

HENRY FORD

SYNAPSE

— *Neurosurgery* —

October 2014



A Look Inside

- Letter from the Chair
- Michigan Spine Surgery Improvement Collaborative
- New Staff Members
- Residents' Corner
- Faculty Feature
- Patient Stories
- Clinical Trials
- 2014 Publications

LETTER FROM THE CHAIR

Dear Colleagues and Friends,



I am incredibly humbled and proud to begin a new journey as chair of the Department of Neurosurgery and co-chair of the Neuroscience Institute at Henry Ford. I strongly embrace the trust placed in me by these appointments, and I want to thank all of you for your support during this transition period over the last few months. I look forward to creating an environment of relentless academic discovery with superior clinical outcomes for our patients, as we work together to take Henry Ford Neuroscience to even greater heights.

Innovations

Thanks to the exemplary leadership of Dr. Mark Rosenblum over the past 22 years, the Henry Ford team begins this journey from an enviable position, already powered by an extraordinary team of specialists regarded as some of the finest in the world. We continue to offer more treatment-specific clinical trials for brain tumors than anywhere in the Midwest, bolstered by the molecular and genetic breakthroughs from our Hermelin Brain Tumor Center tumor bank, which is now the second-largest in the world. The Michigan Spine Surgery Improvement Collaborative (MSSIC) is also led by Henry Ford, as we coordinate spine patient outcomes and treatment protocols for multiple medical centers around the state. Our collaborative partnerships across the Neuroscience Institute, and our commitment to innovation have also led to the implementation of several life-saving “firsts” at Henry Ford, including a full-bore intraoperative MRI suite with functional mapping capability, the Visualase laser thermotherapy ablation system for both refractory brain tumors and epilepsy, and, along with our radiation oncology partners, the new Varian “Edge” stereotactic radiosurgery platform – the first of its kind in North America. Our world-renowned neuro-intensivists recently authored the new national paradigms for brain injury diagnosis and treatment, and our tumor surgeons and neuro-oncologists have spearheaded national guidelines for the treatment of both brain metastases and primary brain tumors.

Most importantly, we are incredibly honored by the trust placed in us by our patients and their families; over 60% of our neurosurgery patients have never before been seen at Henry Ford, and come to us from around the world for hope of a better future.

The road to achieving new successes, however, will mean change and, with it, challenges, but our Henry Ford neurosurgery family has already embraced this unique opportunity to create a top five nationally recognized neurosurgical program within the next five years. Together, along with world-class translational research and innovative treatment solutions, we will bring a heightened sense of accountability and expertise to our patients, to colleagues within the hospital system, and beyond our own walls to reach referring physicians to enhance our trusted partner relationships.

New Team Members

I'm thrilled to announce the following new additions to our team as we build toward this success. Dr. Ellen Air, a renowned epilepsy surgeon from the University of Cincinnati, joined our department two months ago and will work with Dr. Jason Schwalb and our neurology colleagues to build our

movement disorders program. Dr. Victor Chang completed his complex spine surgery fellowship at UCLA and returned home to Henry Ford last month to lead our academic spine initiative and our biomotion laboratory, and he will work closely with Drs. Muwaffak Abdulhak and Mokbel Chedid in our complex spine program. Dr. Charlie Hao from McGill and Emory will join our group this month as the new chief of neuropathology at Henry Ford, along with Dr. Michelle Felicella, who joined us two months ago from UCSF. Dr. Anita Bellail from McGill will also be joining us this Fall as a senior staff scientist in our Hermelin Brain Tumor Center laboratory, where we are also recruiting an additional senior Ph.D. researcher. Finally, we are so fortunate that world-renowned neurosurgeon Beverly Walters, M.D., former chair of neurosurgery at Brown University, has finalized a long-term agreement to serve as a research consultant for our academic programs at Henry Ford for our residents, fellows and senior staff.

Novel Advances

We have also launched several new initiatives over the last two months, including a complete renovation and reconfiguration of our clinic and administrative space at the main campus. We are constructing a state-of-the-art neurosurgical telemedicine library with 3-D video links to the operating room, along with worldwide telemedicine capabilities for teaching and patient referrals. We are partnering with our neurology colleagues to provide seed grants for multidisciplinary one-stop treatment centers and research support for conditions such as movement disorders and epilepsy, and we are collaborating with our orthopedic, physical medicine and rehab and pain service colleagues to design a comprehensive spine center. In addition to all new microscopes, instruments and headlights for the neurosurgery operating rooms, we have also made major investments in our anatomy and cadaver labs with new electronic imaging and live video feeds for resident teaching and for complex case simulation and training.

With humility, collegiality, innovation and a true passion for neurosurgery, we can, together, build a neurosurgery department of tomorrow, to serve as a shining example for the country. My goals focus on superior patient care and outcomes, perfect referring physician relationships, life-saving translational, molecular and personalized medicine research, mentoring and educating our residents and medical students to serve as leaders in the future, designing new technologies, bolstering synergistic relationships with other departments for our neuroscience enterprise, and always respecting the people who work so diligently to make all of our successes possible.

I look forward to a year of growth, transformation and unprecedented success, in partnership with our colleagues both near and far, in the service of our patients who place their trust in us.

Finally, please save the date of **Friday, April 24, 2015**, when we will be hosting the first-ever Henry Ford Neuroscience Symposium in Detroit, in honor of Henry Ford Hospital's 100th Anniversary and to celebrate Dr. Mark Rosenblum's tenure as chair.

Most sincerely,

STEVEN N. KALKANIS, M.D.



