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A publication of Aurora Health Care

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*Aurora Neuroscience  
Innovation Institute®*

# Research corner

## Efficacy and safety of ofatumumab compared to teriflunomide in patients with relapsing multiple sclerosis (ASCLEPIOS 1)

A Randomized, Double-Blind, Double-Dummy, Parallel-Group Study Comparing the Efficacy and Safety of Ofatumumab Versus Teriflunomide in Patients With Relapsing Multiple Sclerosis (MS)

- Clinical trials identifier: NCT02792218
- Local principal investigator: Akram Dastagir, MD
- Research coordinator: Carol Halliday, RN, BA
- Sponsor: Novartis Pharmaceuticals
- Phase: III

## Breaking down barriers in brain cancer

With almost 20 years in the laboratory, senior research scientist Santhi Konduri, PhD, is on the cusp of translating her research into a clinical trial, providing a new investigational option in the fight against brain cancer.

Since joining Aurora Research Institute in July 2013, Dr. Konduri has focused on combining existing chemotherapy drugs with drugs approved for other indications in an attempt to increase survival and decrease toxic effects in hard-to-treat cancers.

Dr. Konduri and her team evaluated the FDA-approved drug disulfiram as part of a combination therapy that significantly decreased tumor cell growth in both pancreatic and breast cancers.

Applying these initial results, Dr. Konduri is testing combinations on brain cancer, specifically glioblastoma multiforme, a rapidly growing and aggressive brain tumor.

“Some of these patients are dying within six to nine months of their diagnosis,” Dr. Konduri said. “It is too difficult for many drugs to penetrate the brain, which makes them ineffective.”

Disulfiram can cross the blood-brain barrier. But it needs help.

Dr. Konduri found that disulfiram plus copper inhibited tumor growth almost 90 percent. With the addition of copper, less disulfiram is needed; high levels of disulfiram may cause neurotoxicities, which destroy normal brain cells.

Taking the research further, Dr. Konduri added the chemotherapy drug temozolomide, which is approved for treatment of glioblastoma multiforme.

She is currently working with neuro-oncologist George Bobustuc, MD, and other researchers at Aurora to determine what types of patients may be eligible for a clinical trial and most appropriate for this type of therapy. Principal biostatistician, Maharaj Singh, PhD, is aiding with statistical analysis.

Going forward, Dr. Konduri wants to use this type of collaboration to continue to develop new combination approaches to prevent or treat various tumor types. ■

## Aurora St. Luke's EEG lab accreditation

The Laboratory Accreditation Board of ABRET has granted the EEG Laboratory at Aurora St. Luke's Medical Center a five-year accreditation. This award is based on an evaluation of the technical quality of the EEGs performed in this lab and on a review of specific

policies from the Policy and Procedure Manual. The lab has been commended on their desire to promote excellence and competency in the department, which has had a positive influence. There are only 156 accredited labs in the country. ■

## We're excited to welcome new providers to our team



**Taylor Finseth, MD**, believes in the role of the physician as educator to empower patients and their caregivers to lead the best life possible. Dr. Finseth provides management of movement disorders, including Parkinson's Disease, tremor, dystonia, restless legs and deep brain stimulation programming; he also performs botulinum toxin (BOTOX) injections for dystonia, chronic

migraine and other conditions. He encourages the use of nonpharmacological treatments, such as exercise and other complementary modalities.

Dr. Finseth earned his medical degree at The Ohio State University College of Medicine in Columbus, and completed both his residency in Neurology and fellowship in Movement Disorders at the University of Colorado in Aurora. He is Board-certified by the American Board of Psychiatry and Neurology. In his free time, Dr. Finseth enjoys playing soccer, live music and spending time outside.

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**Aaron H. Bubolz, DO**, is skilled in procedures such as BOTOX, nerve blocks, trigger point injections, osteopathic medical therapy and EEGs. He also provides treatment for ailments such as headache, face pain, neck pain, nerve pain/neuropathy, seizures, stroke, multiple sclerosis, Parkinson's disease, tremors, ALS and myasthenia gravis. His

areas of interest include headache, epilepsy and stroke. Dr. Bubolz received his medical degree from Des Moines University, Iowa. He completed his residency in neurology at the University of Kansas. He also completed a fellowship in headache medicine at Mayo Clinic, Rochester, Minn.

