

# **Contents**



#### Introduction

| From the chairs                             | 4  |
|---|----|
| Oregon's only public academic health center | 5  |
| About the OHSU Brain Institute              | 6  |
| Neurological surgery                        |    |
| Focused ultrasound expands portfolio        | 8  |
| Movement disorders                          |    |
| Improving well-being in patients            | 11 |
| Cutting-edge wearable sensors               | 12 |
| Nerve center                                |    |
| Unique model of eight specialties           | 14 |
| Research highlights                         |    |
| Movement disorders                          | 18 |
| Stroke                                      | 20 |
| Pituitary disorders                         | 22 |
| Traumatic brain injury                      | 25 |
| Brain surgery education                     |    |
| Influencing national educational policy     | 28 |
| Faculty                                     |    |
| Department of Neurology                     | 30 |
| Department of Neurological Surgery          | 31 |
| Recent representative publications          |    |
| Neurology                                   | 33 |
| Neurological surgery                        | 35 |



# From the chairs

#### Dear colleagues and friends,

The pace of change in the neurosciences is staggering, despite the challenges of the pandemic. At OHSU, we're comfortable with setting that pace as we embrace innovation and challenge the status quo. Our focus on health and sciences creates a unique environment where new ideas take root and barriers continue to be broken.

Throughout the past year of pandemic fluctuations, our faculty provided leading-edge clinical care. Our latest innovation is bringing incisionless neurosurgery to Oregon as a surgical option for essential tremor.

Internally, we created an unprecedented multidisciplinary network to diagnose and treat peripheral nerve disorders and injuries - the OHSU Nerve Center. Externally, we provided collaborative leadership in creating consensus guidelines in pituitary disease, progressive supranuclear palsy and neurosurgical education.

Our research has a track record of transforming human health locally and globally. A few recent highlights include creating new preclinical models for movement disorders, investigating factors affecting outcomes in traumatic brain injury and setting new timelines for follow-up of incidental pituitary adenomas.

Through all this work, we are also educating the next generation of physicians, surgeons and researchers as well as improving diversity in medicine.

We are honored to share with you some annual highlights of how the OHSU Brain Institute is delivering breakthroughs for better health.

Hel. Lat lotten & Seller

Sincerely,



Helmi Lutsep. M.D., FAAN, FAHA Interim Chair and Professor, Neurology



Nathan R. Selden. M.D., Ph.D., FACS, FAAP Campagna Chair and Professor, Neurological Surgery

# Oregon's only public academic health center

Based in Portland, we have more than 1 million patient visits each year. We operate the top-ranked adult and children's hospitals in Oregon, and secure competitive research funding of nearly \$400 million. As a public corporation serving the best interests of Oregon and the region, we also provide services to the most vulnerable Oregonians as well as outreach that improves health in communities across the state.



**\$129M+** Funding focused on clinical trials

100/201 In 2021, OHSU disclosed 100 new inventions and

**#42 World's Most Innovative** OHSU ranks No. 42 on the *Reuters* 100:

**Top 20 Innovation Ranking** OHSU placed in the top 20 of *Nature's Index* 2017 institutions and universities worldwide.

#### **Facilities and employees**

19,136 Employees

**400 acres** OHSU owns and leases space beyond its campuses. Altogether, OHSU occupies more than 8.7 million square feet on about 400 acres.



#### **Education**

OHSU helps educate over 5,400 students and trainees each year.

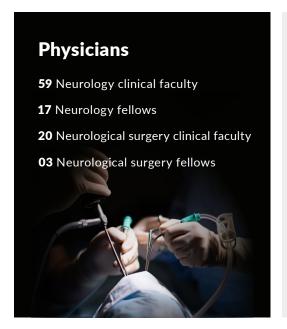
## **Community service**

OHSU has more than 200 community health care programs, reaching out to vulnerable groups in urban areas as well as underserved rural communities throughout the state. In 2021, OHSU had a community benefit contribution of \$522 million.



# **About the OHSU Brain Institute**

The OHSU Brain Institute is internationally recognized for its work in neuroscience, translational research and clinical studies, and provides the most comprehensive care for neurological conditions in our region.





# Research and funding

#### 300+

Neuroscience researchers

#### \$124M

Current neuroscience research funding

## Partnerships and clinical collaborations

As Oregon's only academic medical center, we work with hospitals around the state to expand exceptional care to patients in their home communities.

#### Pediatric neurological surgery

Legacy-Randall Children's Hospital, Portland Shriners Hospital for Children, Portland

#### Adult neurological surgery

OHSU Health Hillsboro Medical Center VA Portland Health Care System

#### Adult neurology

OHSU Health Hillsboro Medical Center Adventist Health Portland St. Charles Medical Center, Bend VA Portland Health Care System



**Accreditations and recognitions** 

Ranked as a top 50 hospital for adult and pediatric

Level 4 Comprehensive Epilepsy Center (Adult and Pediatric)

One of 33 NIH Alzheimer's Disease Centers in the country





# Focused ultrasound expands portfolio of transformative therapies for tremor

OHSU has long been at the forefront of surgical interventions for movement disorders, including pioneering asleep deep brain stimulation (DBS) in 2011. In 2021, we took another leap forward by becoming the only resource between San Francisco and Seattle for focused ultrasound, an incisionless neurosurgery for the treatment of essential tremor and tremor-dominant Parkinson's disease.

"Tremor is not life threatening, but it can take away people's independence and quality of life," said Ahmed Raslan, M.D., FAANS, clinical director of the focused ultrasound program. "As a neurosurgeon, I'm excited to provide an alternative that can have such a meaningful impact without the standard surgical risks. This technology joins our existing spectrum of interventions for people who struggle with daily living tasks due to tremor."

Currently, OHSU offers this procedure for patients with <u>essential tremor</u> or tremor-dominant <u>Parkinson's disease</u>. Essential tremor is the most common movement disorder in the U.S., with an estimated 10 million people affected.

The brain is a high target area of research opportunity for focused ultrasound. As the only academic research center in our region, OHSU is developing clinical trials for additional applications of focused ultrasound in neurosurgery.

#### Focused ultrasound procedure

During the procedure, the patient wears a helmet fixed to a stereotactic frame. Through the helmet, cold water circulates around the scalp. To keep the patient motionless, pins secure the helmet. Our team provides a local anesthetic to patients for the placement of the pins. Patients are awake and responsive during the procedure.

The surgeon uses low-energy sonication to pinpoint the target, typically the ventral intermediate nucleus. This is a gradual, stop-start process that requires feedback and testing with the patient (e.g., drawing spirals or raising arms) to assess tremor improvement throughout the treatment. The surgeon also receives real-time feedback about temperature changes in the brain.

To ablate the target tissue, beams of ultrasonic sound pass through the scalp and skull, converging to create a tiny, discrete lesion. Patients see the improvement in tremor immediately.



Ahmed Raslan, M.D., FAANS,
Clinical director of the
focused ultrasound program



10M

People are affected by essential tremor — the most common movement disorder in the U.S.



