Innovations in Neurosciences

OHSU tram.
Dear Colleague,

We are proud to present to you our first joint publication describing some of the discoveries, innovations and advancements occurring in neuroscience clinical care, research and education at Oregon Health & Science University (OHSU).

OHSU is Oregon's only academic medical center and has a long history of leadership in both basic and clinical neuroscience. We have a strong tradition of teamwork and interdisciplinary care between the departments of Neurology and Neurosurgery as well as many other departments and divisions at OHSU.

Our programs have regional and national prominence. We are utilizing the power of world-class advanced imaging facilities to identify and treat the most complicated medical and surgical problems of the human nervous system, including major new investments in cyclotron ligand design and PET imaging, as well as high Tesla intraoperative MR imaging. Our teams are leveraging telemedicine to extend highly subspecialized care programs to patients across our region in a wide variety of areas such as stroke, deep brain stimulation and Alzheimer's. Finally, we are a center for educating and training the next generation of compassionate practitioners. Our innovative educational programs have changed the way leading neuroscience physicians are trained across the United States.

The following pages highlight just a few of our programs that make OHSU a leader in neuroscience care. We are proud to share with you some of our innovations that are transforming how we provide care. Please contact us if we can provide any additional information about our services and programs.

Sincerely,

Dennis Bourdette, M.D., F.A.N.A., F.A.A.N.
Roy and Eulalia Swank Research Professor and Chair
Department of Neurology

Nathan R. Selden, M.D., Ph.D.
Mario and Edith Campagna Professor and Chair
Department of Neurological Surgery

Drs. Dennis Bourdette and Nathan R. Selden.
OHSU Art of Neuroscience competition finalists
"The Brightest Crayon in the Box" by Kathleen Beeson and "The Basis of Fear" by David Grayson.

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The environment: OHSU is transforming patients’ lives each and every day by increasing our capacity to innovate, discover and teach. In just the last two years, we have:

- Raised $1 billion for cancer care
- Opened a new medical school campus
- Broken ground for a facility to house families and patients traveling for care
- Launched a population health partnership with other leading Oregon hospitals
### Facts, figures and highlights*

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<thead>
<tr>
<th>$64m</th>
<th>Neuroscience research funding 2015–2016</th>
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<tbody>
<tr>
<td>8th</td>
<td>In NIH funding in 2015</td>
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<tr>
<td>1st</td>
<td>• Comprehensive Stroke Center in Pacific Northwest, via The Joint Commission</td>
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<td></td>
<td>• To show lipoic acid slows brain atrophy in secondary progressive MS</td>
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<td>• Pediatric hospital on West Coast with 3.0 Tesla iMRI, part of a major pediatric sedated imaging and intervention center</td>
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<td>• Neuronal stem cell transplantation 2007; first CNS stem cell transplantation of any kind in children</td>
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<td>• To perform awake and asleep DBS in the U.S., 1991 and 2011 respectively</td>
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<td>Neuroscience graduate students</td>
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*Includes Pediatrics.

**Includes fellows.

33,619 Total patient visits FY16
Cross-disciplinary approach enhances Parkinson’s care

OHSU is a leader not only in surgical approaches for Parkinson’s disease, but also in disease progression research. The close collaboration between OHSU’s neurologists, neurosurgeons and researchers has led to groundbreaking advances in Parkinson’s disease care.

Asleep DBS: Safer, more precise, more cost-effective

In 1991, OHSU’s Kim Burchiel, M.D., F.A.C.S., was the first U.S. surgeon to treat Parkinson’s disease with DBS (deep brain stimulation). In 2011, Burchiel pioneered “asleep” DBS with patients under general anesthesia. Surgery is faster, outcomes are better and patient satisfaction is far higher than with awake DBS. Most centers still perform DBS with patients awake and responsive. At OHSU, the team fuses high-resolution presurgical MRI with intraoperative CT scans for a precise map of the brain, placing the electrodes correctly — on the first attempt — 90 percent of the time. By contrast, standard microelectrode-guided placement requires an average of five brain penetrations for a single electrode.

OHSU’s team is now one of the nation’s most experienced DBS provider groups, attracting patients from around the world. A recent three-year analysis placed OHSU in the top four U.S. academic medical centers for DBS.

