



A LOOK INSIDE



Hope is a passion for the possible.
-Søren Kierkegaard

I came across this quote related to our System's cancer survivor celebrations and it felt particularly appropriate at this inflection point – for the pandemic and for our neuroscience advances.

ADAPTING AND GROWING DURING COVID-19

Similar to others across the country, southeast Michigan is finally able to envision an end to the pandemic, with statewide restrictions lifting by July 1. Despite our second surge of cases last fall, our team pushed forward with innovative solutions to everything from virtual residency interviews to surgical scheduling shuffles. Through it all, we were able to move forward with significant advances for our patients, our System and the Henry Ford Neuroscience Institute.

NEW INITIATIVES, IMPROVEMENTS AND MORE

In January, we shared the news of two initiatives that will have a profound impact on our academic mission, research and neuro-oncologic care: our landmark, 30-year partnership with Michigan State University and the opening of our long-envisioned cancer facility in Detroit. This issue of *Synapse* highlights these advances, along with remarkable improvements in spine care, new options for treating glioblastoma, an extensive list of our colleagues' publications, and a tribute to our Director of Clinical Research within our neurosurgical resident education program.

A FOCUS ON COLLABORATION

As a profession and here at Henry Ford, our collective "passion for the possible" drives us to continue our neuroscience research, our first-in-world clinical trials and advanced treatments. We move forward by sharing our learnings across the globe. Thank you for taking the time to see what our team has done to push the boundaries of what is possible in neurosurgical care.

Jack Rock, M.D.
Interim Chair, Department of Neurosurgery
Co-Director, Skull Base, Pituitary and Endoscopy Center





Henry Ford and MSU finalize partnership

Henry Ford Health System and Michigan State University, two of the state's leading education, research and health care institutions, are partnering to make Michigan a national leader in providing access to exceptional health care for all residents, and scientific discovery and education for providers, patients and families.

In a landmark partnership that will last for at least 30 years, both institutions are committed to aligning efforts across key departments and programs to achieve critical health care and educational goals, while addressing social issues that impact health outcomes for patients in Michigan and beyond. The signing of this agreement comes just seven months after Henry Ford and MSU signed a letter of intent to significantly expand their long-term partnership.

Key features of the agreement include fostering innovative, groundbreaking research; providing best-in-class cancer care; interprofessional training; increasing diversity among the next generation of health care professionals; and addressing the needs of traditionally underserved communities.

"Our research programs will seek to engage underrepresented communities in meaningful ways to identify potential interventions and reduce or eliminate health care disparities," says Dr. Steven Kalkanis, M.D., chief executive officer and senior vice president and chief academic officer of Henry Ford Health System. Dr. Kalkanis is also the inaugural president of the Health Sciences Center, a joint research institute that is being developed as part of this partnership.

MSSIC UPDATE

Michigan spine collaborative makes improvements in several key areas

Support for the Michigan Spine Surgery Improvement Collaborative (MSSIC) is provided by Blue Cross Blue Shield of Michigan (BCBSM) and Blue Care Network (BCN) as part of the BCBSM Value Partnerships program.

Henry Ford Health System is the Coordinating Center for MSSIC, which has 30 hospital sites and two ambulatory surgery centers. It has been a busy year for MSSIC:

ERAS ROLLOUT

We are in Phase 1 of the rollout of Enhanced Recovery After Surgery (ERAS) programs at all MSSIC sites. ERAS is a systematized and validated perioperative management model based on best available evidence. ERAS pathways decrease surgical stress, maintain physiological homeostasis and improve postoperative recovery.

It has been demonstrated that ERAS positively influences patient subjective well-being with better health-related quality of life. The MSSIC ERAS patient education video (vimeo.com/451937093) was released at the August 28, 2020, MSSIC collaborative-wide meeting. It is a valuable resource for sites and clinics to use in patient education to introduce ERAS principles at the patient level.

WEBSITE RESOURCE UPDATES

MSSIC made significant upgrades to the Provider and Patient resource section on the website (MSSIC.org/resources). These improvements were introduced and demonstrated on the April 17th MSSIC collaborative-wide meeting and continue to be updated to meet consortium needs.

ACS PARTNERSHIP

MSSIC has partnered with the American College of Surgeon's quality program, "Strong for Surgery" (tinyurl.com/4djnpc3y). Strong for Surgery empowers hospitals and clinics to integrate evidence-based, best practice, risk-assessment checklists into the preoperative phase of clinical practice for elective operations. The checklists are used to screen patients for potential risk factors that can lead to surgical complications, and to provide appropriate interventions to ensure better surgical outcomes.