Fewer than 100 centers worldwide offer focused ultrasound.



MR imaging provides real-time data during focused ultrasound procedure. OHSU is the only Oregon hospital to offer focused ultrasound for essential tremor and tremor-dominant Parkinson's disease.
(Photo credit: Insightec)

# About focused ultrasound

| Results           | Most patients have <b>70-80%</b> improvement in tremor within the same day of the procedure.                  |
|-------------------|---|
| Recovery          | Overnight hospital stay or potentially outpatient.  Most patients return to normal activity within a week.    |
| Tremor medication | Medication is weaned following surgery.   |
| Side effects      | Rare but possible side effects include temporary skin irritation, nausea and vomiting, weakness or imbalance. |
| Recurrence        | Tremor may recur in 15–20% of patients, but the procedure can be repeated.                                    |



# Improving well-being in patients with progressive supranuclear palsy

OHSU is one of 25 specialized centers in the U.S. and Canada treating this rapidly degenerative form of parkinsonism.

Researchers at OHSU joined a consortium of neurodegeneration specialists in North America to create a consensus document in 2021 on best practices around progressive supranuclear palsy (PSP). Contributors from OHSU included Marian Dale, M.D., M.C.R., and Martina Mancini, Ph.D., both assistant professors of neurology, and Jenny Wilhelm, D.P.T., NCS.

PSP is a rare but deadly disease, affecting six in 100,000 people with death in an average of seven years from its onset. Dale, who is also the director of the OHSU CurePSP Center of Care, highlights the ongoing challenges facing patients with PSP and their providers.

"We think it's underdiagnosed," she said.

"The symptoms of PSP get confused with
Parkinson's disease, but the pathology is
closer to Alzheimer's disease. It can take a long
time for many patients to get a diagnosis. An
astute physical therapist or ophthalmologist
might pick it up, but PSP gets missed a lot."

The consensus document highlighted many features of PSP, including its epidemiology, pathophysiology (and relationship with other neurodegenerative disorders), characteristic symptomatology and natural history. Additionally, the document provides guidance to clinicians regarding diagnosis and management of this difficult condition. Contributors emphasized early diagnosis and treatment as factors that can improve the outlook for patients. While there is no definitive disease-modifying treatment for PSP, early management with speech therapy, physical therapy and occupational therapy can be beneficial.

"It extends patients' longevity and well-being to be on the right regimen of symptomatic and supportive therapies early on," Dale said.

OHSU established the only CurePSP Center of Care in Oregon or Washington in 2019. The center coordinates patient care through a multidisciplinary team.



Marian Dale, M.D., director of CurePSP Center of Care



# 6 in 100,000

People are affected by progressive supranuclear palsy (PSP), a rare but deadly disease.



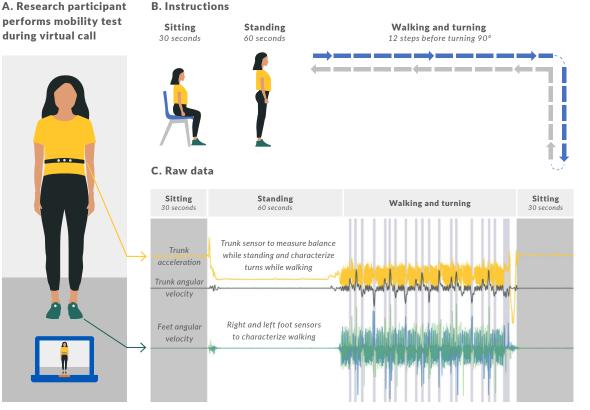
1 of 25

OHSU is one of 25 specialized centers in the U.S. and Canada treating PSP.

# **Cutting-edge wearable** sensors measure mobility during COVID-19 restrictions

The Balance Disorders Laboratory at OHSU is at the forefront of developing and implementing objective measures to quantify balance deficits in people with neurological disorders. Our team was among the first to demonstrate the feasibility of using wearable sensors to quantify gait and turning characteristics during daily life and in people's natural environments. The impact of this work continues to expand. During COVID-19, our lab actively enrolled new participants to our studies and provided rehabilitation treatment opportunities despite most in-person research being either limited or prohibited. Here are a few examples of virtual outreach utilizing these mobile technology innovations developed by APDM:

- Gait/mobility evaluations: In their homes, patients with Parkinson's disease wear inertial sensors on an elastic belt and inside special socks. They wear the sensors all day for a week to characterize normal mobility in daily life. Then the participants perform a short series of tasks while wearing the sensors during a secure video meeting with our providers.
- Clinical virtual exam: Certified assessors evaluate the severity of Parkinson motor symptoms from the MDS-Unified Parkinson's Disease Rating Scale exam performed over secure video. The lab is also actively working on predicting the clinical motor score with wearable inertial sensor data during a brief, prescribed task at home.
- Virtual vestibular rehabilitation: Physical therapists conduct the sessions while participants are wearing sensors for visual feedback about their head movements. While the patient does exercises in their home, the physical therapist can see the sensor data about the head movements in real time.



#### 90° turn

5 steps before turning around

180° turn follow path back to sit

#### Virtual gait and mobility

tests: During a video meeting, researchers watch Parkinson's disease patients perform a task with wearable sensors (Fig. B). Raw data collected by three sensors (Fig. C) characterizes the quality of balance, walking and turning in a very short test at home. Project initiated with 20 individuals, with the intention of expanding to 100-plus in the coming years.

# Nerve center

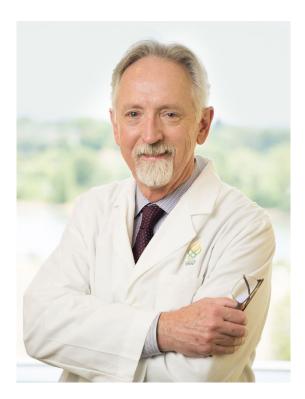
# Unique model of eight specialties streamlines treatment of complex nerve disorders

Patients come from across the U.S. for the expertise and advanced therapies available for nerve disorders and injuries at the OHSU Nerve Center.

"OHSU has created a multidisciplinary nerve center that may well be a unique model for other national institutions interested in the treatment of nerve disorders," said Kim Burchiel, M.D., FACS, professor and immediate past chair of the department of neurological surgery at OHSU. "It offers a high level of expertise while facilitating collaboration on the management of these complex conditions."

The OHSU Nerve Center streamlines care for patients, which can be critical for timely interventions and successful outcomes in nerve dysfunction. Patients come from across the U.S. for the expertise and advanced therapies available for all nerve disorders and injuries.

"OHSU has an unprecedented network that triages nerve problems into the appropriate provider team for diagnosis, medical management and, when necessary, surgical treatment," Burchiel said.