DBS care through telemedicine

The OHSU Parkinson Center’s telemedicine program is starting a new clinical process which will soon allow certain patients, depending on their needs, to attend appointments and have DBS stimulators programmed from a clinic in their home community. Some patients may also complete pre- and postoperative appointments by telemedicine, traveling to OHSU’s main campus only for surgery and initial programming.
Pioneering surgical approaches, understanding disease progression and utilizing telemedicine are just some of the ways OHSU is leading the way in Parkinson’s care. OHSU neurologists and neurosurgeons collaborate to provide the most advanced treatment and follow-up to patients with Parkinson’s disease and other movement disorders. This partnership ensures individualized specialty care at every stage of therapy, optimizing function and quality of life.

**Leading the way in Parkinson’s disease research**

Fay Horak, Ph.D., conducts innovative research on Parkinson’s disease effects and progression. Her work uses wearable sensors to identify patients with the highest fall risk. “By looking at velocity of turns and number of steps, we can measure Parkinson’s disease fluctuation over the day,” says Dr. Horak. “Turn variability may be a good predictor of fall risk.” The Horak lab has found that even patients with advanced neurological disorders, such as Parkinson’s disease and multiple sclerosis, can improve their balance with practice.
The OHSU Advanced Imaging Research Center collaborates with neuropathology services to collect high-resolution brain stem images. In Parkinson’s disease, cells within the substantia nigra degenerate. When a certain percentage are lost, a person exhibits early PD. Working with colleagues at the University of Washington, OHSU investigators scan this area with 12-Tesla MRI for early detection of structural changes in the substantia nigra.

Diffusion tensor imaging reveals the brain’s white matter pathways. A team led by Fay Horak, Ph.D., found that patients with PD and gait “freezing” had fewer paths between the right brainstem and locomotor center.

Matthew Brodsky, M.D., along with the imaging center, uses 7-Tesla MRI to evaluate patients in the earliest stages of PD and those at high risk of developing this disorder. Definitive early diagnoses will allow earlier intervention.

Left: Sixty-three-year-old individual with six months of PD symptoms on only the left side of his body, with corresponding loss of nigrosome 1 signal in the right midbrain. Right: Sixty-three-year-old without PD with healthy nigrosome 1 signal.
A study of 60 OHSU patients found unmatched precision and very low risk for “asleep” deep brain stimulation. The OHSU team’s complication rates are among the lowest in the United States. A recent three-year analysis showed 30-day readmission rates of just 3.7 percent.

In addition to being safe, effective and comfortable, asleep DBS is also cost effective, as shown in a 2016 OHSU analysis.
Brain space: Using intraoperative MRI and brain mapping to treat tumors and other neurological conditions

OHSU's Department of Neurological Surgery has the most advanced resources available for treating brain tumors, epilepsy and other intractable neurologic conditions. While few centers offer either functional brain mapping or advanced Tesla 3.0 intraoperative magnetic resonance imaging (iMRI) — OHSU stands out for having both.

**iMRI for precision tumor removal**

In OHSU’s dedicated surgical imaging suite (opened in March 2016), a 10-ton iMRI glides into the operating room on overhead rails during surgery, retracting when the scan is finished. The iMRI precisely delineates the borders of brain tumors and other lesions to help surgeons ensure a complete resection. The iMRI is especially useful for lesions against or even within parts of the brain that control critical functions. The iMRI maps brain shift during surgery, allowing complete tumor resection without damage to vital nearby structures. It also gives surgeons confirmation of a safe resection before closing, improving immediate outcomes.

**Brain mapping to preserve function**

Since maximal resection with preservation of essential neurological function is the crux of brain surgery decision-making, the team customizes every surgery to retain functions of greatest importance to the patient, such as language or memory. OHSU neurosurgeon Ahmed Raslan, M.D., calls this approach “functional neuro-oncology.” Occasionally, awake brain mapping during surgery is critical to preserving language and memory function.

Brain mapping is used to identify eloquent areas of the brain using direct stimulation. Almost any function that an awake patient can perform during surgery can be mapped. The team takes pride in personally knowing each patient to determine where mapping is most crucial for the best individual outcome. “It’s a matter of millimeters,” says Raslan. “Anatomic descriptions of motor and language areas are wrong more than 20 percent of the time. Using these precise techniques makes an enormous difference to patients.”