DISCLAIMER STATEMENT: Although Blue Cross Blue Shield of Michigan and MSSIC work collaboratively, the opinions, beliefs and viewpoints expressed here do not necessarily reflect the opinions, beliefs and viewpoints of BCBSM or any of its employees.

Henry Ford leads new low back pain quality initiative

The Michigan Back Collaborative (MIBAC) is the newest BCBSM Value Partnership Collaborative Quality Initiative (CQI). It will focus on improving the quality of care and outcomes for patients with low back pain across the state of Michigan. Henry Ford Health System is the Coordinating Center for MIBAC.

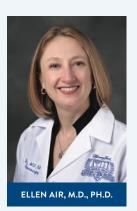
Initial participants in the collaborative will be "first contact providers" for low back pain – primary care physicians and chiropractors. Specialists, including physical medicine and rehabilitation, spine surgeons, ER physicians and physical therapists, will be involved in later stages of the collaborative.

Three "levels" of MIBAC participation are planned: provider training in evidence-based care pathways, collection of patient-reported outcomes using smartphone technology, and the full set of clinical data abstraction, registry-based data analysis and collaborative QI activities characteristic of all the other BCBSM-supported quality collaboratives.

More information is available on the website (mibac.org), including a recording of a live webinar that was presented to potential Physician Organization (PO) participants in February.



HENRY FORD NEUROSURGEON HELPS LEAD NEW PROFESSIONALISM POLICY DEVELOPMENT



Ellen Air, M.D., Ph.D., director of the Neurosurgery Residency Program at Henry Ford Health System and Chair of the American Association of Neurological Surgeons (AANS)/ Congress of Neurological Surgeons (CNS) Joint Section on Women in Neurosurgery, is co-author of a new Professionalism and Harassment Model Policy created to provide a code of ethical behavior that

promotes professional growth and the free exchange of ideas at neurosurgical meetings, educational courses, conferences and other sponsored events.

The policy was a collaborative effort by the American Academy of Neurological Surgery (AAcNS), AANS, American Board of Neurological Surgery (ABNS), CNS, and Society of Neurological Surgeons (SNS). Unlike events held at one's home institution, professional gatherings held at neutral locations often do not have clear rules and jurisdiction regarding professional conduct. The One Neurosurgery Summit Taskforce on Professionalism and Harassment, on which Dr. Air serves, has developed this foundational policy to establish common expectations for behavior and a unified roadmap for the prompt response to behavior that violates these expectations.

"Annual conferences, educational courses, and other meetings bring together a diverse community of individuals, yet also create a unique environment in which sensitivities vary by individual."

- ELLEN AIR, M.D., PH.D.

"Annual conferences, educational courses, and other meetings bring together a diverse community of individuals, yet also create a unique environment in which sensitivities vary by individual," Dr. Air says. "What may feel appropriate for one person based on beliefs or culture may not be appropriate for others gathered at the same event. Through this new policy, we aim to bring greater attention to everyone's responsibility for ensuring a safe and respectful space for education, and hope that other medical organizations will establish their own meeting and conference policies."

The new policy – which was co-published in Neurosurgery (PMID: 33755153) and in The Journal of Neurosurgery (PMID: 33761456) – also sets forth expectations of host organizations to ensure the code of ethical behavior is followed and to provide a procedure for investigating complaints. It requires the participating organizations to adopt their own codes of ethics that will be consistent with the Professionalism and Harassment Model Policy.



DETROIT STROKE CONFERENCE: NOVEMBER 2021

The Henry Ford Neuroscience Institute is pleased to host the 2021 Detroit Stroke Digital Conference from 8 a.m. to 4:30 p.m., Wednesday, Nov. 3. We are busy finalizing our agenda and topics for this live, virtual event. For the latest information, visit HenryFord.com/DetroitStrokeConference.

HENRY FORD TO HOST ANNUAL SNS IN MAY 2022

The Henry Ford Neuroscience Institute is planning exciting experiences and insights as we gear up to host the annual Society of Neurological Surgeons Annual Meeting in Detroit from May 21-24, 2022. Further details will be shared with members later this year.

HENRY FORD FIRST IN U.S. TO OFFER NEXT GENERATION DBS SYSTEM FOR PARKINSON'S

The Parkinson's Disease and Movement Disorder Center at Henry Ford Health System was the first in the United States to offer a new FDA-approved device to help treat the symptoms of Parkinson's disease. Neurosurgeon Jason Schwalb, M.D., surgically implanted the Vercise Genus™ Deep Brain Stimulation (DBS) System, which stimulates a targeted region of the brain through implanted leads that are placed in the brain. The leads are powered by a device called an implantable pulse generator, which sits under the skin in the chest.