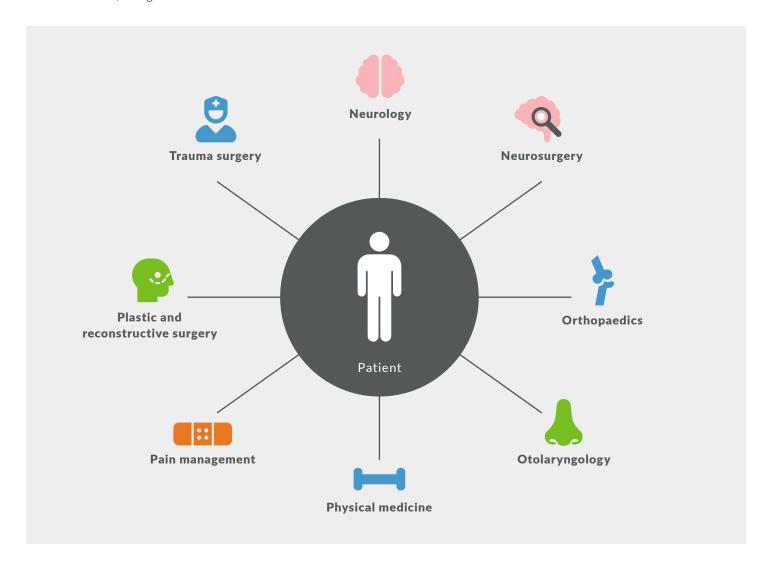
Burchiel is joined by neurological surgery
Assistant Professor Jos'Lyn Woodard and a
team of providers in the fields of orthopaedics,
otolaryngology, plastic and reconstructive surgery
and trauma surgery, who are experts in the most
advanced therapies and surgical techniques to
treat nerve disorders. Additionally, the team
includes pain experts and physical medicine
specialists that help maximize outcomes.

"Nerve tumors can occur anywhere. As a result, the anatomy and surgical approach to these is often complex, and not something that most surgeons are eager to treat. The benefit of the OHSU Nerve Center is the combination of experience and team approach to these lesions."

Kim Burchiel, M.D., FACS

#### The center's surgical options include the following:

- **Nerve repair surgeries:** The team employs exacting techniques needed to treat nerves and the delicate structures in the hands, face and other parts. These include nerve repair surgery to reattach two damaged nerve ends and nerve graft surgery that stitches a nerve between two damaged ends to serve as a bridge while the injured nerve heals.
- **Facial reanimation surgery:** This surgery can restore symmetry and bring a smile back to the face of a patient with acute or prolonged facial paralysis from nerve damage, a stroke or congenital paralysis and who may have been told nothing could be done.
- **Nerve transfer surgery:** OHSU surgeons are the only providers in Oregon to offer this innovative procedure, in which one end of a normal but less important nearby nerve is used to bypass a damaged nerve to restore function to an affected muscle.
- **Nerve tumor surgery:** Patients may have an undiagnosed noticeable mass, pain or numbness and weakness; a history of nerve tumors/neurofibroma; or even a family history. Some may be diagnosed with a singular tumor schwannomas, benign or cancerous.



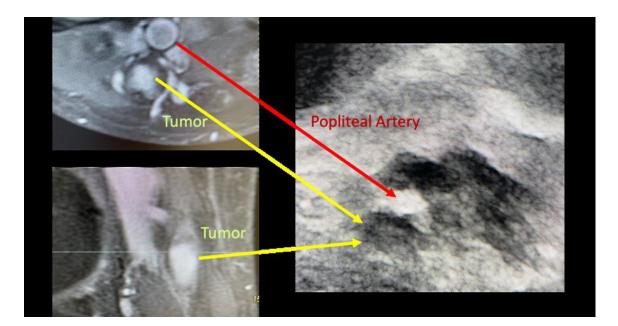


OHSU neurologist Nizar
Chahin, M.D., leads the
neuromuscular program
and has extensive experience
diagnosing and treating
patients with nerve disorders.



The OHSU Nerve Center offers medical, surgical and palliative treatments for all peripheral nerve disorders and injuries, including:

- Acute onset of neuropathies with uncertain etiologies
- Brachial plexus injuries
- Congenital nerve disorders
- Facial nerve disorders (Bell's palsy, blepharospasm, facial paralysis, facial synkinesis, hemifacial spasm, nerve disorders from head trauma)
- Hand surgery for quadriplegic patients
- Nerve entrapment (carpal tunnel, cubital tunnel)
- Nerve tumors (neurofibroma, schwannoma, malignant peripheral nerve sheath tumor)
- Other nerve conditions (amyloidosis, Lambert-Eaton myasthenic syndrome, Parsonage Turner syndrome, spinal muscular atrophy)
- Painful neuromas
- Penetrating and blunt trauma nerve injuries
- Peripheral neuropathies
- Phantom limb pain
- Quadriplegic/tetraplegic hand disorders
- Spasticity in upper and lower extremities



**A tumor** imaged by MRI and intraoperative ultrasound.



# Research highlights

#### Movement disorders

The OHSU Parkinson Center and Movement Disorders Program is committed to improving therapies for Parkinson's disease and all the diseases in our field through compassionate care, research opportunities and collaborations.

#### **Exploring connections between** digestion and erratic motor function

Delaram Safarpour, M.D., M.S.C.E.,

showed an association between medication. absorption and gastrointestinal transit times affecting levodopa efficacy in patients with Parkinson's disease. She presented her findings at the International Movement Disorders Society in September and was also honored with a Top 10 Abstract award from the XXVI World Congress on Parkinson's Disease and Related Disorders.

Safarpour compared 10 typical levodopa responders to 10 erratic responders. To track transit time, each participant took a SmartPill, a motility testing system that sends data to a wearable wireless device as it progresses through the whole gastrointestinal tract. A serum levodopa level was also measured every 30 minutes after taking the usual morning dose of levodopa.

The results showed a pattern of wide variation in transit time through the stomach and small intestine in both groups, which was more prominent among erratic responders.

"We were able to successfully measure transit time in all segments of the gastrointestinal tract in patients with Parkinson's disease," Safarpour said. "This study confirms the feasibility of a new technique that can be used in measuring gastrointestinal motility in Parkinson's disease."

Safarpour plans to work with the Balance Disorders Laboratory to continue the study using objective measurements to verify "on" and "off" fluctuations.

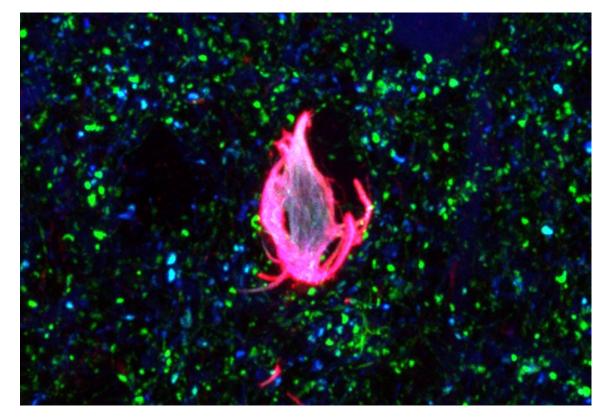




"Treating motility disorders in the gastrointestinal tract is an important step in improving the response to levodopa. Fewer fluctuations and 'off' episodes will improve quality of life for persons with Parkinson's disease."