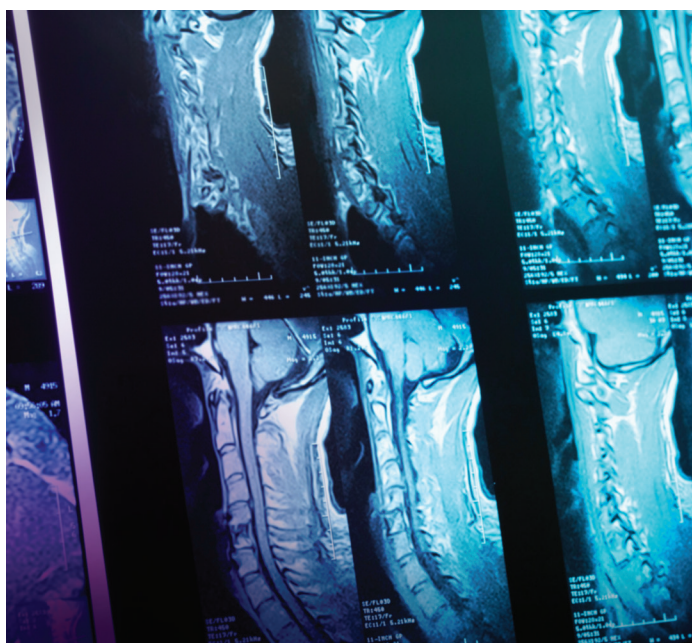
MICHIGAN SPINE SURGERY IMPROVEMENT COLLABORATIVE

TO MAKE AN APPOINTMENT, GO TO
henryford.com/neuro or call (313) 916-1340



The Michigan Spine Surgery Improvement Collaborative (MSSIC) is a statewide quality improvement collaborative involving hospitals, orthopaedic surgeons, and neurosurgeons who seek to measure and improve the care and outcomes of patients who undergo spine surgery. It is supported by Blue Cross Blue Shield of Michigan and Blue Care Network as part of the "Value Partnerships" program. The Coordinating Center of MSSIC is housed in the Department of Neurosurgery, with offices at OFP.

MSSIC was launched Sept. 13, 2013, with seven participating hospitals (Borgess Medical Center, Henry Ford Hospital, Henry Ford West Bloomfield, Marquette General, McLaren-Flint, Sparrow Hospital of Lansing, St. Joseph Mercy-Ann Arbor). Data collection began February 2014. A second wave of recruitment is currently underway, with up to seven new hospitals expected to join the Collaborative.



Scope of Clinical Activity

MSSIC is focusing on cervical and lumbar spine surgery, as opposed to the broader domain of back pain. Within the domain of spine surgery, the collaborative is focusing on surgeries for indications like stenosis, disk herniation, and degenerative disease for which pain relief and restoration of function are primary treatment goals. Surgeries for tumors, traumatic fractures, severe scoliosis, or spinal cord injury are not within the scope (at least initially) of MSSIC.

Areas of QI Focus

MSSIC is initially focusing its activities on a limited set of quality domains, and then gradually expanding that focus as a base of experience develops in the group and leaders for other domains step forward. Participating hospitals and surgeons decide on initial areas of focus as a group. The initial areas of focus include:

- Prevention of surgical complications, including deep-vein thrombosis (DVT), wound infection, nerve damage, urinary tract infections (UTIs), and adjacent-segment disease for patients receiving fusion procedures;
- Frequency and management of the "failed back chronic pain syndrome";
- Use of minimally invasive procedures;
- Use of fusion vs. non-fusion procedures;
- Choice of multi-level vs. simpler procedures;
- Methods for tracking patients post-surgery, including collection and analysis of self-reported outcomes data.

Registry

The project uses a patient registry to maintain and analyze data on patient characteristics, treatment processes, and outcomes of care. Data is collected by abstractors under the direction of Surgeon Champions at each site. The registry is maintained by ArborMetrix of Ann Arbor – a group that is already providing registry support services for several other BCBSM quality collaboratives. Participants have access to their own data, as well as to aggregate, de-identified data to be used for benchmarking and comparison purposes. The MSSIC registry uses a limited data set so a patient cross-walk document must be maintained at each participating site.

MSSIC TEAM

Directors:

Muwaffak Abdulhak M.D.
Stephen Bartol, M.D.

Associate Directors:

David Nerenz, Ph.D.
Jason Schwalb, M.D.

Program Manager:

Lisa Pietrantonio

Surgeon Champions, Henry Ford Hospital:

Donald Seyfried, M.D.
Stephen Bartol, M.D.

Surgeon Champions, Henry Ford West Bloomfield:

Mike Chedid, M.D.
Stephen Bartol, M.D.

Please Welcome our NEW STAFF MEMBERS



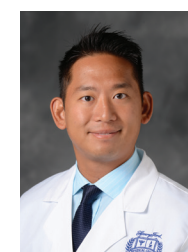
ELLEN L. AIR, M.D., PH.D.

Co-Director, Functional Neurosurgery Program
Henry Ford Department of Neurosurgery

Ellen L. Air, M.D., Ph.D., specializes in the surgical treatment of epilepsy, movement disorders (such as Parkinson's Disease, tremor and dystonia), and pain, including facial pain. After earning both her M.D. and Ph.D. degrees at the University of Cincinnati, she completed residency at the University of Cincinnati Medical Center. She then completed a fellowship in Epilepsy, Stereotactic and Functional Neurosurgery at the University of California San Francisco.

Dr. Air has published more than 30 peer-reviewed articles, co-authored book chapters, and received several awards, including being named one of Cincinnati Magazine's "Top Doctors" and a Cincinnati Business Courier's "Forty Under 40."

Dr. Air is an advocate for her patients and strongly believes that chronic illness should not keep individuals from enjoying the pleasures of life.



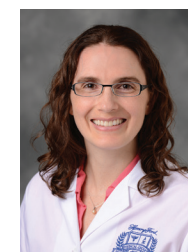
VICTOR CHANG, M.D., PH.D.

