., resident (left), Samy A. Elhammady, M.D., chief resident, M. Ali Aziz-Sultan, M.D., Assistant Professor of Neurological Surgery, Koji C. Ebersole, M.D., endovascular fellow, and Ramsey R. Ashour, M.D., resident, in the endovascular suite, Jackson Memorial Hospital.



Dileep Yavagal, M.D., Director of Interventional Neurology (center), and colleague Baowin Lin, M.D., voluntary faculty, examine adult mesenchymal stem cells in the endovascular laboratory with Steven Amatangelo, M.S., research assistant.

endovascular therapy for acute stroke. In the last three years, he has published eight peer reviewed articles and presented 13 abstracts at national and international meetings. ■

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*NeuroFocus is produced by the Departments of Neurological Surgery and Neurology at the University of Miami's Miller School of Medicine in affiliation with Jackson Health System.*

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## NEUROLOGY

### Ethnic/Racial Variations of Intracerebral Hemorrhage (ERICH)

Hemorrhagic stroke occurs in approximately 100,000 persons in the U.S. each year, of which 40%-50% die within 30 days. Despite comprising less than 20% of all strokes, hemorrhagic stroke accounts for 50% of the mortality associated with stroke and 30% of stroke-related costs. Intracerebral hemorrhage (ICH) accounts for two-thirds of all hemorrhagic strokes. In ICH, half of the mortality occurs in the first two days after stroke and at present, there are no proven effective treatments. Decades of research demonstrate the disproportionate burden of ICH among non-Hispanic African Americans and Hispanics, but only a few hundred cases have been collected with DNA available in either minority group. The long-term goal of the Ethnic/Racial Variations of Intracerebral Hemorrhage (ERICH) study is to perform a genome-wide association study (GWAS) to identify genes that affect risk of ICH including African Americans and Hispanics. This can be achieved by performing a multi-center case-control study of ICH. All cases and controls will be recruited using identical interview processes and phenotype definitions, handling of biologic samples, centralized neuroimaging analysis and case and control identification using identical methods. This methodology would represent a critical advantage to performing a large genome-wide association study of ICH including minorities.

PI - Sebastian Koch, M.D.

For more information on Neurology clinical trials please call 1-877-977-7724

## NEUROLOGICAL SURGERY

### Brain Metastasis

Analysis of the mechanisms by which systemic cancers metastasize to the brain. The Department of Neurosurgery laboratory has identified a receptor protein produced by brain metastases from many different primary cancer types, which is not produced by most cancers that have not yet metastasized. The ligand (binding protein) for this receptor is also produced by brain metastases. The laboratory is currently performing experiments to more carefully analyze the roles of these proteins in brain metastasis. These proteins may be targets for future treatments of brain metastasis.

PI – Ronald J. Benveniste, M.D., Ph.D.

### Cerebral Aneurysms

#### Neuroform Microdelivery Stent System

There is currently no approved method for the treatment of wide-necked cerebral aneurysms. The FDA has designated the Neuroform Microdelivery Stent System as a Humanitarian Use Device (HUD), the use of which provides physicians with a tool to treat these difficult aneurysms, that was previously not available. The Neuroform Microdelivery Stent System is intended for use with embolic coils for the treatment of wide neck, intracranial, saccular aneurysms arising from a parent vessel that are not amenable to treatment with surgical clipping. Patients are being enrolled for the study through Jackson Memorial Health Systems and the University of Miami.

PI – M. Ali Aziz Sultan, M.D. ■

For more information on Neurological Surgery Clinical trials please call 1-800-996-3783

# UM Neurology Team Finds Insulin Resistance Association with Stroke Risk

**I**NSULIN RESISTANCE APPEARS to be associated with an increased risk of stroke in individuals without diabetes, according to a report by a team of Miller School of Medicine Neurology researchers published in the October issue of Archives of Neurology, one of the JAMA/Archives journals. Their data suggests that insulin resistance is a marker of stroke risk independent of obesity and other components of metabolic syndrome indicating existence of alternative pathways, directly related to inflammation, atherosclerosis and stroke risk. The condition contributes to the risk of cardiovascular disease, but whether it predicts ischemic stroke is still a matter of debate.