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**Shawn Whitton, MD**, is skilled in providing video EEG, ambulatory EEG, evoked potentials, WADA testing, lumbar punctures, intraoperative/extraoperative mapping and vagus nerve stimulation. His areas of interest include epilepsy/seizures and neurology.

Dr. Whitton received his medical degree from Ross University School of Medicine, Portsmouth Dominica, West Indies. He completed his residency in neurology at the University of Missouri. Dr. Whitton also completed an epilepsy fellowship at the University of Michigan.

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**Willson H. Luy Tan, MD**, provides general neurology care for issues such as headache; movement disorders; epilepsy; behavioral neurodegenerative disorders, including Alzheimer's disease and other dementias; autoimmune disorders, including multiple sclerosis; cerebrovascular disorders, including stroke; neuro-otology; neuromuscular disorders; and sleep disorders.

Dr. Luy Tan also provides electroencephalography (EEG), electromyography (nerve conduction/EMG) lumbar punctures, skin biopsy for peripheral neuropathy, and therapeutic BOTOX injections (dystonias). His areas of

interest include neurodegenerative disorders, Parkinson's disease, epilepsy and cerebrovascular disorders.

Board-certified in neurology, Dr. Luy Tan received his medical degree from the University of the Philippines. He completed a residency in neurology at the University of Pittsburgh. ■

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# Raising awareness about MS



**By Dr. Lea Rayman**  
**Neurology**  
**Aurora Health Care**  
**(offices in Summit and Waukesha)**

Eating breakfast ... writing your grocery list ... walking to the car. Most of us do these activities without a second thought. But for a person with a movement disorder, the easiest daily living tasks can be challenging—or even dangerous. One well-known neurological disorder that often results in problem with movement is multiple sclerosis (MS).

MS is considered an immune-mediated disease in which the body's immune system mistakenly attacks myelin in the central nervous system. In multiple sclerosis, damage to the myelin, and to the nerve fibers themselves, interferes with transmission of nerve signals between the brain and spinal cord and other parts of the body.

MS is an unpredictable, often disabling disease. It affects women more than men and most commonly begins between the ages of 20 and 40.

Doctors aren't sure of the cause of multiple sclerosis. Most theories point to a virus, a genetic defect or a combination of both. Some scientists believe the disease is triggered by an unidentified environmental factor in a person who is genetically predisposed to respond.

## What are the symptoms of MS?

No two people have the exact same multiple sclerosis symptoms, but there are certain signs that are widespread, such as:

- fatigue
- numbness or tingling
- weakness
- walking problems
- vision problems
- dizziness
- bladder or bowel problems
- emotional changes
- balance problems

If you have multiple sclerosis symptoms, your doctor (a neurologist) will thoroughly evaluate you and may order a series of tests in order to make a diagnosis. He or she will:

- work to understand your full medical history
- conduct a neurologic exam

- perform other tests, including an MRI and spinal fluid analysis

These evaluation techniques will help your doctor make an accurate diagnosis. After receiving a diagnosis of MS, a neurologist can work with you to determine the best way to slow the destruction of your nerves' protective coating (myelin).

MS is an unpredictable, often disabling disease. It affects women more than men and most commonly begins between the ages of 20 and 40.

It's important to treat MS early on. The right MS treatment can significantly reduce symptoms and prevent them from becoming disabling. Multiple sclerosis treatment options include:

- injectable therapies
- oral pills
- IV or oral steroids
- anti-cancer drugs that suppress the immune system
- plasma exchange therapy (plasmapheresis)

## A comprehensive treatment plan for MS should include:

- education on managing MS symptoms
- recommended lifestyle modifications to enhance health
- information on health and community resources
- guidance on nutrition, exercise planning, physical therapy
- counseling for emotional issues

If you or a loved one is dealing with a diagnosis of MS, please seek medical care that treats the whole person—including the person's spiritual, physical and emotional needs. There are many support groups and patient education resources available for patients who have MS and their families. ■



# Couple's love transcends early-onset dementia

**Milwaukee Journal Sentinel**  
**By Crocker Stephenson**

Mike Grassel loves Julie Grassel and Julie loves Mike. That's the way it is and that's the way it has been for more than 30 years. And someday, Julie says, when they die and join each other in heaven, she will remind Mike of all that has happened.