Henry Ford Department of Neurosurgery

Victor Chang, M.D., attended medical school at University of Michigan and completed his post-graduate education at Henry Ford Hospital in Detroit, Michigan and UCLA Medical Center in California.

Dr. Chang's research interests encompass a full range of spine related questions. He is involved in biomechanical and motion analysis research to improve understanding of spinal diseases, in order to innovate new treatment options for the spine. He is also involved in outcomes research to help improve the delivery of care to patients.

His philosophy is to maximize patient care with the least-invasive means possible. Dr. Chang endeavors to treat spinal disorders based on the latest techniques supported by the most current and robust medical evidence.



MICHELLE MADDEN FELICELLA, M.D.

Senior Staff Neuropathologist
Henry Ford Department of Pathology & Neurosurgery

Michelle Madden Felicella, M.D., joins us as a Senior Staff Neuropathologist with dual appointments in the Departments of Pathology and Neurosurgery.

Most recently she served as Director of Neuropathology - Surgical Pathologist at Pathology Consultants of South Broward, Memorial Healthcare System in Hollywood, Florida.

Dr. Felicella received her doctorate in Medicine from the University of Vermont College of Medicine, Burlington, Vermont in 2006. She is board certified in Anatomic, Clinical and Neuropathology.

Dr. Felicella is a member of the United States and Canadian Academy of Pathology, College of American Pathologists, American Society for Clinical Pathology and National Association of Medical Examiners.

FOR MORE INFORMATION CONTACT LISA PIETRANTONI, LPIETRAI@HFHS.ORG, 313-874-1892 (OFFICE), 313-399-7263 (MOBILE).

RESIDENTS' CORNER

The Henry Ford Neurosurgical Training Program has embraced the concepts of Evidence-Based Practice by implementing a new Journal Club that is structured around a recognized format for critical appraisal of the medical literature. Once a month, the topics of randomized controlled trials, prognostic studies, case-control studies (such as those for causation), cross-sectional studies (such as used in assessing diagnostic tests) or clinical findings are studied in rotation. Every month, two articles pertaining to neurosurgical issues are discussed under the leadership of two of the residents designated ahead of time. After a thorough discussion, the group decides whether to accept the conclusions or recommendations in the article based upon methodological rigor, and whether it is applicable to their everyday care of patients. Besides creating an atmosphere of knowledgeable criticism among the residents regarding the literature, this exercise sets the stage for implementation of their own research with subsequent appropriate publication.

Along with the structured Journal Club, the residents have a new focus on an organized approach to research during their training. Every month, they meet with the new Clinical Research Consultant to the Department – Dr. Beverly C. Walters, a neurosurgeon and clinical epidemiologist. Using a targeted outline, the residents meet to discuss all of their ongoing projects, including the topic area, the faculty who are mentoring them, and the details of their progress through the steps necessary for reaching their publication goal. These include:

- Statement of the clinical question being addressed by the study
- Articulating the specific research question
- Searching the appropriate medical literature
- Creating a bibliography in citation management software
- Deciding on the study design
- Creating a database for data collection (if appropriate)
- Seeking Institutional Review Board approval
- Gathering the data
- Submitting the findings to statistical analysis
- Writing the manuscript and receiving faculty approval for submission
- Submitting and publishing the manuscript



RECENT RESIDENT PUBLICATIONS

In the course of implementing the program, resident productivity has increased exponentially. Having a specific person to whom they are responsible for the development and progress of their research plans is helpful in overcoming inertia and promoting momentum in the research process. The Journal Club helps to set the expectations for excellence in clinical research and generally to set a higher bar for academic achievement.

Over the past year, the neurosurgical residents at Henry Ford have presented their research at several national and regional meetings, and many manuscripts have been submitted for review. Some recent resident publications include:

Pabaney AH, Robin AM, Schwalb JM. **New technique for open placement of paddle-type spinal cord stimulator electrode in presence of epidural scar Tissue Neuromodulation.** 2014 Apr 11. doi: 10.1111/ner.12174. [Epub ahead of print]

Robin AM, Kalkanis SN, Rock J, Lee I, Rosenblum ML. **Through the patient's eyes: an emphasis on patient-centered values in operative decision making in the management of malignant glioma.** J Neurooncol. 2014 Jun 25. [Epub ahead of print]

Robin AM, Walbert T, Mikkelsen T, Kalkanis SN, Rock J, Lee I, Rosenblum ML. **Through the patient's eyes: the value of a comprehensive brain tumor center.** J Neurooncol. 2014 Jul 16. [Epub ahead of print]

Mazaris P, Hong X, Altshuler D, Schultz L, Poisson LM, Jain R, Mikkelsen T, Rosenblum M, Kalkanis S. **Key determinants of short-term and long-term glioblastoma survival: a 14-year retrospective study of patients from the Hermelin Brain Tumor Center at Henry Ford Hospital.** Clin Neurol Neurosurg. 2014 May;120:103-12. doi: 10.1016/j.clineuro.2014.03.001. Epub 2014 Mar 12.

Greiner HM, Horn PS, Arya R, Holland K, Turner M, Alsaidi MH, Leach JL, Mangano FT. **Acute postoperative seizures and long-term outcome following pediatric epilepsy surgery.** Seizure. 2014 Jun;23(6):483-6. doi: 10.1016/j.seizure.2014.02.010. Epub 2014 Feb 28.

Ali R, Yang LJ, Henning PT. **Posterior interosseus nerve palsy resulting from inflammatory myofibroblastic pseudotumor: case presentation.** PM R. 2014 Jul;6(7):659-61. doi: 10.1016/j.pmrj.2013.12.016. Epub 2014 Jan 31.