Using the homeostasis model assessment (HOMA) to estimate insulin sensitivity, the Miller School team assessed insulin resistance for 1,509 non-diabetic participants in the Northern Manhattan Study, a study assessing stroke risk, incidence and prognosis in a multi-ethnic urban community. Participants were followed for an average of 8.5 years.

During the follow-up period, vascular events occurred in 180 participants, including 46 who had fatal or non-fatal ischemic strokes, 45 who had fatal or non-fatal heart attacks and 121 who died of vascular causes.

Individuals in the top one-fourth (quartile) of HOMA index had an increased risk of stroke compared to those in the other three quartiles of the HOMA index. Adjusting for established cardiovascular risk factors—including glucose level, obesity and metabolic syndrome—did not diminish the association. The relationship between insulin resistance and the risk of first stroke was stronger in men than women but did not vary by racial or ethnic group.

Individuals in the top quarter of insulin resistance had a 45 percent greater risk of any type of vascular event. However, insulin resistance was not associated with heart

attack or vascular death separately.

“This epidemiological study shows that pre-diabetes or insulin resistance is very important among people with non-diabetes, as it is clearly associated with increased risk of stroke,” said Tatjana Rundek, M.D., Ph.D., associate professor of neurology and lead author of the study. “This knowledge can really help assess and target people with an increased risk of stroke and not yet diabetic. We would need well designed clinical trials to determine how to treat these people moving forward, but for now the new knowledge may prompt the physician to treat the risk factors in a patient with pre diabetes much more aggressively.”

“There are several possible reasons for the stronger effect of insulin resistance on the risk of ischemic stroke than of myocardial infarction in the present study compared within other studies,” the authors write. It may be because individuals with a history of heart attack were excluded from this study or because factors associated with insulin resistance—including high blood pressure, high triglyceride levels and low HDL or “good” cholesterol levels—are more significant risk factors for stroke than for heart attack. ■



Tatjana Rundek, M.D., Ph.D., lead author of the insulin resistance study.

## Traumatic Brain Injury Surviving an AK-47



(From left) Daisy Bourges, R.N., M. Ross Bullock, M.D., Ph.D., Clinical Director of the Neurotrauma Program, and Yasniel Ravelo, fully recovered, in the Jackson Memorial Hospital ICU.

**Y**asniel Ravelo, a 19-year-old Miami resident, experienced a severe head trauma when an AK-47 bullet entered his head directly below his left eye on the evening of October 28, 2008. Survival after a direct hit in the head, by an AK -47 bullet, is almost unknown, due to the huge energy, large size, and high velocity, of the bullet.

Ravelo was target shooting with an AK on his family’s farm in Homestead, Florida, with his brother and cousin when the incident occurred. A shot was fired, and Ravelo was seen falling directly on to his face, and bleeding heavily, from the wound.

Within minutes, Ravelo’s family dialed 9-1-1 and made their way to the closest major intersection. Ravelo recalls losing consciousness and then experiencing extreme nausea and vomiting. A trauma unit arrived on the scene shortly after with an emergency helicopter that quickly medevaced Ravelo to the Ryder Trauma Center at Jackson Memorial Hospital (JMH), the only Level 1 Trauma Center in south Florida.

Ravelo received a sedative from the EMT before he was transported to JMH. He recalls being reassured, “Don’t worry, you are just going to go to sleep for while . . .”

# Epilepsy Surgery Increasingly Encouraged

## As a Treatment for Seizure Patients

**D**r. Sanjiv Bhatia, Associate Professor of Clinical Neurosurgery, strongly feels that medically refractory epilepsy is an imminently surgical disorder and that all patients who are refractory to medication should be actively investigated to consider their feasibility for surgical treatment.