Over the past 25 years, more than 160,000 DBS systems have been surgically implanted in patients worldwide to help treat movement disorders, such as Parkinson's disease. The new Vercise system, which is the fourth generation of the platform and received FDA approval in January 2021, is small and thin, and allows patients to safely undergo MRI scans, when certain conditions are met.

When the Vercise Genus DBS System is turned on, the implanted pulse generator sends a pre-determined program of mild electrical impulses to stimulate the brain. Unlike traditional DBS systems that are built from pacemaker technology, the Vercise technology is developed from a foundation of cochlear implant technology and the precise stimulation of auditory nerves it uses to replicate hearing.





RESIDENT NEWS

Highlighting our two new neurosurgical residents

Henry Ford draws strong candidates for our neurosurgical residency program, and next year is no exception. The two residents who matched with us are both already accomplished in several ways, including publications.

ANISSE CHAKER



Anisse earned his B.A. from Vanderbilt in Neuroscience and his M.D. at University of Illinois at Chicago. He won several awards in medical school including the Silver Scalpel Award. He received the Dr. C.M. Craig Summer Research Fellowship and was named the Class of 2021 James Scholar for his work on exosome delivery for brain and spinal injury.

PRANISH KANTAK



Pranish earned his B.S. from Lehigh, his MPH at University of North Carolina and his M.D. at University of North Dakota. He is a NERF (Neurosurgery Education and Research Fellowship) awardee. His work using optogenetics to understand dopaminergic control of reward-seeking behaviors has been published in Cell, Nature Communications and PNAS.



NEW CANCER PAVILION

Henry Ford Cancer Institute - Detroit: A new home for hope

The Henry Ford Cancer Institute – Detroit brings together the most advanced, patient-centered cancer treatments, clinical trials and research, and enhanced support services.

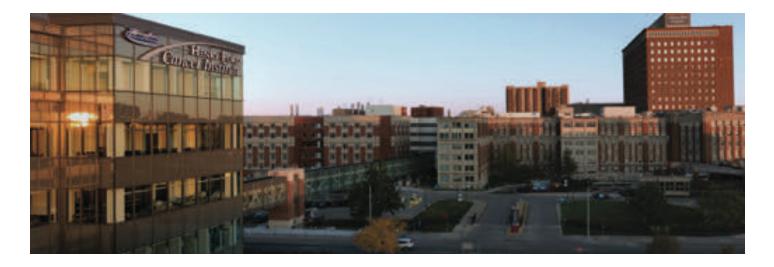
For patients, this historic investment brings to life a transformative care pathway that we have developed, where our medical, radiation and surgical oncologists, genomics and clinical trials experts and other specialists come together in disease-specific clinics.

This approach creates a truly seamless experience that's unique to each patient's cancer journey. As the new "hub" for our Cancer Institute services, we ensure seamless connections to our additional cancer care facilities

throughout southeast and south central Michigan.

"There has never been a better time to offer the kind of hope that is built into the very walls of this new cancer pavilion," notes Steven Kalkanis, M.D., CEO, Henry Ford Medical Group and Chief Academic Officer, Henry Ford Health System.

"The bridge that connects the cancer pavilion to Henry Ford Hospital is a symbolic testament and visual affirmation of our roots in innovation and world class patient care. In 1925, some of our founding physicians introduced the region's first cancer research program. From there, we've soared to extraordinary heights – introducing many world-first advancements in cancer research and treatment."



SYNAPSE - SUMMER 2021



FEATURES OF THE 187,000 SQUARE FEET, SIX-FLOOR FACILITY INCLUDE:

- Disease-specific tumor boards, along with molecular tumor boards, where every patient is presented
- The Hermelin Brain Tumor Center and 13 other disease-specific clinics, where comprehensive care teams come to the patient, bringing multidisciplinary care to new levels
- OncoStat Clinic for same day urgent care
- Clinical Trials Office, staffed with research nurses, to provide patients access to the latest clinical trials
- The most advanced imaging technology for diagnosis and treatment planning, including a fixed PET CT and MRI
- A healing environment with art and music therapy, natural light throughout and supportive services, including nurse navigation, financial counseling, social work, genetic counselors, cancer nutritionists, psych-oncology and integrative medicine services
- A skywalk connection to Henry Ford Hospital

Henry Ford activates two world-first treatments

Henry Ford Cancer Institute is the first site in the world to activate two new treatments for glioblastoma (GBM), the deadliest form of brain cancer, as part of a patient-centered adaptive platform trial known as GBM AGILE (Glioblastoma Adaptive Global Innovative Learning Environment).