Basheer A, Jain R, Anton T, Rock J. **Bilateral iliopsoas hematoma: Case report and literature review.** Surg Neurol Int. 2013 Sep 20;4:121. doi: 10.4103/2152-7806.118561. eCollection 2013.

FACULTY FEATURE

ASIM MAHMOOD, M.D.

Henry Ford Department of Neurosurgery

Asim Mahmood, M.D., has had a very distinguished career. He has completed multiple residencies and fellowships around the world, in some of the most renowned neurological surgery facilities. He joined Henry Ford Hospital in 1994 as a senior staff neurosurgeon.

Asim moved to the United States in 1984/1985 and was awarded a Clinical Fellowship in Neurological Surgery at Long Island College Hospital in Brooklyn, New York. Residencies followed, firstly in General Surgery at Easton Hospital in Easton, Penn., from 1986 to 1988 and then in Neurological Surgery here at Henry Ford Hospital from January 1989 to December 1993. In 1989, he was awarded the F.R.C.S. (Fellow of Royal College of Surgeons) from the Royal College of Surgeons of Edinburgh in Scotland. After his residency at HFH, he completed a fellowship in Skullbase surgery at the University of Cincinnati, Ohio. He returned to Henry Ford Hospital as a Senior Staff Physician Jan. 1, 1994.

Dr. Mahmood's main research interest is neurosurgical trauma with a focus on trauma to the brain and spinal cord. Traumatic brain injury (TBI) is a significant health concern worldwide; approximately 1.7 million people in the U.S. sustain TBI each year and more than 5 million people are coping with disabilities from TBI at annual cost of over \$60 billion. Dr. Mahmood coordinates clinical head injury trials testing novel therapeutic agents and directs NIH-funded laboratory research using bone marrow stromal cells and pharmacologic manipulation for neuroregeneration in the preclinical pneumatic model of cerebral contusions. There is no effective treatment to repair biostructural damage following TBI, hence Dr. Mahmood's Cerebral Injury Protection Laboratory has been focused on investigating the pathophysiology of TBI and exploring cell-based and pharmacological therapies using animal TBI models.

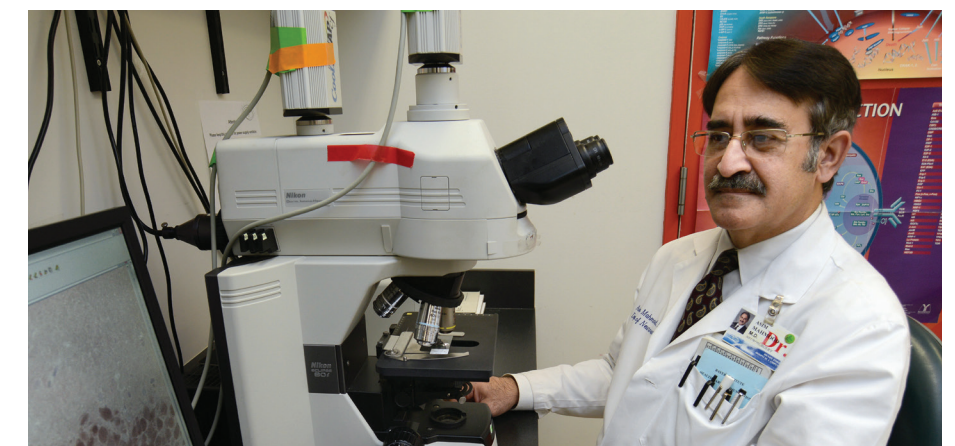
Dr. Mahmood's research projects have received NIH funding six times. His ongoing studies follow:

- Thymosin beta 4 (TB4) is a major G-actin-sequestering peptide in all eukaryotic cells, and promotes angiogenesis, cell migration and differentiation. The lab is investigating TB4 as a neuroprotective and neurorestorative agent to improve outcomes after TBI. Preclinical animal experiments have yielded positive results and clinical trials will soon be initiated. The lab is also investigating a tetrapeptide acetyl-aspartyl-lysyl-proline (AcSDKP) generated from TB4 as a potential pharmacological agent to treat TBI instead of using the entire TB4 molecule.
- Cerebrolysin is a mixture of neuropeptides derived from purified brain proteins by standardized enzymatic proteolysis and it has neuroprotective and neurotrophic properties. It is hoped that cerebrolysin will reduce the biostructural damage after TBI and improve functional outcome. Cerebrolysin reduces matrix metalloproteinase-9 and elevates vascular endothelial growth factor (VEGF) and this more than likely contributes to neurorestoration.
- Tissue plasminogen activator (tPA) is the only U.S. Food and Drug Administration- approved drug for treatment of acute ischemic stroke.

In addition to inducing thrombolysis tPA is extensively involved in synaptic plasticity, dendritic remodeling and axonal outgrowth in the developing and injured central nervous system. Experiments using tPA show that using intranasal tPA after TBI improves cognitive and sensorimotor function. tPA enhances neurogenesis as well as axonogenesis and may be a potential treatment for TBI.

- The lab is using exosomes derived from bone marrow stromal cells (MSCs) administered systemically to improve recovery and neurovascular remodeling in rats after TBI. If successful, this process will provide cell-free exosome treatment as a potential therapy for TBI and other neurological disorders.
- Magnetic resonance imaging (MRI) is being examined as a possible means to monitor structural changes following neural injury and repair following the different cell-based treatment (MSCs). This NIH-funded project is attempting to correlate functional outcomes with structural changes.

Along with these intensive research studies, Dr. Mahmood has authored or co-authored approximately 200 abstracts and peer-reviewed manuscripts, many of them involving the outcome and treatment of traumatic brain injury.