A recent successful patient case, the treatment of Ricardo Ibarra, an adult male who experienced his first seizure in elementary school, is a testament to the surgery's effectiveness.

Prior to receiving surgery, Mr. Ibarra experienced secondary generalized seizures with convulsions. He was taken to the emergency room multiple times and on one occasion experienced 10 sequential seizures requiring intubation and prolonged hospitalization. "While I was hospitalized, I woke up and my brother told me that my heart had stopped during one of my seizures" notes Mr. Ibarra.

Over the years, he has been prescribed a total of 8 different antiepileptic medications, some in monotherapy and others polytherapy, but no combination had ever controlled his seizures. At that time he was diagnosed with refractory epilepsy was referred to the Epilepsy Division at the Department of Neurology at the University of Miami Miller School of Medicine.

In April 2010, Mr. Ibarra was referred for long-term video EEG monitoring at Jackson Memorial Hospital to determine the area of the brain responsible for the generation of his seizures. During the monitoring he had multiple complex partial seizures that were diagnosed to be originating from the left temporal lobe.

After identifying the onset of his seizures, further data was gathered and obtained as part of his pre-surgical evaluation. A dedicated epilepsy protocol brain MRI was

performed at the University of Miami's Appelbaum's Diagnostic Imaging Center that demonstrated left mesial temporal sclerosis (MTS). A FDG PET scan showed decreased glucose metabolism in the left temporal lobe which correlated anatomically to Mr. Ibarra's EEG spike activity and MRI findings. Mr. Ibarra's language and memory function was evaluated with a Wada test performed by Dr. Enrique Serrano. From the results of the Wada test, it was determined that Mr. Ibarra should be able to undergo surgery without developing significant worsening of his memory.

Mr. Ibarra's case was then discussed in a comprehensive epilepsy surgical conference with a team of neurosurgeons and epileptologists from the UM Departments of Neurology and Neurosurgery. The team agreed that his best treatment option would be to go ahead with left anterior temporal lobectomy and amygdalohippocampotomy following intraoperative electrocorticography to assist in the delineation of the epileptogenic region. He was then scheduled for surgery with Dr. Bhatia at Jackson Memorial Hospital on August 30, 2010.

Mr. Ibarra underwent the surgery without any complications. Following the surgery, Ricardo has remained seizure free and has not experienced any worsening of his memory. "The surgery gave me back my independence" reports Mr. Ibarra, "I'm now making plans to move



(From left) Ricardo Ibarra, Sanjiv Bhatia, M.D., and Enrique Serrano, M.D., discuss the surgery's success during Mr. Ibarra's follow up visit.

out of my parents' home and finally become more self-sufficient". Dr. Bhatia has been extremely thrilled at the outcome.

In a follow up visit with his treating epileptologist, Dr. Enrique Serrano, Mr. Ibarra continued to report no seizures. "Medial temporal lobectomy was definitely a good option for Mr. Ibarra as he had mesial temporal sclerosis resulting in medically refractory epilepsy," states Dr. Serrano. The option of surgical intervention for patients like Mr. Ibarra gives them a chance towards seizure freedom or significant reduction of medications.

In addition to Dr. Bhatia, University of Miami faculty member, Dr. Jonathan R. Jagid, Assistant Professor of Neurological Surgery, also performs epilepsy surgery cases in conjunction with Jackson Memorial Hospital. ■

.". Ravelo resumed consciousness 3 surgeries and 21 days later.

Miraculously, Ravelo was able to obey commands right from his initial presentation. Preliminary CT scans, and emergency angiography revealed that the AK bullet had passed under the front part of the brain, between the eyes, under the optic nerves, between the two carotid arteries, and then entered the posterior fossa, via the petro-clinoid region on the right, then passed through the space between the basilar, and middle cerebellar arteries, without damaging the vessels, a real miracle (Figures 1, 2).