Led by Global Coalition for Adaptive Research (GCAR), GBM AGILE tests multiple therapies for patients with newly diagnosed and recurrent GBM. Henry Ford Cancer Institute was first-in-the-world to enroll a patient in GBM AGILE when enrollment began in 2019.

"We are excited for this major step forward in the GBM AGILE trial, and especially for the hope it provides those battling glioblastoma brain cancer," says Tom Mikkelsen, M.D., principal investigator for GBM AGILE at Henry Ford Cancer Institute, and medical director of the Precision Medicine Program and Clinical Trials Office at Henry Ford Health System. "Through global collaboration, GBM AGILE is making it possible for some of the world's foremost experts in glioblastoma research and treatment to collaborate and advance the pace at which scientific and clinical breakthroughs can be achieved."

After opening at Henry Ford Cancer Institute, the two new interventions – VAL-083 from Kintara Therapeutics, Inc., and paxalisib from Kazia Therapeutics Limited – will subsequently open at more than 35 trial sites across the United States, with additional global sites in Canada, Europe and China to follow. VAL-083 is being evaluated in all three glioblastoma patient subtypes: newly diagnosed methylated MGMT, newly diagnosed unmethylated MGMT and recurrent. Paxalisib is being evaluated in newly diagnosed unmethylated and recurrent glioblastoma.

VAL-083 is a "first-in-class" small molecule that has been studied in more than 40 Phase I and Phase II clinical trials in multiple indications sponsored by the National Cancer Institute.

Paxalisib is a small molecule inhibitor of the PI3K / AKT / mTOR pathway. The PI3K pathway appears to be disordered in more than 85% of cases of glioblastoma, making this pathway a high-potential target for new glioblastoma therapies.





Robotic spine surgery: Greater accuracy and control

Robotic-assisted spine surgery has a long history. However, it's only been in recent years, as both robotics and the related navigation technology have advanced, that these procedures have become increasingly used in fusion surgery, particularly for low back pain.

"Robotics is a logical extension of navigation," says Victor Chang, M.D., neurosurgeon and co-director of minimally invasive and deformity spine surgery at Henry Ford Health System. "If you have navigation to show you where your screws should go and real-time feedback on the patient's anatomy, this can greatly assist you in surgery."

The evolution in spine care in recent years (see related story on p. 10) has also been driven by a greater knowledge of the spine itself.

"We have a greater appreciation of sagittal balance and achieving good alignment, particularly in the lumbar spine," Dr. Chang says.

ROBOTIC SPINE SURGERY UNDERUTILIZED

While the majority of patients with low back pain don't need surgery, one challenge is convincing those who do. "We see people who have had issues for a while," Dr. Chang says. "Sometimes even when surgery is recommended, they dismiss it due to the misconception that spine procedures have to be heavily invasive."

However, in many degenerative cases, patients only need a level 1 or 2 thoracolumbar fusion, which can make a significant difference in their symptoms and quality of life.

ROBOTIC-ASSISTED SCREW PLACEMENT

Currently, all spinal fusion surgery requires placing pedicle screws. Any of these procedures can be performed with robotic assistance. Henry Ford's team performs these procedures with the ExcelsiusGPS®, the most advanced robotic spine technology available. It offers several advantages over previous systems, including improved,

Spine Prehab helps prepare patients, improve surgical outcomes

Our presurgical Spine Prehab program is designed to prepare patients for their surgical experience, inpatient stay and postsurgical spine therapy. One key element is increasing a patient's level of aerobic activity and strengthening core muscles prior to surgery. This improves surgical outcomes by decreasing pain, improving mobility and helping them return more quickly to a normal routine. The program also provides comprehensive information and in-person or online video instructions from experts on everything from ways to safely conduct activities of daily living after surgery to brace demonstrations.



Before Surgery



Day of Surgery



Initial Recovery



Pain Expectations & Management



Therapy



Transitioning Home

"We're heavily focused on clinical trials and research. We rely on our public health sciences department for analytics and are constantly looking for ways to innovate and optimize our spine care."

- VICTOR CHANG, M.D.

automated accuracy using GPS technology; automatic compensation for patient movement; reduced risk of unnecessary tissue damage; little to no radiation exposure for OR team and patient; safer, more consistent and smaller incisions; faster recovery times; and reduced risk of postoperative pain and complications.