Delaram Safarpour, M.D., M.S.C.E.

An OHSU study showed the feasibility of using the SmartPill in patients with Parkinson's disease. Future studies that take advantage of pro-motility medications will be able to rely on this technique. Photo credit: ©2021 Medtronic. All rights reserved. Used with the permission of Medtronic.



Composite image of Lewy bodies. OHSU's characterization of this preclinical model is excellent for identifying the initial location of Lewy pathology formation and propagation in vivo. It also allows careful study of peripheral-tocentral spread of Lewy pathology in vivo.

#### Increasing research possibilities with real-time brain data

Seeing Lewy body formation and resulting brain changes in real time opens new research pathways for exploring treatment strategies in Parkinson's disease and dementia with Lewy bodies. In 2020, Vivek K. Unni, M.D., Ph.D., developed a new transgenic model for the preclinical evaluation of potential therapeutics in both diseases. He uses a unique approach involving in vivo cranial imaging. The new model expresses human A53T alpha-synuclein fused to the green GFP protein and allows for rigorous study of the neurodegeneration associated with alpha-synuclein aggregation.

This model is already a promising tool for basic and therapeutic research. Unni used the model to study the function of specific kinase inhibitors in 2021. He will also use this model to investigate the synergies between alpha-synuclein and beta-amyloid in neurodegeneration, with support from a recent grant from the National Institutes of Health.

For next steps, Unni and Randy L. Woltjer, M.D., Ph.D. director of the Oregon Brain Bank, will evaluate the real-time interaction of these neuropathologies in Parkinson's disease, dementia with Lewy bodies and Alzheimer's disease. Unni serves as the interim director of the Jungers Center for Neurosciences Research, a collaborative effort of the Department of Neurology and the Vollum Institute at OHSU.



"By creating this new model, we are accelerating our ability to test new drugs for Parkinson's disease and dementia with Lewy bodies, hopefully hastening the day when we have our first treatment for these diseases that can stop them from progressively worsening."

Vivek Unni, M.D., Ph.D.

#### Stroke

The OHSU Stroke Program, created in 1979, was the first in the Northwest certified as a comprehensive stroke center. OHSU's telestroke program provides the most advanced lifesaving stroke response when time is critical, augmenting local care across Oregon and Southwest Washington.

#### Pivoting for the pandemic in stroke awareness

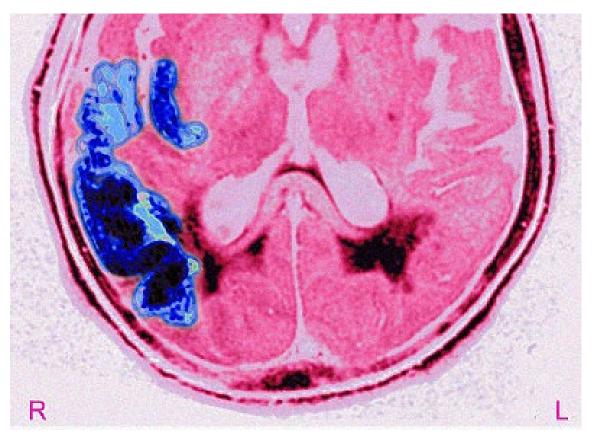
Hospitalizations for stroke declined 19.2% worldwide during the peak months of the pandemic in 2020 according to a <u>study</u> coauthored by <u>Helmi Lutsep</u>, M.D., FAAN, <u>FAHA</u>, a stroke specialist who also serves as interim chair of neurology. The retrospective study measured case volumes in the first three months of the pandemic in 187 comprehensive stroke centers across six continents.

"At OHSU, our volume declined 33% from the same three months a year earlier," Lutsep said. "Stroke didn't suddenly become less common in Oregon, but patients may have become more fearful of seeking medical attention in case they contracted SARS-CoV-2. We realized we needed to quickly pivot by raising public awareness about the consequences associated with lack of stroke treatment."



A worldwide study indicates that fewer people are seeking medical attention for stroke. Helmi Lutsep, M.D., FAAN, FAHA, a coauthor on the study from OHSU, emphasizes the need for broad public awareness of the signs of stroke.





OHSU prioritized outreach efforts, quickly initiating a BE FAST campaign in English and Spanish that included a short song of the acronym of symptoms: balance, eyes, face, arms, speech, time. The song aired on radio stations as well as on www.ohsu.edu/befast. Also at the website, people can download a poster illustrating the signs of stroke and a guide to preventing stroke targeted to women.

"Encouraging patients to recognize the signs of stroke and to get emergency medical treatment is the best way to prevent permanent disability and death at any time, but that education is even more critical to preserve stroke care in a time of crisis," Lutsep said.

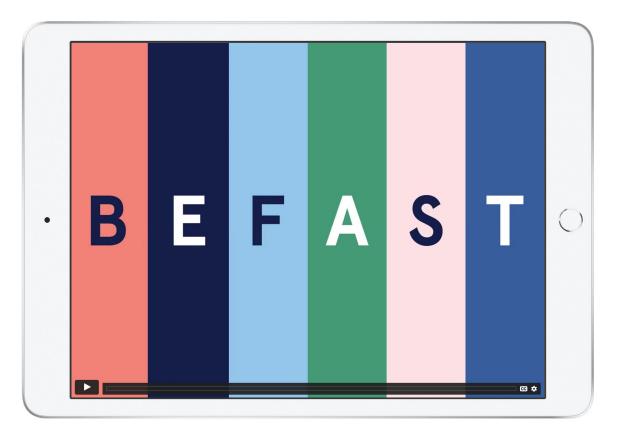
"An important goal of the outreach was to educate young people about stroke, as they may not recognize numbness in the hand or blurred vision as an emergency requiring immediate attention. Some asymptomatic young adults have strokes as their initial symptom of a COVID-19 infection."

Severe COVID-19 infections produce more blood clots than other virus-related illnesses, raising the risk of ischemic stroke.

"COVID-19 can drive stroke cases up, which makes the percentage decline in case volumes even more stark," Lutsep said.



OHSU is a DNV-GL Certified Comprehensive Stroke Center.



#### During the pandemic,

OHSU created a verbal and visual mnemonic to support stroke awareness and the importance of prompt medical attention.

in Neurosciences

#### **Pituitary disorders**

The OHSU Pituitary Center is a premier multidisciplinary program with high patient volume, fulfilling all criteria for a Pituitary Center of Excellence. The center's clinical observations and research are innovating and changing standards of care in neuroendocrinology and pituitary tumors. OHSU Pituitary Center Director Maria Fleseriu, M.D., FACE, is a world-renowned expert in this field, serving as a global primary investigator in several international clinical trials and as lead author of guidelines and other published works influencing diagnosis and treatment of these rare disorders.