Mike remembers some of it, though he remember less than he once did, and in the years to come he will remember less and less. As for now, he remembers meeting Julie on their first day of college, in a psychology class at University of Wisconsin-Milwaukee. As for now, he remembers how it quickly became clear to them both that they would live out their lives together. As for now, he can remember that in their sophomore year, as his mother was driving him to work on Interstate 94, a wheel came loose from an oncoming car, smashed through the windshield of their car and, without harming his mother, hit him in the head. When he regained consciousness a week later, he didn't know who Julie was.

Julie stayed at Mike's side as he re-entered his life. Relearned to walk. Relearned to talk. Relearned the simplest things. People asked Julie why. Even Mike asked her why. He was changed. The man she fell in love with was now a different man. She could go on with her life. Without him. No one would blame her.

Why not go on without him?

"I didn't even understand the question," Julie says. "I had made a commitment. Nothing changed for me."

In time, Mike returned to school and got his degree. He and Julie married, built careers, had two kids—Stephanie and Nick—and settled down in Brookfield.

And then, about seven years ago, Mike began to forget. Connections in his brain came apart. Well-worn neural pathways came to confusing dead ends. Where once there was something, there was now a gap. Mike was just 43 years old, and his doctor thought he might have early-onset Alzheimer's disease. The diagnosis was modified to progressive dementia, the result of his brain injury. But Mike's prognosis remained much the same as it had been for Alzheimer's. He will forget.

Early-onset Alzheimer's affects people younger than 65. The Alzheimer's Association estimates that about 5 percent of the more than 5 million Americans with Alzheimer's have an early onset, sometimes called younger onset, form of the disease.

Early-onset Alzheimer's  
affects people younger  
than 65.

Many people who sustain a severe head injury never develop Alzheimer's disease or dementia. More research is needed to understand the link. Mike and Julie have adjusted their lives so that Mike remains social and connected, and they are very active in the array of programs offered through the Southeastern Wisconsin Chapter of the Alzheimer's Association.

And to Mike's surprise, he has found a new passion: art.

On a recent evening, Julie drops Mike off at the Donna Lexa Art Center, located in a building behind the First Baptist Church in Waukesha. Donna Lexa offers art classes to students with special needs, like cerebral palsy, schizophrenia, brain injury, Down syndrome, stroke, autism and Alzheimer's. The classroom smells like glue and markers. A riot of work hangs on all the walls and covers virtually every horizontal surface. Dolls hang in a set of windows that run the length of a wall and look out on a park across the street.

A dozen students, and about half as many volunteers and staff, sit around a table in the center of the room. The mother of one the students, Mary Green, has died. In grief, Mary has drawn a portrait of her mother on a sheet of cardboard and cut it out. The cutout sits on the chair beside her. The room is already a blur of activity, but everything kicks up a notch when Mike comes in, wearing a T-shirt he's dyed with Packers green and gold. He goes around the room distributing hugs and compliments.

"That's really cool," he says. "Oh that's awesome. Wow, look at that!" The windows darken. Wind pushes against them and there's a lashing of rain. The classroom is warm and bright and loud. Mike puts music on his phone. He gets people to sing with him. He gets them to dance. Mike is working—more or less—on a landscape collage. By the time Julie comes to pick him up, he's only added a few things. The dominant feature of Mike's landscape is a rainbow. Rainbows appear in a lot of his work. They stand for hope, he says.

That's what he's about, he says. Even now. Especially now. Hope.

"I almost died," Mike says. "I was gone and then I was there." "It's all bonus," he says, and then he says it again. "It's all bonus." ■



## Burlington hospital volunteer saves herself

**The Journal Times Racine**  
**By Mark Feldmann**

Listening is a skill. Sometimes it's a lifesaver.

Just ask Burlington resident Dorothy Hakala, who worked as a guidance counselor in the Burlington Area School District for 30 years. It was her open ears and alert mind that helped her avoid a massive—and potentially fatal—stroke earlier this summer.

"It hit me a few days after it was all over that this was something that could have been really bad," said the 69-year-old. "It could have turned out very different."

After retiring in 2005, Hakala started to volunteer at Aurora Memorial Hospital of Burlington. She chairs the scholarship committee, helps families in the day surgery area, and participates in several healthy kids initiatives. She quickly became president of the volunteers at the hospital. As part of their service, Hakala and the other 160 volunteers review stroke education each April and remind themselves how to discern the symptoms of a stroke, said Kathy Galstad, Aurora's manager of ancillary services.