COORDINATED SPINE TREATMENT

While robotic-assisted procedures can help encourage better outcomes, this is just one aspect in Henry Ford's multidisciplinary approach.

"From anesthesiology and radiology, to physical medicine and rehabilitation, integrative medicine services and a spine prehab program (see box at left), we incorporate a full breadth of care," Dr. Chang says. "We're also heavily focused on clinical trials and research. We rely on our public health sciences department for analytics and are constantly looking for ways to innovate and optimize our spine care."

VIRTUAL CARE

During COVID-19, the number of patients seen virtually increased, in part due to patients' fear of coming to the hospital and getting the virus. In addition, in recent years, the Henry Ford spine team has expanded its robotic-assisted treatment to reach more patients outside of the metro Detroit area.

"I have patients who travel a long distance, from remote parts of the state or out of state," Dr. Chang says. "They're interested in the robotic procedures, but don't want to travel and go through the initial steps to even see if they're a candidate. In some cases, I never meet them in person until the day of the surgery. We handle everything else virtually, including consultation, imaging and treatment recommendations."



PATIENT CASE STUDY

Firefighter back to leading his team after robotic procedure

Last year, I treated a 30-year-old man who came in for a second opinion for his low back pain and related symptoms. The patient presented with severe low back and left leg pain, and a foot drop. He had undergone two prior microdiscectomies.

THE DIAGNOSIS & PROCEDURE

Our team diagnosed him with severe degenerative disk disease and recurrent disc herniation, and robotic surgery was recommended. This approach allowed him to minimize functional recovery time. He had been off work because of his symptoms and wanted to go back to work as a firefighter eventually. He had been offered a more invasive procedure elsewhere, but wanted a minimally invasive approach. Surgery performed was an L3-4, L4-5 minimally invasive transforaminal lumbar interbody fusion with robotic assistance.

THE RESULTS & FOLLOW-UP

Initial outcome was near resolved leg pain, with an increase in strength. He eventually started physical therapy, underwent a work-hardening program and within six months postoperatively was back to firefighting at the same level as before. We will continue to follow him for two years after surgery.

VICTOR CHANG, M.D.

Co-director, minimally invasive and deformity spine surgery; vice chair of research; and co-director of the Michigan Spine Surgery Improvement Collaborative



The constant evolution of spine care: Q&A with Dr. Victor Chang



VICTOR CHANG, M.D.

FOCUS AREAS

- Back Pain
- Spine Diseases
- Neurotrauma
- Minimally Invasive and Robotic Spine Procedures
- Spine Outcomes
- Biomechanical and Motion Analysis Research

POSITIONS

- Co-Director, Minimally Invasive and Deformity Spine Surgery
- Vice Chair of Research
- Co-Director, MSSIC
- Clinical Associate Professor
- Senior Staff Neurosurgeor

Dr. Chang received Spine fellowship training at the David Geffen School of Medicine at the University of California – Los Angeles. In addition to his role as co-director of the Michigan Spine Surgery Improvement Collaborative, he serves as co-director of minimally invasive and deformity spine surgery and vice chair of research at Henry Ford. This spring, he performed his 100th robotic spine surgery procedure.

WHAT'S CHANGED IN SPINE CARE SINCE YOUR INITIAL TRAINING?

There's been a constant evolution with more minimally invasive techniques being introduced. We've focused both on reducing the morbidity of surgery and also decreasing the amount of time to get to functional recovery after surgery. We're thinking about the spine from a global architecture standpoint, how it aligns relative to the rest of the body.

WHY IS THERE A MISCONCEPTION THAT SPINE SURGERY ALWAYS HAS TO BE HEAVILY INVASIVE?

That reputation might have been deserved at some point, given that past procedures were more invasive. Things have advanced to a point where, now, patients are surprised to find out that they can be in quite a bit of pain from their condition, and the procedure can still be done on an outpatient basis.

WHEN DID YOU START PERFORMING ROBOTIC SPINE PROCEDURES

December 2019. Modern robotic spine treatments have only emerged in about the last five years. We were able to view the technology early on, but in the beginning it was pretty rudimentary. We acquired the Excelsius GPS a year after its release (see robotic spine feature on p. 8), and this was a game changer. It's been an integral part of the practice since then, and we employ robotassisted procedures for any thoracolumbar fusion that involves pedicle screws.

HOW DID IT FEEL TO PERFORM YOUR 100TH ROBOTIC SPINE SURGERY?