A hematoma developed in the posterior fossa, on day two necessitating decompression surgery performed by Dr. M. Ross Bullock, Clinical Director of the Neurotrauma Program and a Neurological Surgery Professor, but when the clot was removed, the bullet could not be seen (Figure 3). It had migrated, since he was in the prone position, to lie in the middle cerebellar peduncle. On day five, he developed a massive hemorrhage from the nose and angiography showed a false aneurysm, on the anterior ethmoidal artery, which was emergently embolised using Onyx, by Dr. M. Ali Aziz-Sultan. A second posterior fossa surgery was conducted by Dr. Bullock to remove the migrating bullet, in part because he developed meningitis, and also to prevent further migration, of the large ferrous metallic bullet core.

Once Ravelo regained consciousness he remained at JMH for an additional seven days and was cared for by the ICU team, which included Daisy Bourges, R.N., the nurse primarily responsible for Ravelo's treatment. Following his discharge from JMH, Ravelo underwent

intense rehabilitation at JMH South, which included re-learning how to walk, balance training, etc.

The mystery of how Ravelo survived the injury, and how the bullet could have hit him while he was standing right next to the weapon, was solved by an astute police detective who searched the dirt pile into which they had been firing, and found a thick steel truck wheel rim, with a fresh metallic gouge, to show that the bullet had hit the rim, and spun 180 degrees round the wheel, to come back hitting Ravelo as a ricochet, thus absorbing most of its energy, before hitting the patient.

Today, Ravelo's left eye waters occasionally and he no longer has a sense of smell, but apart from these minor side effects he is fully functional, and works 8 hour days running his family's farm.

"Dr. Bullock and the ICU team at Jackson Memorial saved my life. My family and I are so grateful for the care I received. I am thankful to be alive," said Ravelo. ■

**Figure 1.** Initial sagittal CT angiogram, showing multiple metallic fragments from the bullet jacket, and indicating the Trajectory into the posterior-fossa.

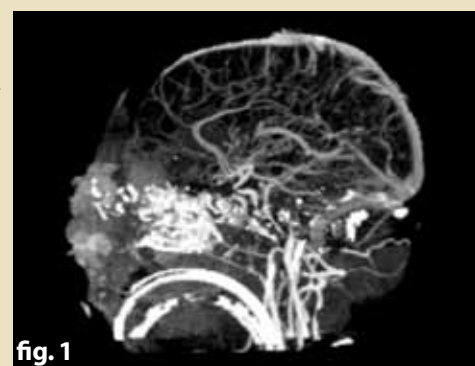


fig. 1

**Figure 2.** CT image to show bullet lodged near the surface of the Rt cerebellum, after passing through the middle cerebellar peduncle, and between the middle cerebellar artery, and the basilar.

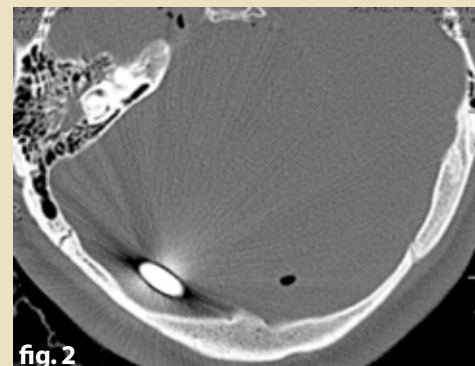


fig. 2

**Figure 3.** "Moving Bullet" now laying in the middle Cerebellar peduncle, prior to removal, while the patient was prone.

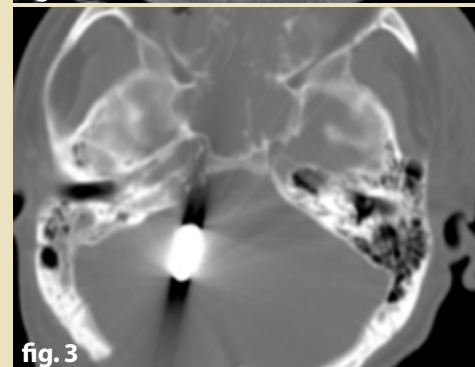


fig. 3



## In The News

### University of Miami to Host the 2012 AANS Scientific Meeting

**April 14-18, 2012**

**Miami, Florida**

Miami was named the location of the 2012 AANS Scientific Meeting. The four day symposium, which draws expertise from medical and scientific communities, is especially designed for neurological surgeons. The 2011 Scientific Program will include practical clinics, breakfast seminars, oral paper presentations and electronic poster presentations.