"Because we are a primary stroke center, we need to have our volunteers have a refresher on stroke signs every year," Galstad said. "We want to get that message out." Hakala paid close attention in the inservice, even though she was hearing the presentation for the eighth time. Never in her wildest dreams did she think the person she would save using her stroke knowledge would be herself.

### Sensing the symptoms

About two months after taking the stroke course, Hakala and her husband, John, were returning from Galena, Ill., where they were celebrating their 48th wedding anniversary. Hakala noticed her left arm went

completely numb for almost 10 seconds. "Looking back, I remembered feeling some tingling sensation, but I figured it was probably nothing," she said. "But this time it was so heavy and limp."

Recalling her stroke training, Hakala surmised she might be having a stroke. The couple drove directly to the Midwest Medical Center in Galena, where she was assessed in the emergency room and told she was right: She had experienced a transient ischemic attack (TIA), where blood flow to part of the brain is blocked or reduced by a clot.

The emergency room physician in Galena stabilized Dorothy and sent her home, but told her she should see her primary care physician immediately upon her return for more tests. She did the next day. She underwent several tests during the next five days. Doctors discovered that one of her arteries was almost 95 percent blocked. "There was only a trickle of blood flowing," she said. "The doctors told me that I could have had a massive stroke at any time."

### Surgery and recovery

On July 1, she underwent surgery to clear the blockage. Lief Erickson, a surgeon who specializes in vascular and laparoscopic surgery, performed the four-hour operation. She went home the next day, and three weeks later, returned to the hospital to volunteer.

"I feel very lucky and very blessed," Hakala said. "I have a strong faith and I believe God still has work for me to do."

For Hakala, finding out she had severe artery blockage was a shock. "I had no idea," she said. "I think I'm a pretty healthy person and I stay active. But so many people ignore symptoms. Your body will send you signals. When it does, it's usually trying to tell you something." ■

# B.E.F.A.S.T. is an easy way to remember the sudden signs of stroke



**Balance**



Do you have sudden loss of balance or coordination?



**Eyes**



Is your vision blurred? Do you have double vision or sudden trouble seeing out of one or both eyes?



**Face**



Can you smile? Does one side of the face sag or droop?



**Arms**



Can you raise both arms? Or does one arm drift downward?



**Speech**



Is your speech slurred or strange-sounding? Can you repeat a single sentence?



**Terrible Headache**



Sudden onset of a terrible headache or “the worst headache of your life.” Every minute counts! Call 9-1-1 immediately if you are experiencing any of these symptoms.

# Initial experience with a robotically operated video optical telescopic-microscope in cranial neurosurgery: feasibility, safety, and clinical applications

**Lior Gonen, MD; Srikant S. Chakravarthi, MD; Alejandro Monroy-Sosa, MD; Juanita M. Celix, MD, MPH; Nathaniel Kojis, Maharaj Singh, PhD; Jonathan Jennings, MD; Melanie B. Fukui, MD; Richard A. Rovin, MD' and Amin B. Kassam, MD**

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Technological innovation is an important driver in the development of new medical procedures and surgical techniques. The concept of robotics and integration especially has been a recent topic of interest in the surgical realm, with an effort to create more efficient operative platforms (6, 13).

The development of surgical robotic devices is founded on the principle of a human-machine interface, which is integral to the definition of a robot. By programming an integrated computer unit, this platform can be referred to as human-computer-machine interface. We consider surgical robotics in the following three broad classifications:

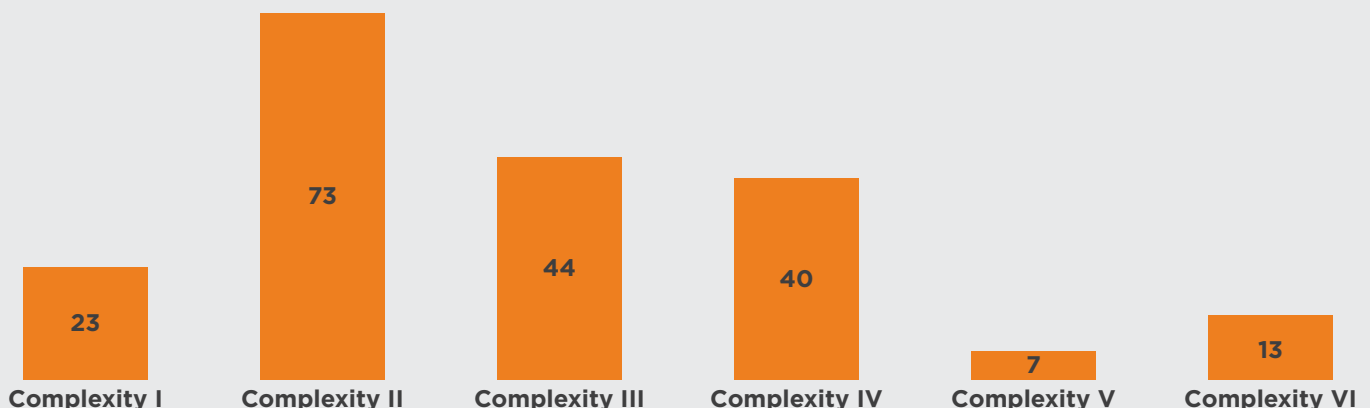
- Detectors are robotic devices that enhance optical visualization (i.e., equivalent to the human eye)
- Effectors are robotic devices that enhance dexterity, maneuverability and scale motion (i.e., equivalent to the human hand)
- Integrative/intelligent robotic devices capture information through iterative processes and are able to predict and define a series of steps based on this “learned information” (i.e., equivalent to the human brain)

Explicitly, detector, effector and integrative systems may also be referred to as “robotic eyes,” “robotic hands,” and the “robotic mind,” respectively.

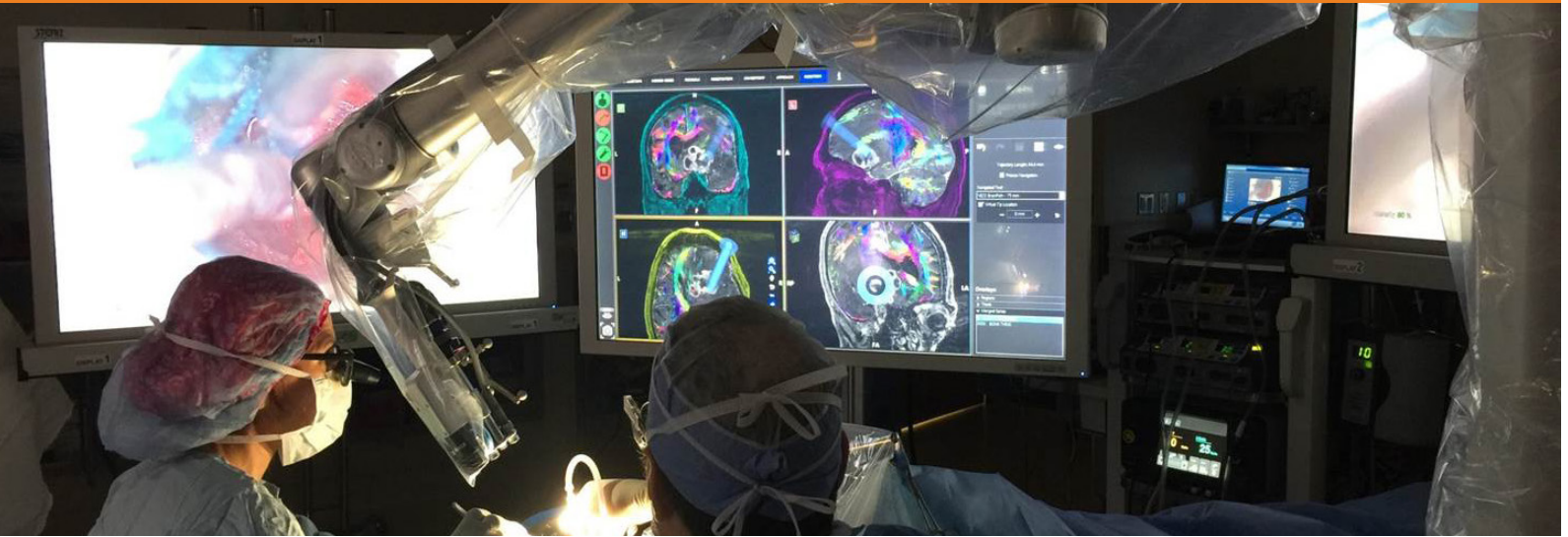
Historically, interest in surgical robotics has been primarily focused on effector robots for the purposes of enhanced dexterity and superior micromanipulation. Such devices have been recently introduced into other surgical subspecialties (7, 10, 11, 21). However, as noted by Peter Jannetta in a personal communication, one of the first neurosurgeons to document and integrate the microscope into neurosurgery in 1968, “... the hand cannot perform if the eye cannot see ...” (25). This may have been why the development of effector robots in neurosurgery has been profoundly limited; specifically, inadequate visualization has been a rate-limiting step. In other words, the enhanced maneuverability that might be achieved by effector robotic devices would only become valuable once the visualization scale demands it. Therefore, the first step toward a meaningful integration of robotics into neurosurgery should focus on the detector system, followed by the effector.