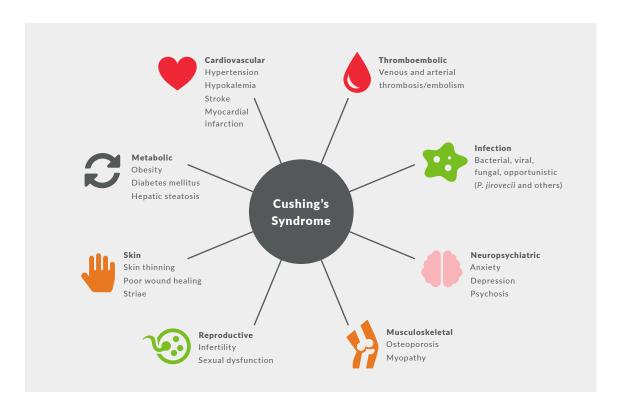
#### Establishing new international guidelines for Cushing's disease

Published in The Lancet D&E in October, lead author Fleseriu presented the consensus opinion regarding recommendations for use of laboratory tests, imaging and treatment options as well as

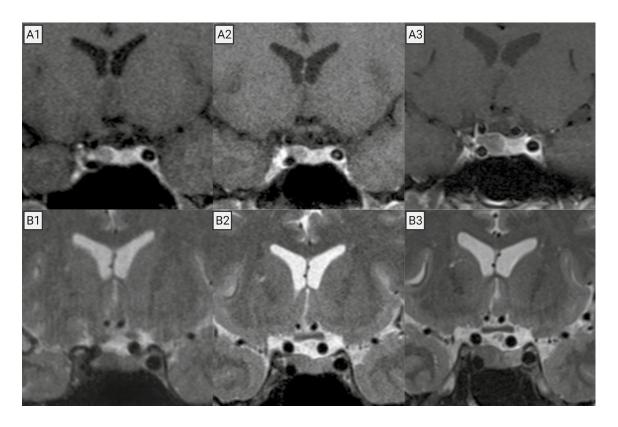
algorithms for both diagnosis and management of Cushing's disease (also known as Cushing's syndrome). The new guidelines also present key considerations for novel medical therapies.

"In the last decade, we have seen advances in novel screening and diagnostic modalities in addition to new treatments approved for use," Fleseriu said. "Much of the data and strategies for disease-related and treatment-related complications of Cushing's disease are new. We highlight the importance of treating complications in parallel with the cause of cortisol excess to improve patient outcomes and quality of life."

Fleseriu co-chaired the consensus workshop of the Pituitary Society that established these unified guidelines for Cushing's disease. OHSU endocrinologist Elena V. Varlamov, M.D., joined Fleseriu and more than 50 academic researchers and clinical experts from 13 countries and five continents in the work group meetings held in 2020.



The new guidelines update the standards of care for Cushing's syndrome, which can have systemic impact.



An MR image shows minimal change in nonfunctioning pituitary microadenoma over time.

#### Recommending extended intervals for imaging nonfunctioning pituitary microadenomas

Once thought to be rare, incidental pituitary tumors are being detected by advanced imaging more than ever before. As many as one in four people may have small pituitary adenomas without any symptoms. Most are benign but merit evaluation and monitoring. In the largest single-center study, consisting of 347 patients, Fleseriu, Varlamov and Ashley Han, a medical student at the OHSU School of Medicine, concluded that the follow-up timeline for MR imaging of nonfunctioning pituitary adenomas can be extended to up to three years as opposed to the annual one previously recommended.

Exceptions include patients with a lesion close to the optic chiasm, troubling mass effect symptoms or new pituitary deficiencies.

Extending the imaging timeline reduces the economic burden on patients and the medical system. This revised timeline could be especially impactful for young people, who can also be spared excess gadolinium contrast with frequent MR imaging over a lifetime.



People may have small pituitary adenomas without any symptoms.

in Neurosciences



## **Pituitary disorders** and COVID-19

**OHSU Pituitary Center has contributed** extensively to the international literature guiding the safe management of patients with pituitary disease during the COVID-19 pandemic. Patients with pituitary diseases have experienced both direct and indirect effects from the pandemic. Several pituitary disease components (acute visual loss, tumor mass effects) or chronic conditions (adrenal insufficiency, hypopituitarism, Cushing's disease or growth hormone excess/acromegaly) can have tremendous interplay with COVID-19, increasing morbidity and mortality. Major disruptions in services, postponement of elective surgeries and cessation of clinical trials have also played a role in changing the complex care for pituitary disease during the pandemic, creating a new normal.



#### Leading treatment research in acromegaly

Fleseriu was global investigator and lead author on MPOWERED, a phase 3 multicenter international trial assessing the response in patients to oral octreotide capsules compared to monthly injectable somatostatin receptor ligands (SRLs), published in The Lancet D&E. Interestingly, while oral and injectable versions of treatment have similar biochemical efficacy, patients reported fewer symptoms with the oral option. Based on these results, physicians can present options considering patient preference.

Also as global primary investigator, Fleseriu and colleagues shared the results of the global ACROSTUDY of the real-world experience of the GH receptor antagonist pegvisomant (PEGV) in acromegaly patients. This large, noninterventional international study of patients followed over 14 years demonstrated a favorable benefit-to-risk profile (including improved quality of life) for using PEGV as a single treatment or in combination with SRLs or dopamine agonists, and highlighted the need for dose optimization.

**Growth hormone** deficiency is among Elena V. Varlamov, M.D.'s particular interests.

#### Traumatic brain injury

As one of only two Level 1 trauma centers in Oregon, OHSU is a critical regional resource for the advanced care of traumatic injuries. Special resources include a Neurosciences Intensive Care Unit with neurointensivists on duty 24/7 at OHSU and an advanced pediatric intensive care at OHSU Doernbecher Children's Hospital.

#### People of color twice as likely to die after traumatic brain injury

In the first study to review racial and ethnic disparities in the field of neurosurgical trauma, OHSU researchers revealed that people of color are more than twice as likely to die after a traumatic brain injury as white people.

The retrospective study analyzed more than a decade of data related to the health outcomes and demographics of thousands of patients treated for traumatic head injuries at OHSU Hospital.

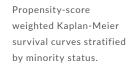
Weighted for severity of injury, age and other factors, researchers calculated an inhospital mortality hazard ratio of 2.21 for minority patients compared to white patients. Researchers noted that the increased risk was not a factor of bias in treatment but highlights underlying disparities in health that disproportionately affect people of color.