[www.aans.org](http://www.aans.org)

### UM Brain Bank Receives NIH Award for Genotype-Tissue Expression Project

The University of Miami/National Parkinson's Foundation Brain Endowment Bank, directed by Deborah Mash, Ph.D., the Jeanne C. Levey Professor of Neurology and Molecular and Cellular Pharmacology, is the recipient of a three-year award from the NIH to partner with researchers across the country for the Genotype-Tissue Expression project (GTEx). A two-year, \$25 million pilot project supported by the NIH Common Fund, GTEx is designed to generate data for the systematic study of how gene expression is regulated in different organs in the human body, a key step to explaining the underlying biology of many organ-specific diseases, such as heart disease or mental illness.

<http://commonfund.nih.gov/GTEx/>

## What's Next

### Eleventh Annual Hubert L. Rosomoff Research Day

**Saturday, March 26, 2011**

The Department of Neurological Surgery will host the eleventh Hubert L. Rosomoff Research Day on Saturday, March 26, 2011 from 8:30 a.m. to 1:00 p.m. in the Lois Pope LIFE Center, seventh-floor auditorium. The event will showcase research by neurological surgery residents, fellows and faculty. The visiting professor will be Edward R. Laws, Jr., M.D., F.A.C.S. Director, Pituitary/Neuro-endocrine Center, Brigham & Women's Hospital Harvard University.

For further information, call 305-243-6751.

### Neurology Update and Stroke Intensive 2011

**February 24-26, 2011**

**The Alexander Hotel, Miami Beach, FL**

Neurology Update and Stroke Intensive 2011 is designed to provide clinicians with the most recent developments in the diagnosis and management of neurologic disorders, including stroke. The stroke seminar on Saturday is a stand-alone 8-hour CME activity that will provide the annual CME credits needed for stroke team personnel. For those planning to receive stroke center status, this course will provide stroke teams with the most up-to-date evidence in the field. This activity has been approved for AMA PRA Category 1 Credit™.

[www.cme.med.miami.edu](http://www.cme.med.miami.edu)

## New Multiple Sclerosis Division Director

### Kottil W. Rammohan, M.D.

Kottil W. Rammohan, M.D., recently joined the department of neurology as Professor and Director of the Multiple Sclerosis Center at the University of Miami. He is board certified by the American Board of Internal Medicine, American Board of Psychiatry and Neurology with special competence in Neurology, and The American Society of Neurorehabilitation.

Dr. Rammohan previously served as Professor and Director of Multiple Sclerosis Center at Ohio State University. A graduate of Madras Medical College in Chennai, India, Dr. Rammohan completed an internship at the Cook County Hospital in Chicago, and trained as a resident in Internal Medicine and Neurology at the Ohio State University. He was a Fellow and Senior Clinical Associate at the National Institutes of Health.

A participant in a number of investigator and industry initiated clinical trials, Dr. Rammohan's main research interest is in understanding the pathogenesis and treatment of multiple sclerosis (MS). In particular, he has been involved with understanding mechanisms of fatigue, and designing treatments for this disabling symptom. Magnetic resonance imaging, specifically, imaging MS brain abnormalities at Ultra high field strength (8 tesla). His contributions include developing novel and simple techniques for examination of abnormalities in the cerebrospinal fluid in MS. At a basic level, his interests include exploring autoimmunity to ion channels in MS and exploring mechanisms of action of the presently used disease modifying therapies in multiple sclerosis.

Integrally involved in the study of MS, Dr. Rammohan has served the National Multiple Sclerosis Society as a member of both the Medical Advisory Board and the Clinical Care Committee. He chaired the Clinical Advisory Committee at the National level.