PATIENT STORIES



DONALD M. SEYFRIED, M.D.
Henry Ford
Department
of Neurosurgery

"I had the great privilege of having Dr. Seyfried as my surgeon in May. Both he and his staff were incredible in providing care and taking care of me and helping me through a very difficult experience; I came to Dr. Seyfried as a patient, just days before my own medical school graduation. After four long years of medical school, I had just matched at my top choice residency program and was preparing to move to California when suddenly, I discovered that I had ruptured a disc in my cervical spine which left my right arm partially paralyzed. Dr. Seyfried understood my situation right away and the potential implications that this would have for my career. He was able to schedule my surgery immediately and spent a lot of time going over my images with me and answering my questions. He was incredibly detailed in explaining his

reasoning for every step of the process. He also made sure that I was able to walk at my medical school graduation ceremony despite it being only 10 days after my operation and then worked with me to help make sure I could move safely across the country and start my residency program on time. I want to commend not only Dr. Seyfried, but also the residents on his service. The resident who operated with him took incredible ownership of me as a patient and was able to answer my questions and check in with me whenever I had questions over the next several months, regardless of the time difference and my own busy schedule as a new intern. I was humbled and amazed by the time and effort both she and Dr. Seyfried spent to help keep me healthy and able to work. The physical outcome of the surgery is evidence enough of their excellent surgical skills; my pain has disappeared and I have full function and mobility of my arm. As a young woman in her mid-20s, I had been concerned about scarring on my neck. Because of Dr. Seyfried's skill and attention to detail, the scar on my neck is almost invisible. Their attention to helping me transition

and stay functional speaks to their kindness, compassion and dedication to caring for the whole patient. As a physician myself, I know how much time and energy it takes to provide that kind of care, and I could not be more pleased or grateful for their service."



JACK P. ROCK, M.D.
Henry Ford
Department
of Neurosurgery

"I had my first experience at Henry Ford with Dr. Rock, division head of Neurosurgery, and Dr. Gary Talpos, Surgery. Dr. Jack Rock not only has a wonderful team, but is extremely thorough and patient. I don't think I have met a kinder man than Dr. Talpos. He made me feel completely at ease. It is obvious that everyone at Henry Ford truly cares about the patient experience."

Head for the Cure HENRY FORD BRAIN TUMOR WALK AND RUN!

We had a very successful inaugural Head for the Cure Henry Ford Brain Tumor Walk and Run! Close to 600 patients, families, supporters and runners attended the event. So far, we have raised over \$52,000 for brain tumor research! Thank you to everyone involved for making this event such a success!



Henry Ford Head for the Cure Team

CLINICAL TRIALS

IRB 7763 – Mechanomyography for Evaluation of Pediclin Screw Placement – (SentioPed)

IRB 8436 – Tissue Bank for Patients Referred for Potential Normal Pressure Hydrocephalus

IRB 8231 – The Development of a Pre-Operative Predictor Model of Outcomes in Patients Undergoing Lumbar Spine Fusion

IRB 8138 – Occipital Nerve Stimulation (ONS) for Migraine (OPTIMISE), IDE# G120051

IRB 8522 – Visualase Ablation in Uni-Lateral Temporal Site

IRB 8842 – Trial of Laser Interstitial Thermal Therapy for Cerebral Radiation Necrosis

ABTC 1302 – Drug Distribution and Pharmacodynamics Study of Pulsatile Lapatinib in Surgically Accessible EGFR-Amplified Recurrent High-Grade Glioma

BTTClI-01 – Randomized, Double-Blind, Placebo-Controlled Trial of Lacosamide for Seizure Prophylaxis in Patients with High-Grade Gliomas

BTTClI-02 – Phase I/II Adaptive Randomized Trial of Bevacizumab versus Bevacizumab plus Vorinostat in Adults with Recurrent Glioblastoma

CERN09-02 – Phase II Trial of Carboplatin and Bevacizumab for the Treatment of Recurrent Low-grade and Anaplastic Supratentorial, Infratentorial and Spinal Cord Ependymoma in Adults

CTSUN0577 – Phase III Intergroup Study of Radiotherapy versus Temozolomide Alone versus Radiotherapy with Concomitant and Adjuvant Temozolomide for Patients with 1p/19q Codeleted Anaplastic Glioma

HFHS 11-01 – Prospective Study of Stereotactic Radiosurgery Using Diffusion-weighted Abnormality for Recurrent Glioblastoma After Second Line Chemotherapy

N-HFHS 09-08 – An Open-Label, Phase 2 Trial of Orally Administered PF-00299804 in Adult Patients with Relapsed/Recurrent Glioblastoma (GBM)

Pharm DCVax_020221 – A Phase II Clinical Trial Evaluating DCVax-Brain, Autologous Dendritic Cells Pulsed with Tumor Lysate Antigen for the Treatment of Glioblastoma Multiforme

Pharm Novocure EF-14 – A Prospective, Multi-Center Trial of NovoTFF-100A Together With Temozolomide Compared to Temozolomide Alone in Patients with newly Diagnosed GBM

Pharm STML-701-0114 – A Phase I/II Study of SL-701, a Subcutaneously Injected Multivalent Glioma-Associated Antigen Vaccine, in Adult Patients with Recurrent Glioblastoma

Pharm Tocagen 511-08-01 – A Phase 1 Ascending Dose Trial of the Safety and Tolerability of Toca 511 in Patients with Recurrent High Grade Glioma

Pharm Tocagen 511-09-01 – A Continuation Protocol for Patients Previously Enrolled in a Study of Toca 511

RTOG 0834 – Phase III trial on Concurrent and Adjuvant Temozolomide Chemotherapy in Non-1P/19Q Deleted Anaplastic Glioma. The CANTON Intergroup trial

RTOG 0925 – Natural History of Postoperative Cognitive Function, Quality of Life, and Seizure Control in Patients with Supratentorial Low-Risk Grade II Glioma