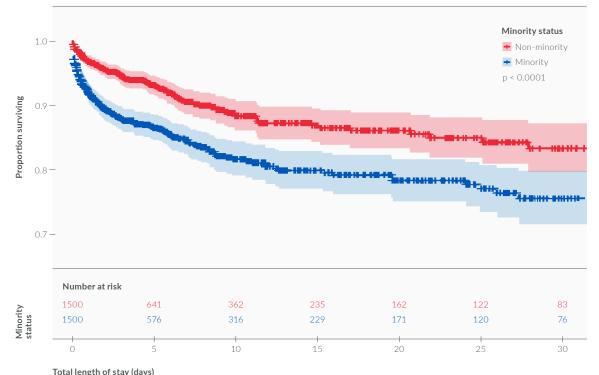
"If you ran the same analysis with patients with pneumonia, you might find the same results," said senior author Ahmed M. Raslan, M.D., FAANS, associate professor of neurological surgery in the OHSU School of Medicine. "Our findings point to the problem in a more robust and clear way. The problem is rooted in social determinants of health, including factors such as diet, lifestyle, occupations and access to health care."

The study is published in the journal Frontiers in Surgery.



In-hospital mortality hazard ratio for minority patients compared to white patients.





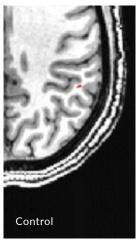
Non-minority Minority

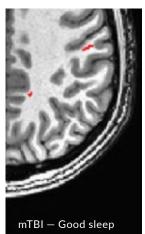
#### Sleep a powerful therapy in healing mTBI

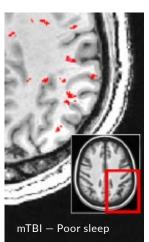
An OHSU-led study of military veterans puts sleep at the epicenter of recovery in mild traumatic brain injury.

"This study has huge implications for the armed forces as well as civilians," said lead author Juan Piantino, M.D., M.C.R., assistant professor of pediatrics (neurology) in the Papé Family Pediatric Research Institute - Neuroscience Division, OHSU School of Medicine and Doernbecher Children's Hospital. "The results suggest sleep may play an important role in clearing waste from the brain after traumatic brain injury — and if you don't sleep very well, you might not clean your brain as efficiently."

The researchers from OHSU and other collaborators used data collected from 56 veterans. Using an automated imaging segmentation tool developed at OHSU, researchers objectively quantified whole-brain perivascular spaces in number, volume, location and morphology.







Among veterans in the study, those who slept poorly had more evidence of these enlarged spaces and more post-concussive symptoms. Therefore, sleep disturbances represent a modifiable treatment target for potentially improving outcomes in patients with mTBI.

The study is published in the Journal of Neurotrauma.



# Technique measures brain's wasteclearance system through MRIs

Developed at OHSU, a technique for autoidentification of perivascular spaces in white matter using clinical field strength T1 and FLAIR MR imaging measures enlarged perivascular spaces (ePVS) in the brain. Created under the direction of Lisa Silbert, M.D., M.C.R., director of the Neuroimaging Laboratory at the Layton Oregon Aging and Alzheimer's Disease Center, this tool provides positive predictive values and detailed assessments of ePVS burden in white matter on routinely acquired MRI sequences.

Piantino said the technique could be useful for older adults.

"Longer term, we can start thinking about using this method to predict who is going to be at higher risk for cognitive problems including dementia," he said.

#### Imaging showing the effect of mTBI and poor sleep on perivascular space burden.

Axial T1-weighted image slices through the posterior quadrant of the centrum semiovale (box) in a control subject with no history of mTBI and good sleep, a subject with mTBI and good sleep, and a subject with mTBI and poor sleep. Perivascular spaces (in red) were identified with a semiautomated detection algorithm. Note the increased number of PVS in the posterior region in the subject with mTBI and poor sleep.



# Influencing national educational policy for clinical neuroscience

Our inventive educational programs have changed how neurosurgeons receive training in the United States.

At OHSU, we challenge conventions in education and pioneer new ways of teaching. In 2021, a study co-authored by 24 neurosurgeons across the country summarized 20 years of educational improvements resulting in cohesive nationwide standards. Several evolutionary jumps in neurosurgery training, including boot camps and crisis simulators, originated at OHSU.

"This is a report of two decades of work that has made neurosurgery training in America radically more effective and safer, and is turning out better neurosurgeons," said lead author Nathan R. Selden, M.D., Ph.D., chair of neurological surgery. "By creating immersive environments to practice techniques under stress in conjunction with intensive faculty mentorship, we are making a whole generation of surgeons more capable and confident."

Selden serves as secretary of the Society of Neurological Surgeons and chaired its collaboration with the Accreditation Council for Graduate Medical Education to develop uniform national training milestones. Study co-author Kim J. Burchiel, M.D., professor and former chair of neurological surgery in the OHSU School of Medicine, led the creation of a new national "matrix" curriculum for neurosurgery that remains in use today. Burchiel is a past president of the SNS and its current historian.



"At OHSU, we are committed to creating new models for realistic, hands-on experiences," Selden said. "We have been a leading center driving this nationwide effort since piloting the first boot camps in 2009. Those first camps have become models for resident training in other surgical disciplines. We have put shaping outcomes-based neurosurgical education at the forefront of our priorities for the purpose of improving patient care here in Oregon and elsewhere."

Education is only one component of graduating successful neurosurgeons, however. In the report, Selden and colleagues also outlined progress in the field of neurosurgery in advancing racial and gender equity, anti-harassment and physician wellness.

The report is published in the Journal of Neurosurgery.

A first-year neurosurgery resident drills through a 3D-printed model of a skull as he trains with a brain surgery simulator developed at OHSU. Such hands-on training is among the innovations that have transformed the training of America's brain surgeons, according to a report published in the Journal of Neurosurgery.

# Faculty

in Neurosciences

# **Faculty**

## **Department** of Neurology

Helmi Lutsep, M.D., FAAN, FAHA

Professor and Interim Chair

Prakash Ambady, M.D.

Shannon Anderson, M.P.A.S., P.A.-C.

Zach Beattie, Ph.D.

Jacqueline Bernard, M.D.

Eilis Boudreau, M.D., Ph.D.

Hormozd Bozorgchami, M.D.

William Brewster-Smith, M.D.

Matthew Brodsky, M.D.

Michelle Cameron, M.D.

Nizar Chahin, M.D.

Chris Chou, M.D.

Kathryn Chung, M.D.

Wayne Clark, M.D.

Dana Colgan, Ph.D.

Raina Croff, Ph.D.

Marian Dale, M.D.

Proleta Datta, M.D.

Walt Dawson, Ph.D.

Alexandra Dimitrova, M.D.

Hiroko Dodge, Ph.D.

Nancy Doolittle, Ph.D.

Julia Durrant, M.D.

Jonathan Elliott, Ph.D.

Ben Emery, Ph.D.

Lia Ernst, M.D.

Melanie Fried-Oken, Ph.D.

Nora Gray, Ph.D.

Nathan Hantke, Ph.D.

Amie Hiller, M.D.

Holly Hinson, M.D., M.C.R.

Scott Hofer, Ph.D.

Fay Horak, Ph.D., P.T.

Cinda Hugos, M.S., P.T.

Kim Hutchison, M.D.

Stefanie Kaech-Petrie, Ph.D.