Enhanced visualization represents the very essence of microscopy (from the Greek mikros, “small,” and skopein, “to look”). This can occur with binocular visualization with conventional stereoscopic microscopes or other alternative systems (18, 28). In this report, we present the application of a novel detector system, namely, the robotically operated video optical telescopic-microscope (ROVOT-m; BrightMatter Servo System, Synaptive Medical). Specifically, within this optical chain, three individual components were designed in an attempt to leverage the synergistic performance of the overall chain:

## DISTRIBUTION OF THE FIRST 200 PATIENTS REGARDING THE COMPLEXITY OF THE CASE







*The operating room setup for the ROVOT-m. As shown, the 5 optical chain components include the optical payload (1), light source (2), camera (3), holder (4), and display monitor (5). In this specific case, the setup was designed for a right-sided lesion. The general setup principles are applied, and include the following: 1) The position of both the robotic arm and its base depends on the location of the pathology and the resultant patient positions. In our experience, the robotic arm is typically positioned on the ipsilateral side of the lesion, with its base placed at the patient's hip level. 2) All joint angles are initially placed at 90° to allow for maximum unencumbered movement without creating singularity (i.e., locking the joints). 3) The operating room setup must provide the surgeon and assistants with an unobstructed view of the monitors that display the surgical view. We use at least 2 high-definition display monitors that, as a default, are positioned on the opposite side of the robotic arm unit: one monitor directly in front of the surgeon and the other at a slight angle to allow for "stereoscopic" input with optics and navigation. 4) The image navigation guide system is positioned on the contralateral side of the robotic arm to allow for visualization.*

- The payload: telescopic microscope (BrightMatter Vision). This is an exoscope, distinct from existing standalone exoscopes, in that it is purpose-built for the ROVOT-m.
- The navigation system: (BrightMatter Guide). This system creates an automated human-machine interface, tracking the relative position of the payload and a series of instruments within the operative field.
- The positioning system: automated holding robotic arm (BrightMatter Drive). This system uses the computer-interfaced global positioning system to automatically and robotically position the payload.

As a feasibility-only study, there are three objectives of this report: to describe an initial experience in cranial neurosurgery with the ROVOT-m, to assess the feasibility and safety of this system in cranial applications, and to describe the incremental experience needed to overcome the associated learning curve.

## Objective

The move toward better, more effective optical visualization in the field of neurosurgery has been a focus of technological innovation. In this study, the authors' objectives are to describe the feasibility and safety of a new robotic optical platform, namely, the robotically operated video optical telescopic-microscope (ROVOT-m), in cranial microsurgical applications.

## Methods

A prospective database comprising patients who underwent a cranial procedure between April 2015 and September 2016 was queried, and the first 200 patients who met the inclusion criteria were selected as the cohort for a retrospective chart review. Only adults who underwent microsurgical procedures in which the ROVOT-m was used were considered for the study. Preoperative, intraoperative and postoperative data were retrieved from electronic medical records. The authors address the feasibility and safety of the ROVOT-m by studying various intraoperative variables and reporting perioperative morbidity and mortality, respectively. To assess the learning curve, cranial procedures were categorized into six progressively increasing complexity groups. The main categories of pathology were I) intracerebral hemorrhages (ICHs); II) intraaxial tumors involving noneloquent regions or noncomplex extraaxial tumors; III) intraaxial tumors involving eloquent regions; IV) skull base pathologies; V) intraventricular lesions; and VI) cerebrovascular lesions. In addition, the entire cohort was evenly divided into early and late cohorts.