RTOG 1119 – Phase II Randomized Study of Whole Brain Radiotherapy in Combination With Concurrent Lapatinib in Patients With Brain Metastasis From HER2-Positive Breast Cancer; a Collaborative Study of RTOG and KROG

Pharm CA209143 – A Randomized Phase IIB Open Label Study of Nivolumab or Nivolumab in Combination with Ipilimumab versus Bevacizumab in Adult Subjects with Recurrent Glioblastoma (GBM)

CONGRATULATIONS TO DR. PETER LEWITT AND DR. JASON SCHWALB, recipients of the first Henry Ford Neuroscience Research Award Characterization of a Novel Tremor Model in Mice due to GABAA Receptor Subunit $\alpha 1$ Knockout

This research plan describes a promising mouse genetic knockout whose phenotype includes limb tremors that show pharmacological responsiveness to several drugs known to be useful for essential tremor. This model will be characterized further as to its tremor mechanisms (including thalamic and cerebellar recordings, possibly other lab methods to determine tremor circuitry in the brain) and will be used in the start of screening for novel anti-tremor medications and treatments.



Henry Ford Department of Neurosurgery

The Henry Ford Department of Neurosurgery offers a broad spectrum of neurosurgical services, each backed by strong teaching and research programs, providing patients the most recent advances in diagnosis and treatment technologies. The Department works in close collaboration with the other eight departments in the nationally recognized Henry Ford Neuroscience Institute. The Departments of Neurology and Neurosurgery are staffed by a team of nationally recognized clinicians and researchers in the following areas of expertise:

Neurosurgery Senior Staff

Steven Kalkanis, M.D.,
*Department Chairman,
Vlasic Family Chair*
313-916-1340

Ghaus Malik, M.D.,
*Exec. Vice Chairman,
John R. Davis Chair*
313-916-1093

Mark L. Rosenblum, M.D.,
Chair Emeritus

Tamer Abdelhak, M.D.

Muwaffak Abdulhak, M.D.

Ellen L. Air, M.D., Ph.D.

Stephen Bartol, M.D.

Chaya Brodie, Ph.D.

Victor Chang, M.D.

Mokbel Chedid, M.D.

Jorge Gutierrez, M.D.

Max Kole, M.D.

Ian Lee, M.D.

Asim Mahmood, M.D.

Horia Marin, M.D.

Tom Mikkelsen, M.D.

David Nerenz, Ph.D.

Suresh Patel, M.D.

Laila Poisson, Ph.D.

Aditya Raghunathan, M.D., MPH

Mohammed Rehman, D.O.

Jack Rock, M.D.

Norbert Roosen, M.D., Dr. med

William Sanders, M.D.

Jason Schwalb, M.D.

Donald Seyfried, M.D.

Panayiotis Varelas, M.D., Ph.D.

Tobias Walbert, M.D., MPH

Ye Xiong, M.D.

Ritu Zacharias, M.D.

HERMELIN BRAIN TUMOR CENTER:

313-916-1340

Steven Kalkanis, M.D.
Chairman and Center Co-Director

Tom Mikkelsen, M.D.
*Center Co-Director, Director, Medical
Neuro Oncology*

Jack P. Rock, M.D.
Surgical Clinic Co-Director

Ian Lee, M.D.

Salim Siddiqui, M.D.
Radiotherapy

Tobias Walbert, M.D., MPH
Medical Neuro Oncology

METASTATIC TUMOR PROGRAM:

313-916-1094

Steven Kalkanis, M.D.

Ian Lee, M.D.

Jack Rock, M.D.

Salim Siddiqui, M.D.

NEUROVASCULAR PROGRAM:

313-916-1093

Max Kole, M.D.
Surgery and Endovascular

Ghaus M. Malik, M.D.
Vice Chairman and Director

Horia Marin, M.D.
Endovascular

Asim Mahmood, M.D.

William Sanders, M.D.
Director, Endovascular

Donald M. Seyfried, M.D.

SKULL BASE SURGERY PROGRAM:

313-916-1094

Jack P. Rock, M.D.
Director

Asim Mahmood, M.D.

Ghaus M. Malik, M.D.

EPILEPSY SURGERY PROGRAM:

313-916-3528

Ellen L. Air, M.D., Ph.D.
Co-Director

Jason Schwalb, M.D.
Co-Director

PAIN/SPASTICITY SURGERY PROGRAM:

313-916-3528

Ellen L. Air, M.D., Ph.D.
Co-Director

Jason Schwalb, M.D.
Co-Director

MOVEMENT DISORDER AND BEHAVIORAL NEUROSURGERY PROGRAM:

313-916-1340

Jason Schwalb, M.D.
Co-Director

Ellen L. Air, M.D., Ph.D.
Co-Director

PEDIATRIC NEUROSURGERY PROGRAM:

313-916-3528

Ghaus M. Malik, M.D.

Ellen L. Air, M.D., Ph.D.

SPINAL DISORDERS AND NEUROTRAUMA PROGRAM:

313-916-2682

Muwaffak Abdulhak, M.D.
Director, HFHS Spine Program

Mokbel Chedid, M.D.
Director, Spine Surgery, West Bloomfield

Victor Chang, M.D.

Ellen L. Air, M.D., Ph.D.

Stephen Bartol, M.D.
Co-Director, HFHS Spine Program

Steven Kalkanis, M.D.

Ian Lee, M.D.

Max Kole, M.D.

Asim Mahmood, M.D.
Director, Neurotrauma Program

Ghaus M. Malik, M.D.

Jack P. Rock, M.D.

Norbert Roosen, M.D., Dr Med

Norman Rotter, M.D.

Jason Schwalb, M.D.

Donald M. Seyfried, M.D.

Ritu Zacharias, M.D.