It's been exhilarating to see what's possible with this technology, and how you can change lives. Many people associate spinal fusion surgery with permanent disability, but with robotic-assisted minimally invasive surgery, patients can return to an active lifestyle or physically demanding career (see case study on p. 9).

HOW IMPORTANT IS RESEARCH TO ADVANCING SPINAL CARE?

The way we offer spine care is very different than 5-10 years ago, and our understanding is evolving quickly. We need research to validate the latest thinking, and to update older principles that have been taken as dogma before. But we also need to weigh how spine care is beneficial for patient outcomes, and how we can improve these. We address this in one of our clinical quality initiatives, MSSIC (see p. 3).

WHAT'S ON THE HORIZON FOR ADVANCED SPINE CARE?

Eventually, we may also be able to integrate robotics and its image guidance to help facilitate other minimally invasive spine approaches, to get real-time feedback on patient anatomy. This would also allow us to avoid the ionizing radiation that everyone is subjected to in the OR with the fluoroscopybased imaging that's currently used in these procedures.

10



Clinical Trials

The Henry Ford Department of Neurosurgery is active in clinical research, and is currently offering these prospective clinical trials as a treatment option. For more information about these or other current studies, please call (313) 916-1756.

BRAIN TUMORS

ABTC 1401: Phase 1 Dose Escalation and Drug Distribution Study of Oral Terameprocol in Patients with Recurrent High Grade Glioma

ABTC 1403: A Phase I and Pilot Study of the Effect of rhIL-7-hyFc (NT-I7) on CD4 Counts in Patients with High Grade Gliomas and Severe Treatment-Related CD4 Lymphopenia after Concurrent Radiation and Temozolomide

ABTC 1603: Phase I Study of Neoadjuvant GMCITM Plus Immune Checkpoint Inhibitor Combined with Standard of Care for Newly Diagnosed High-Grade Gliomas

ABTC 1604: Phase 0/I Study of AMG 232 Concentrations in Brain Tissue in Patients with Recurrent Glioblastoma and of AMG 232 in Combination with Radiation in Patients with Newly Diagnosed Glioblastoma and Unmethylated MGMT Promoters

ABTC-1701: Pilot Surgical PK Study of BGB324 in Recurrent Glioblastoma Patients

ABTC-1801: Phase I/II Study of BGB-290 with Temozolomide in Recurrent Gliomas with IDH1/2 Mutations

ABTC-1802: A Phase II Study of Binimetinib in Combination with Encorafenib in Adults with Recurrent BRAF V600-Mutated High-Grade Astrocytoma or other Primary Brain Tumor

AG881-C-004: A Phase 3, Multicenter, Randomized, Double-blind, Placebo-Controlled Study of AG-881 in Subjects With Residual or Recurrent Grade 2 Glioma With an IDH1 or IDH2 Mutation

BED-FLC-312: An Open-label, Single-arm, Single-dose, Prospective, Multicenter Phase 3 Study to Establish the Diagnostic Performance of F-Fluciclovine Positron Emission Tomography (PET) in Detecting Recurrent Brain Metastases after Radiation Therapy (REVELATE)

BMX-MBM-001: Safety Lead-In/Randomized Phase 2 Study of BMX-001 as a Therapeutic Agent for Treatment of Cancer Patients with Multiple Brain Metastases Undergoing Whole-Brain Radiotherapy

BTTC 17C0034 Pembro: A Randomized, Double Blind Phase II Trial of Surgery, Radiation Therapy plus Temozolomide and Pembrolizumab With and Without HSPPC-96 in Newly Diagnosed Glioblastoma (GBM) in Patients with Recurrent or Progressive Glioblastoma following Initial Therapy

CTSU EAF151: Change in Relative Cerebral Blood Volume as a Biomarker for Early Response to Bevacizumab in Patients with Recurrent Glioblastoma

DB102-01: A Randomized, Double-Blind, Placebo-Controlled Phase 3 Study of Enzastaurin Added to Temozolomide During and Following Radiation Therapy in Newly Diagnosed Glioblastoma Patients Who Possess the Novel Genomic Biomarker DGM1

GBM AGILE GLOBAL ADAPTIVE TRIAL MASTER PROTOCOL

MEK-NF-201: Phase 2b Trial of the MEK 1/2 Inhibitor (MEKi) PD-0325901 in Adult and Pediatric Patients with Neurofibromatosis Type 1 (NF1)-Associated Inoperable Plexiform Neurofibromas (PNs) that are Causing Significant Morbidity