Jeffrey Kaye, M.D.

Marissa Kellogg, M.D., M.P.H.

Ed Kim. M.D.

Laurie King, Ph.D.

Eran Klein, M.D.

Jeff Kraakevik, M.D.

Michael Lane, M.D.

Noona Leavell, M.D.

Miranda Lim, M.D.

Allison Lindauer, Ph.D., NP

Mary Logan, Ph.D.

Pippa Macdonald, M.D.

Martina Mancini, Ph.D.

Ian Martin, Ph.D.

Matthew McCaskill, M.D.

Anusha Mishra, Ph.D.

Paul Motika, M.D.

Leslie Muldoon, Ph.D.

Andrew Natonson, M.D.

Edward Neuwelt, M.D.

Halina Offner-Vandenbark, Ph.D.

Barry Oken, M.D., Ph.D.

Ron Pfeiffer, M.D.

Aimee Pierce, M.D.

Juliette Preston, M.D.

Joseph Quinn, M.D.

Emily Riddle, M.D.

Delaram Safarpour, M.D., M.S.C.E.

Martin Salinsky, M.D.

Sonemany Salinthone, Ph.D.

Lynne Shinto, N.D., M.P.H.

Elizabeth Silbermann, M.D.

Lisa Silbert, M.D.

Asha Singh, M.D.

Amala Soumyanath, Ph.D.

Rebecca Spain, M.D., M.S.P.H.

David Spencer, M.D.

Peter Spencer, Ph.D.

Lauren Talman, M.D.

Andrew Treister, M.D.

Desire Tshala-Katumbay, M.D., Ph.D.

Tarvez Tucker, M.D.

Vivek Unni, M.D., Ph.D.

Arthur Vandenbark, Ph.D.

Shawn Westaway, Ph.D.

Gary Westbrook, M.D.

Katherine Wild, Ph.D.

Anson Wilks, M.D.

Lindsey Wooliscroft, M.D.

Kirsten Wright, N.D.

Letisha Wyatt, Ph.D.

Vijayshree Yadav, M.D., M.C.R.

Ilker Yaylali, M.D., Ph.D.



# **Department of Neurological Surgery**

Nathan R. Selden, M.D., Ph.D., FACS, FAAP Campagna Professor and Chair

Nabil Alkayed, M.D., Ph.D.

Peter Andersen, M.D.

Kim J. Burchiel, M.D., FACS

Jeremy N. Ciporen, M.D.

Kelly L. Collins, M.D.

Aclan Dogan, M.D.

Maria Fleseriu, M.D., FACE

Mary M. Heinricher, Ph.D.

Susan L. Ingram, Ph.D.

Ines Koerner, M.D., Ph.D.

Jesse Liu, M.D.

Christopher J. Madden, Ph.D.

Shirley McCartney, Ph.D.

Shaun F. Morrison, Ph.D.

Gary Nesbit, M.D.

Edward Neuwelt, M.D.

Josiah Orina, M.D.

Ahmed M.T. Raslan, M.D.

Donald A. Ross, M.D.

W.H. Andrew Ryu, M.D., M.Sc., M.T.M., FRCSC

Olabisi Sanusi, M.D.

Christina M. Sayama, M.D., M.P.H.

Domenico Tupone, Ph.D.

Kamila Vagnerova, M.D.

Elena Varlamov, M.D.

Jesse Winer, M.D., FAANS

Jos'Lyn Woodard, M.D.

Christina Wright, M.D., M.P.H.

James Wright, M.D.

Chris Yedinak, M.N., F.N.P., D.N.P.

Garrett Zoeller, M.D., FAANS, FACS, FAAP



# Recent representative publications

#### **Neurology**

Chaudhary P, Marracci GH, Calkins E, Pocius E, Bensen AL, Scanlan TS, **Emery B, Bourdette DN.**Thyroid hormone and thyromimetics inhibit myelin and axonal degeneration and oligodendrocyte loss in EAE. *Journal of Neuroimmunology*. 2021;13(9).

Ernst LD, Steffan PJ, Srikanth P, Wiedrick J, Spencer DC, Datta P, Joseph NM, Wernovsky M, Becker DA. Electrocorticography Analysis in Patients with Dual Neurostimulators Supports

Desynchronization as a Mechanism of Action for Acute Vagal Nerve Stimulator Stimulation.

J Clin Neurophysiol. 2021;12(1).

Fiedler SE, Spain RI, Kim E, Salinthone S. Lipoic acid modulates inflammatory responses of monocytes and monocyte-derived macrophages from healthy and relapsing-remitting multiple sclerosis patients. *Immunology and Cell Biology*. 2021;(4).

Hinson HE, Gonzales NR. On increasing the visibility of women and other groups underrepresented in medicine: To be it, you must see it. *Neurology*. 2020;21(6).

Jung SH, Hasegawa N, Mancini M, King LA, Carlson-Kuhta P, Smulders K, Peterson DS, Barlow N, Harker G, Morris R, Lapidus J, Nutt JG, Horak FB. Effects of the agility boot camp with cognitive challenge (ABC-C) exercise program for Parkinson's disease. npj Parkinson's Disease. 2020;23(7):1056-1071.

Kisby GE, Eriksen JL, Chlebowski AC, **Spencer PS.** Cycad Genotoxin. Methylazoxymethanol Disrupts the Brain Ubiquitin-Proteasome Pathway, Tau and α-Synuclein, as Reported in ALS-PDC. Journal of neuropathology and experimental neurology. 2021;41(5):823.

Scott GD, Lim MM, Drake MG, Woltjer R, Quinn JF. Onset of Skin, Gut, and Genitourinary
Prodromal Parkinson's Disease: A Study of 1.5 Million Veterans. Movement Disorders. 2021;11(1).

Shoamanesh A, Hart RG, Connolly SJ, Kasner SE, Smith EE, Martí-Fàbregas J, Liu YY, Uchiyama S, Mikulik R, Veltkamp R, O'Donnell MJ, Ntaios G, Muir KW, Field TS, Santo GC, Olavarria V, Mundl H, Lutsep H, Berkowitz SD, Sharma M. Microbleeds and the Effect of Anticoagulation in Patients with Embolic Stroke of Undetermined Source: An Exploratory Analysis of the NAVIGATE ESUS Randomized Clinical Trial. JAMA Neurology. 2021;12(1).

Stoler J, Miller JD, Brewis A, Freeman MC, Harris LM, Jepson W, Pearson AL, Rosinger AY, Shah SH, Staddon C, Workman C, Wutich A, Young SL, Adams E, Ahmed F, Alexander M, Asiki G, Balogun M, Boivin MJ, Carrillo G, Chapman K, Cole S, Collins SM, Eini-Zinab H, Escobar-Vargas J, Ghattas H, Ghorbani M, Hagaman A, Hawley N, Jamaluddine Z, Krishnakumar D, Maes K, Mathad J, Maupin J, Owuor PM, Melgar-Quiñonez H, Morales MM, Moran J, Omidvar N, Rasheed S, Samayoa-Figueroa L, Sánchez-Rodriguez EC, Santoso MV, Schuster RC, Sheikhi M, Srivastava S, Sullivan A, Tesfaye Y, Triviño N, Trowell A, Tshala-Katumbay D, Tutu R. Household water insecurity will complicate the ongoing COVID-19 response: Evidence from 29 sites in 23 low- and middle-income countries. International Journal of Hygiene and Environmental Health. 2021;23(3):348.