RADIOSURGERY PROGRAM:

313-916-1094

Salim Siddiqui, M.D.
Director

Steven Kalkanis, M.D.
Brain and Spine Tumors

Ian Lee, M.D.
Brain and Spine Tumors

Ghaus M. Malik, M.D.
AVMs

Tom Mikkelsen, M.D.
Brain Tumors

Jack P. Rock, M.D.
Brain and Spine Tumors

ADVANCED CLINICAL TRIALS

Under the direction of the Neuroscience Institute's Clinical Trials and Outcomes Center, Dr. David Nerenz and Tom Mikkelsen support novel clinical trials in all Disease Programs within the department of neurosurgery.

To Schedule Appointments:

Henry Ford Hospital, Detroit:
313-916-2241

Henry Ford West Bloomfield Hospital:
248-661-6417

Henry Ford Wyandotte Hospital:
734-246-6966

2014 PUBLICATIONS

Lee I, Omodon M, Rock J, Schultz L, Ryu S. Stereotactic radiosurgery for high-grade metastatic epidural cord compression. *JRSBRT* 2014;3(1):51-58.

Griffith B, Vallee P, Krupp S, Jung M, Slezak M, Nagarwala J, Loeckner CP, Schultz LR, Jain R. Imaging utilization in the emergency department: Results and lessons learned from a multi-phase practice quality improvement initiative. *J Am Coll Radiol* 2014;11(2):139-144. Feb.

Kalkanis S, Kast RE, Rosenblum ML, Mikkelsen T, Yurgelevic S, Nelson KM, Raghunathan A, Poisson LM, Auner GW. Raman spectroscopy to distinguish grey matter, necrosis, and glioblastoma multiforme in frozen tissue sections. *J Neurooncol* 2014;116(3):477-485. Feb.

Walbert T, Khan M. End-of-life care in patients with primary malignant tumors - A systematic literature review. *J Neuro-oncol* 2014;117(2):217-224. April.

McDonald C, Chang V, McDonald M, Rammo N, Bey M, Bartol S. Three-dimensional motion analysis of the cervical spine for comparison of anterior cervical decompression and fusion versus artificial disc replacement in 17 patients. *J Neurosurg Spine* 2014;20(3):245-255.

Chwang WB, Jain R, Nejad-Davarani SP, Iskander ASM, VanSlooten A, Schultz L, Ewing JR, Arbab AS, Bagher-Ebadian H. Measurement of rat brain tumor kinetics using an intravascular MR contrast agent and DCE-MRI nested model selection. *JMRI* 2014 Jan. 13 [Epub ahead of print]

Hasselbach LA, Irtenkauf SM, Lemke NW, Nelson KK, Berezovsky AD, Carlton ET, Transou AD, Mikkelsen T, deCarvalho A. Optimization of high grade glioma cell culture from surgical specimens for use in clinically relevant animal models and 3D immunochemistry. *J Vis Exp* 2014;83:e51088. PMID:24429465 [pubmed-inprocess] doi:10.3791/51088. Jan.

Mahmood A, Wu H, Qu C, Mahmood S, Ye X, Kaplan D, Chopp M. Suppression of neurocan and enhancement of axonal density in rats after treatment of traumatic brain injury with scaffolds impregnated with bone marrow stromal cells. *J Neurosurgery* 2014;120(5):1147-1155. May.

Mazaris P, Hong X, Altshuler D, Schultz L, Poisson L, Jain R, Mikkelsen T, Rosenblum M, Kalkanis S. Key determinants of short-term versus long-term glioblastoma survival: A 14-year retrospective study of patients from Henry Ford Hospital. *Clin Neurol Neurosurg* 2014;120:103-112. May.

Mahmood A, Wu H, Qu C, Mahmood S, Xiong Y, Kaplan D, Chopp M. Down-regulation of Nogo-A by collagen scaffolds impregnated with bone marrow stromal cell treatment after traumatic brain injury promotes axonal regeneration in rats. *Brain Res* 2014;1542:41-48. Jan. PMID24177046.

Varelas PN, Abdelhak T, Corry JJ, James E, Rehman MF, Schultz L, Mays-Wilson K, Mitsias P. Clevidipine for acute hypertension in patients with subarachnoid hemorrhage: A pilot study. *Int J Neurosci* 2014;124(3):192-198. March.

Walbert T. Integration of palliative care into the neuro-oncology practice: Patterns in the United States. *Neuro-oncology Practice* 2014;1(1):3-7. March.

Berezovsky AD, Poisson LM, Cherba D, Webb CP, Transou AD, Lemke NW, Hong X, Hasselbach LA, Irtenkauf SM, Mikkelsen T, deCarvalho AC. Sox2 promotes malignancy in glioblastoma by regulating plasticity and astrocytic differentiation. *Neoplasia* 2014;16(3):193-206. March.

Kim E-Y, Yechieli R, Kim J-K, Mikkelsen T, Kalkanis SN, Rock J, Rosenblum M, Ryu S. Patterns of failure after radiosurgery to two different target volumes of enhancing lesions with and without FLAIR abnormalities in recurrent glioblastoma multiforme. *J Neurooncol* 2014;116(2):291-297. January. PMID 24173682.

Mueller C, deCarvalho AC, Mikkelsen T, Lehman NL, Calvert V, Espina V, Liotta LA, Petricoin III EF. Glioblastoma cell enrichment is critical for analysis of phosphorylated drug targets and proteomic-genomic correlations. *Cancer Res* 2014;74(3):818-828. Feb. doi: 10.1158/0008-5472. PMID:24346432.