NRG-BN003: Phase III Trial of Observation Versus Irradiation for a Gross Totally Resected Grade II Meningioma

NXDC-MEN-301: A Phase 3 Multicenter Study of Gleolan (Aminolevulinic Acid Hydrochloride) to Enhance Visualization of Tumor in Patients with Newly Diagnosed or Recurrent Meningiomas

OKN-007-IV-RMG-201: A Phase II Open-label Study Investigating the Efficacy, Safety, and Pharmacokinetic Properties of OKN-007 Combined with Temozolomide in Patients with Recurrent Glioblastoma

Orbus OT-15-001: A Phase 3, Randomized, Open-label Study To Evaluate the Efficacy and Safety of Eflornithine with Lomustine Compared to Lomustine Alone in Patients with Anaplastic Astrocytoma That Progress/Recur After Irradiation and Adjuvant Temozolomide Chemotherapy

IRB 9736: Functional Assessment of Cancer Therapy – Meningioma (FACT-MNG): Tumor Site Specific Web-Based Outcome Instrument for Meningioma Patients

IRB 9936: Validity and Reliability of Self-Reported Karnofsky Performance Status

IRB 10722: NeMeRe, a Multi-Institutional Retrospective and Prospective Registry of Neoplastic Meningitis in Adults

EPILEPSY

IRB 10701: Stereotactic Laser Ablation for Temporal Lobe Epilepsy (SLATE) Study

PAIN

IRB 12825: High-Frequency Nerve Block for Post-Amputation Pain: A Pivotal Study

IRB 14615: A Randomized, Sham-Controlled, Double-Blind Study of Vagus Nerve Stimulation for Moderate-to-Severe Rheumatoid Arthritis: The RESET-RA Study

SPINE

IRB 9165: Three-Dimensional Motion Analysis in Patients' Status Post Anterior Cervical Fusion and Cervical Disc Arthroplasty, a Clinical Study_ MOTION STUDY (Supported by the Mentored Clinician Scientist program of HFHS)

IRB 10912: Genetic Basis of Diffuse Idiopathic Sclerosing Hyperostosis (DISH)

IRB 12228: Postoperative Pain and Opioid Use Following Spine Surgery

IRB 13512: A Prospective, Single-center, Randomized, Intra-patient Controlled Study Evaluating OsteoStrand™ Plus Demineralized Bone Fibers versus ViviGen® Cellular Bone Matrix in Stand-Alone Anterior Lumbar Interbody Fusion

IRB 14318: A Prospective, Randomized, Single-center Study to Assess the Safety and Performance of MagnetOs Putty Compared to Autograft in Patients Undergoing Two-level Instrumented Posterolateral Lumbar/Thoracolumbar Fusion (PLF) The PROOF Study (MAG-920-023)

VASCULAR

IRB 11254: Decision Support System for Predictions of Aneurysm Rupture and DVT/VTE in Aneurysm Patients

IRB 14209: The Use of Near Infrared Spectroscopy in a Neuro-Intensive Care Unit

EDITORIAL: BY STEVEN KALKANIS, M.D.

Dr. Beverly Walters: A strong legacy at Henry Ford and in the global neurosurgical community

Ever since I had the honor of successfully recruiting Beverly C. Walters, M.D., MSc, FRCSC, neurosurgeon and clinical epidemiologist, to Henry Ford nearly a decade ago, she has served in our Department of Neurosurgery as the Director of Clinical Research within the neurosurgical resident education program.

Dr. Walters came to the department having retired from clinical practice in neurosurgery, but continuing her busy and wide-ranged practice in neurosurgical clinical epidemiology. As she retires at the end of this academic year, I reflect with immense pride, and awe, at her legacy in our department, in our profession globally and in the service of our patients.

A FOCUS ON EVIDENCE-BASED NEUROSURGERY

What Dr. Walters is probably best known for is her efforts in educating her fellow neurosurgeons – both peers and trainees – in evidence-based neurosurgical practice and publication. She completed her degree in Clinical Epidemiology, specializing in Design, Measurement and Evaluation at McMaster University under the mentorship of Dr. David L. Sackett, world-famous founder of Clinical Epidemiology programs at McMaster and Oxford, while carrying out a residency program in neurosurgery at the University of Toronto.

From very early on, Dr. Walters began writing in the surgical/neurosurgical literature on topics that had not previously been seen in the specialty's publications. Most recently, Dr. Walters, along with Dr. Stephen Haines, has posted a link online to 52 recommended papers about Evidence-Based Neurosurgery and Biostatistics: tinyurl. com/3k7hu2ba.