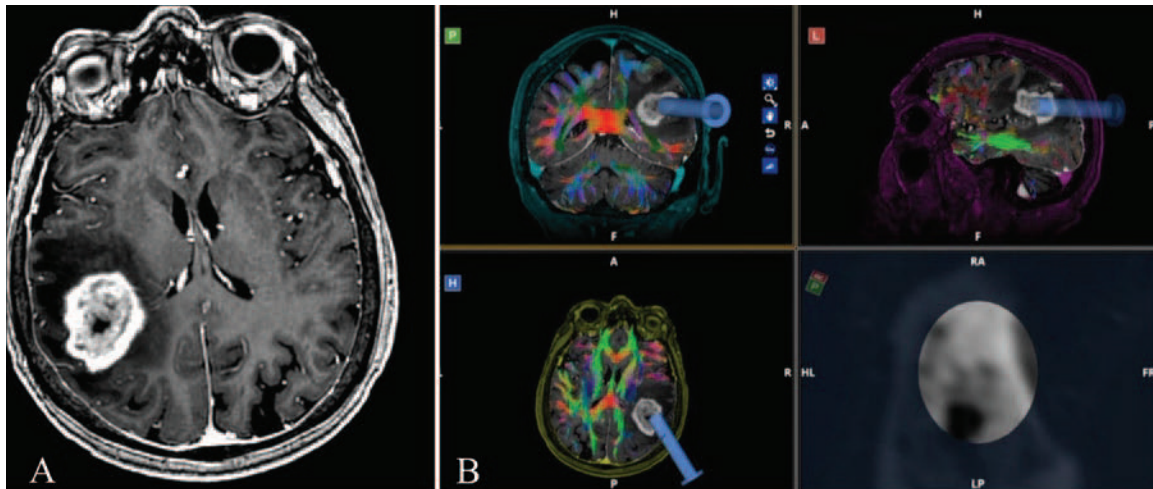
## Results

The patient cohort comprised 104 female (52 percent) and 96 male (48 percent) patients with a mean age of 56.7 years. The most common pathological entities encountered were neoplastic lesions (153, 76.5 percent), followed by ICH (20, 10 percent). The distribution of cases by complexity categories was 11.5 percent, 36.5 percent, 22 percent, 20 percent, 3.5 percent, and 6.5

*(continued on page 10)*

# Initial experience with a robotically operated video optical telescopic-microscope in cranial neurosurgery: feasibility, safety, and clinical applications (continued)

(continued from page 9)



Resection of a right parietal glioblastoma (Category II; corresponds to Video 2). A: Preoperative axial Gd-enhanced T1-weighted MR image showing a right parietal glioblastoma with vasogenic edema. B: Intraoperative photographs showing the trajectory of the port (B), which was designed preoperatively to avoid violating neural tracts in the vicinity of the lesion, and the portal view.

percent for Categories I, II, II, IV, V and VI, respectively. In all 200 cases, the surgical goal was achieved without the need for intraoperative conversion. Overall, the authors encountered three (1.5 percent) major neurological morbidities and six (3 percent) 30-day mortalities. Four of the six deaths were in the ICH group, resulting in a 1 percent mortality rate for the remainder of the cohort when excluding these patients. None of the intraoperative complications were considered to be attributable to the visualization provided by the ROVOT-m. When comparing the early and late cohorts, the authors noticed an increase in the proportion of higher-complexity surgeries (categories IV–VI), from 23 percent in the early cohort to 37 percent in the late cohort ( $p = 0.030$ ). In addition, a significant reduction in operating room setup time was demonstrated ( $p < 0.01$ ).

## Conclusions

The feasibility and safety of the ROVOT-m was demonstrated in a wide range of cranial microsurgical applications. The authors report a gradual increase in case complexity over time, representing an incremental acquisition of experience with this technology. New adopters of the robot system should anticipate a learning curve of both setup and execution phases. Further prospective studies are required to address the efficacy of ROVOT-m. This system may play a role in

neurosurgery as an integrated platform that is applicable to a variety of cranial procedures.

**Full Article:** <https://thejns.org/doi/abs/10.3171/2017.3.FOCUS1712>

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