Yu K, Wild K, Potempa K, Hampstead BM, Lichtenberg PA, Struble LM, Pruitt P, Alfaro EL, Lindsley J, MacDonald M, Kaye JA, Silbert LC, Dodge HH. <u>The Internet-Based Conversational Engagement Clinical Trial (I-CONECT) in Socially Isolated Adults 75+ Years Old: Randomized Controlled Trial Protocol and COVID-19 Related Study Modifications. Front Digit Health. 2021;25(3).</u>

#### **Neurological surgery**

Bouchet C, Eshleman A, Janowsky A, **Ingram S.** <u>Persistent Inflammation Reduces Cannabinoid 1</u> Receptor Function in the Ventrolateral Periaqueductal Gray. *The FASEB Journal*. 2021;35(S1).

Etson CM, Block KF, Burton MD, Edwards A, Flores SC, Fry C, Guillory AN, **Ingram SL**, McGee R, Neely-Fisher DL, Paxson S, Phelan L, Primus C, Suggs K, Vega LR, Vuong E, Hammonds-Odie L, Leibowitz MJ, Zavala M, Lujan JL, Ramirez-Alvarado M, Segarra VA. <u>Beyond Ticking Boxes:</u> Holistic Assessment of Travel Award Programs Is Essential for Inclusivity. *The Biophysicist.* 2021.

Fleseriu M, Auchus R, Bancos I, Ben-Shlomo A, Bertherat J, Biermasz NR, Boguszewski CL, Bronstein MD, Buchfelder M, Carmichael JD, Casanueva FF, Castinetti F, Chanson P, Findling J, Gadelha M, Geer EB, Giustina A, Grossman A, Gurnell M, Ho K, Ioachimescu AG, Kaiser UB, Karavitaki N, Katznelson L, Kelly DF, Lacroix A, McCormack A, Melmed S, Molitch M, Mortini P, Newell-Price J, Nieman L, Pereira AM, Petersenn S, Pivonello R, Raff H, Reincke M, Salvatori R, Scaroni C, Shimon I, Stratakis CA, Swearingen B, Tabarin A, Takahashi Y, Theodoropoulou M, Tsagarakis S, Valassi E, Varlamov EV, Vila G, Wass J, Webb SM, Zatelli MC, Biller BMK.

Consensus on diagnosis and management of Cushing's disease: a guideline update.

Lancet Diabetes Endocrinol. 2021.

Giustina A, Legg E, Cesana BM, Frara S, Mortini P, **Fleseriu M**. <u>Results from ACROCOVID:</u> an international survey on the care of acromegaly during the COVID-19 era. *Endocrine*. 2021.

Greenberg JK, Ahluwalia R, Hill M, Johnson G, Hale AT, Belal A, Baygani S, Olsen MA, Foraker RE, Carpenter CR, Yan Y, Ackerman L, Noje C, Jackson E, Burns E, **Sayama CM**, **Selden NR**, Vachhrajani S, Shannon CN, Kuppermann N, Limbrick DD, Jr. <u>Development and External Validation of the KIIDS-TBI Tool for Managing Children with Mild Traumatic Brain Injury and Intracranial Injuries</u>. *Acad Emerg Med*. 2021.

Gupta R, Saver JL, Levy E, Zaidat OO, Yavagal D, Liebeskind DS, Khaldi A, Gross B, Lang M, Narayanan S, Jankowitz B, Snyder K, Siddiqui A, Davies J, Lin E, Hassan A, Hanel R, Aghaebrahim A, Kaushal R, Malek A, Mueller-Kronast N, Starke R, **Bozorgchami H**, **Nesbit G**, Horikawa M, **Priest R**, **Liu J**, Budzik RF, Pema P, Vora N, Taqi MA, Samaniego E, Wang QT, Nossek E, Dabus G, Linfante I, Puri A, Abergel E, Starkman S, Tateshima S, Jadhav AP. New Class of Radially Adjustable Stentrievers for Acute Ischemic Stroke: Primary Results of the Multicenter TIGER Trial. Stroke. 2021;52(5):1534-1544.

Holland MT, Mansfield K, Mitchell A, Burchiel KJ. <u>Hidden Error in Optical Stereotactic</u>
Navigation Systems and Strategy to Maximize Accuracy. *Stereotact Funct Neurosurg.* 2021:1-8.

Mazur-Hart DJ, Bowden SG, Pang BW, Yaghi NK, Nugent JG, Yablon LD, Domreis WO, Ohm ET, Sayama CM. Standardizing postoperative care for pediatric intradural Chiari decompressions to decrease length of stay. Journal of Neurosurgery: Pediatrics. 2021:1-6.

Paulk AC, Yang JC, Cleary DR, Soper DJ, Halgren M, O'Donnell AR, Lee SH, Ganji M, Ro YG, Oh H, Hossain L, Lee J, Tchoe Y, Rogers N, Kiliç K, Ryu SB, Lee SW, Hermiz J, Gilja V, Ulbert I, Fabó D, Thesen T, Doyle WK, Devinsky O, Madsen JR, Schomer DL, Eskandar EN, Lee JW, Maus D, Devor A, Fried SI, Jones PS, Nahed BV, Ben-Haim S, Bick SK, Richardson RM, Raslan AM, Siler DA, Cahill DP, Williams ZM, Cosgrove GR, Dayeh SA, Cash SS. Microscale Physiological Events on the Human Cortical Surface. *Cerebral Cortex*. 2021.

Richie EA, Nugent JG, Raslan AM. Racial and Ethnic Inequities in Mortality During
Hospitalization for Traumatic Brain Injury: A Call to Action. Front Surg. 2021;8:690971.

**Selden NR**, Barbaro NM, Barrow DL, Batjer HH, Branch CL, **Burchiel KJ**, Byrne RW, Dacey RG, Day AL, Dempsey RJ, Derstine P, Friedman AH, Giannotta SL, Grady MS, Harsh GR, Harbaugh RE, Mapstone TB, Muraszko KM, Origitano TC, Orrico KO, Popp AJ, Sagher O, Selman WR, Zipfel GJ. Neurosurgery residency and fellowship education in the United States: 2 decades of system development by the One Neurosurgery Summit organizations. *J Neurosurg*. 2021:1-10.

**Tupone D, Cetas JS.** In a model of SAH-induced neurogenic fever, BAT thermogenesis is mediated by erythrocytes and blocked by agonism of adenosine A1 receptors. *Sci Rep.* 2021;11(1):2752.