Related to her expertise in evidence-based neurosurgery, many people currently practicing do not remember that at one time, our specialty came very close to losing the right to provide pedicle screw fixation to neurosurgical spine patients. In a class action lawsuit launched against both the CNS and AANS, as well as several well-known neurosurgical spine surgeons, claims were made that no evidence existed



to justify the use of the devices then (and now) commonly employed in the treatment of spinal instability.

In federal court, Dr. Walters testified as an expert witness, explaining that, flawed as it was, the evidence currently available still constituted "evidence" for the use of pedicle screws, and her testimony was cited by Judge Bechtle in his judgement in favor of the defendants and denying the right to a class action suit. Although testifying as an expert, Dr. Walters refused payment from either organization or any of the other defendants in the lawsuit, citing her wish to avoid any conflict of interest with her testimony. This was also noted by those participating on both sides of the case as convincing with respect to her belief in the evidentiary nature of the literature available at that time. Without this testimony, the course of spinal neurosurgery would no doubt have been different. Of interest, Dr. Walters' pivotal role in this legal battle is encapsulated in the federal records of the case.

GUIDELINES AND PUBLICATIONS

Similarly, Dr. Walters is known as a guidelines "guru," having provided leadership and guidance in the development of neurosurgical and other related guidelines since the early 1990s. She was the founding chair of the AANS/CNS Joint Guidelines Committee, and kept that position for over 10 years (in various modified forms), an exception to the rules because of the needs of the organizations.

She has been a co-author – and methodological resource – for over 154 published guidelines, with hundreds of



Dr. Walters oversees a meeting of Henry Ford Neurosurgery's resident research-focused Journal Club.

recommendations. These included: the severe head injury guidelines (2000), the acute spinal cord injury guidelines (2002 and 2013), lumbar fusion guidelines (2005), surgical management of traumatic brain injury (2006), neurobehavioral sequelae of traumatic brain injury (2006), imaging in stroke (2009) and electrophysiological monitoring in spine surgery (2017). Her work in this area on behalf of organized neurosurgery earned her the Congress of Neurological Surgeons Distinguished Service Award in 2005.

Dr. Walters has over 240 publications in the medical literature, excluding books and book chapters. Many of them serve as exemplars of various types of study design so that her colleagues and residents have guides to follow in their own work. She is a co-author of the first case-control study in neurosurgery, the first meta-analysis, the first observer reliability study and one of the first randomized controlled trials. She, along with Dr. Mark Hadley, had the honor of being selected for publication in the Journal of Neurosurgery – Spine to celebrate the 75th Anniversary of the JNS publications.

EDUCATING THE NEXT GENERATION

Since the early 1990s, Dr. Walters has been involved in international educational efforts in neurosurgery. She began this work while still at the University of Toronto, when she brought Ukrainian neurosurgeons and neurosurgical residents from Kiev to observe and discuss neurosurgical treatment. Later, Dr. Walters began an intensive spine education program at the University of Zagreb in Croatia, where she has been a Visiting Professor for many years. She began this work by bringing key neurosurgeons from Zagreb to Brown University to observe contemporary approaches to anterior cervical spine surgery. Dr. Walters is still in demand as a speaker at neurosurgical conferences in Croatia, having now been to the country a total of 28

times. She continues in her post as Visiting Professor, is an honorary member of the Croatian Neurosurgical Society and has been given honorary citizenship of Dubrovnik.

It is likely that most neurosurgeons who know Dr. Walters are unaware of her seminal early activities centering on women in medicine. She was an early recipient of the Ruth Jakoby Lectureship of WINS (Women in Neurosurgery) and was one of the original founding members of that organization. Wherever she works, she serves as a special mentor to the women in the program, both faculty and residents. She listens to, she counsels, and she advocates for these women, while pressing them to provide their very best performance.

In the last few years in her position with residents in neurosurgery at Henry Ford, she has helped to achieve an exponentially greater level of publication on the part of residents and faculty – her primary goal. Dr. Walters is now retiring from her mentorship at Henry Ford, but her legacy will most certainly endure. We have created a special resident research award given at the end of each academic year, in her name. In addition, in the fall of 2021, Dr. Walters will be the first female neurosurgeon to receive the Founder's Laurel award from the Congress of Neurological Surgeons.



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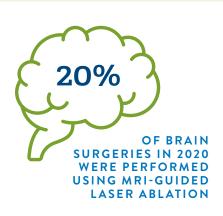


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