Lubanska D, Market-Velker BA, Decarvalho AC, Mikkelsen T, Fidalgo da Silva E, Porter LA. The cyclin-like protein spy1 regulates growth and division characteristics of the CD133+ population in human glioma. *Cancer Cell* 2014;25(1):64-76. Jan. (PMID:24434210)

Hong X, O'Donnell JP, Salazar CR, Van Brocklyn JR, Barnett KD, Pearl DK, Decarvalho AC, Ecsedy JA, Brown SL, Mikkelsen T, Lehman NL. The selective Aurora-A kinase inhibitor MLN8237 (alisertib) potently inhibits proliferation of glioblastoma neurosphere tumor stem-like cells and potentiates the effects of temozolamide and ionizing radiation. *Cancer Chemother Pharmacol* 2014;73(5):983-990. May. PMID24627220

Darwish H, Mahmood A, Schallert T, Chopp M, Therrien B. Simvastatin and environmental enrichment effect on recognition and temporal order memory after mild-to-moderate traumatic brain injury. *Brain Inj* 2014;28(2):211-226. Jan-March.

Jacoby E, Yalon M, Leitner M, Cohen ZR, Cohen Y, Fisher T, Eder S, Amariglio N, Rechavi G, Cazacu S, Xiang C, Mikkelsen T, Brodie C, Toren A. Related to testes-specific, vespid and pathogenesis protein-1 is regulated by methylation in glioblastoma. *Oncol Lett* 2014;7(4):1209-1212. Jan-March.

Owonikoko TK, arbiser J, Zelnak A, Shu HK, Shim H, Robin AM, Kalkanis SN, Whitsett TG, Salhia B, Tran NL, Ryken T, Moore MK, Egan KM, Olson JJ. Current approaches to the treatment of metastatic brain tumours. *Nat Rev Clin Oncol* 2014;11(4):203-222 PMID: 24569448. April.

Zhang Y, Xiong Y, Mahmood A, Zhang ZG, Chopp M. Angiogenesis and functional recovery after traumatic brain injury. *Vascular Mechanisms in CNS Trauma*. Lo EH, Lok J, Ning MM, Whalen MJ, eds. 2014:141-156. Jan-March.

Shankar A, Kumar S, Iskander A, Varma NR, Janic B, Decarvalho A, Mikkelsen T, Frank JA, Ali MM, Knight RA, Brown S, Arbab AS. Subcurative radiation significantly increases cell proliferation, invasion, and migration of primary glioblastoma multiforme in vivo. *Chin J Cancer* 2014;33(3):148-158. PMID:24016393. March.

(Continued)



henryford.com/neuro

2014 PUBLICATIONS

(Continued)

Assi HH, Paran C, VanderVeen N, Savakus J, Doherty R, Petruzzella E, Hoeschele JD, Appelman H, Raptis L, Mikkelsen T, Lowenstein PR, Castro MG. Pre-clinical characterization of signal transducer and activator of transcription 3 small molecule inhibitors for primary and metastatic brain cancer therapy. *J Pharmacol Exp Ther* 2014;349(3):458-469. June.

Greiner HM, Horn PS, Arya R, Holland K, Turner M, Alsaidi MH, Leach JL, Mangano FT. Acute postoperative seizures and long-term outcome following pediatric epilepsy surgery. *Seizure* 2014;23(6):483-486. June. PMID:24680553.

Kondziolka D, Kalkanis SN, Mehta M, Ahluwalia M, Loeffler JS. It is time to re-evaluate the management of patients with brain metastases. *Neurosurgery* 2014;120(5):1147-1155. May. PMID:24662510.

Chang V, Lu DC, Hoffman H, Buchanan C, Holly LT. Clinical results of cervical laminectomy and fusion for the treatment of cervical spondylotic myelopathy in 58 consecutive patients. *Surg Neurol Int* 2014;SI33-SI37. May.

Pabaney AH, Robin AM, Schwalb JM. New technique for open placement of paddle-type spinal cord stimulator electrode in presence of epidural scar tissue. *Neuromodulation* 2014, April 11 [Epub ahead of print]

Corry JJ, Varelas P, Abdelhak T, Morris S, Hawley M, Hawkins A, Jankowski M. Variable change in renal function by hypertonic saline. *World J Crit Care Med* 2014;3(2):61-67. May

Hasselbach LA, Irtenkauf SM, Lemke NW, Nelson KK, Berezovsky AD, Carlton EE, Transou AD, Mikkelsen T, deCarvalho AC. Optimization of high-grade glioma cell culture from surgical specimens for use in clinically relevant animal models and 3D immunochemistry. *J Vis Exp* 2014;83:e51088. PMID: 24429465 January.

Godil SS, McGirt MJ, Glassman SD, Knightly JJ, Mummaneni PV, Oetting G, Kalkanis SN, et al. Defining the effectiveness of lumbar spine surgery in a nationwide, prospective longitudinal quality of life registry: An analysis of variability in patient-reported outcomes and preliminary predictive models of treatment failure. *Neurosurgery* 2014;61(Suppl 1):194-195. June.

Hu J, Gonsahn MD, Nerenz DR. Socioeconomic status and readmissions: Evidence from an urban teaching hospital. *Health Aff (Millwood)* 2014;33(5):778-785. May.

Jarvik JG, Comstock BA, Heagerty PJ, Turner JA, Sullivan SD, Shi X, Nerenz DR, Nedeljkovic SS, Iessler L, James K, Friedly JL, Bresnahan BW, Bauer Z, Avins AL, Deya RA. Back pain in seniors: The Back Pain Outcomes Using Longitudinal Data (BOLD) cohort baseline data. *BMC Musculoskelet Disord* 2014;15:134. April.

Stachler RJ, Schultz LR, Nerenz D, Yaremchuk. PROMIS evaluation for head and neck cancer patients: A comprehensive quality-of-life outcomes assessment tool. *Laryngoscope* 2014;124(6):1368-1376. June.

Synapse – October 2014

Editor: Jason Schwalb, M.D.

Newsletter team: Susan MacPhee and Jennifer Day