In one form of mapping, stimulating the brain surface during surgery allows surgeons to identify eloquent functional areas. Passive mapping uses free-running recording of brain electrical activity and rapid mathematical analysis to precisely localize areas of
function. Mapping is also possible outside the operating room, using surgically implanted electrodes resting on the brain surface. So-called “extraoperative brain mapping” is useful both to identify the focus of seizure onset in patients with severe epilepsy, and to define functional areas that must be preserved during resection. The OHSU neurosurgery team also uses tract mapping of deep brain areas to preserve function, in addition to advanced fiber tractography imaging inside and outside the operating room.

This unusual combination of technological resources is a rare strength at a single academic medical center. With these resources available for OHSU’s top neurosurgeons and outstanding neuro-anesthesia and neurocritical care providers, the OHSU Department of Neurological Surgery is in the vanguard of functional neurosurgery and neuro-oncology.
Many academic MS centers investigate new disease-modifying agents and offer a range of therapies. While the OHSU Multiple Sclerosis Center offers traditional treatments, their investigations into complementary and alternative medicine (CAM) approaches are particularly innovative. As MS Clinical Medical Director Vijayshree Yadav, M.D., M.C.R., F.A.N.A., states, “We are committed to sifting effective therapies from unfounded hope.”

**Patient-centered investigations:**
**False hope or real potential from CAM?**

MS patients often develop a strong interest in “wellness” approaches without evidence-based guidance on their effectiveness. OHSU’s goal is to provide a rigorous investigational approach to such complementary therapies. The Center is funded by the U.S. National Institutes of Health, Department of Veterans Affairs and National MS Society to study exercise, diet and stress reduction for MS management.

**Addressing patients’ realities and evaluating the benefits of wellness approaches**

Well-designed investigations of CAM therapies for MS at OHSU include:

- A placebo-controlled trial of the natural antioxidant lipoic acid in secondary progressive MS by Rebecca Spain, M.D., M.S.P.H. Building on findings by MS Center Director Dennis Bourdette, M.D., F.A.A.N., F.A.N.A., in a murine model, Spain showed that lipoic acid was associated with a 68 percent decrease in brain atrophy rate over the two-year study period compared with placebo.

- Benefits of a low-fat vegan diet on fatigue were demonstrated by Yadav, who is conducting ongoing investigations on dietary approaches in MS.

- Separate, randomized placebo-controlled trials led by Bourdette investigated the benefits of ginkgo biloba on cognitive impairment and American ginseng on fatigue. Neither of these frequently touted supplements was superior to placebo.

- Spain investigated the benefits of aerobic exercise in patients with MS and found that exercise improved fatigue and cognitive performance.
• Angela Senders, N.D., M.C.R., is evaluating the potential benefit of mindfulness meditation for stress reduction in MS.

• Lynne Shinto, N.D., M.P.H., recently completed an investigation of the value of lipoic acid plus omega-3 fatty acids for cognitive impairment in MS.

The OHSU Multiple Sclerosis Center is one of the nation's premier programs for multiple sclerosis, focusing on all aspects of the disease — from diagnosis and lifelong quality clinical care to cutting-edge clinical trials, brain imaging and laboratory research. One of just six programs in the MS Center Without Walls, it is also a National MS Society Partners in MS program and Consortium of MS Centers member.

Japanese macaque encephalomyelitis: An MS mimic in nonhuman primates

The U.S. National Institutes of Health funds just seven regional primate research centers around the country, one of them being the Oregon National Primate Research Center operated by OHSU. A valuable finding has emerged from this long-standing, internationally known center. Approximately 25 years ago, Center investigators noted the spontaneous emergence of an MS-like disease in various members of the Japanese macaque colony. They learned that this disease, now known as Japanese macaque encephalomyelitis, was associated with a unique herpes virus infection. It continues to affect 1 to 3 percent of the macaque colony each year. Today, Primate Center scientists in collaboration with Bourdette and other MS Center researchers are conducting genetic research into the possibility of a similar virus affecting humans with MS.
7-Tesla MRI reveals MS-related brain changes

Bill Rooney, Ph.D., head of OHSU’s Advanced Imaging Research Center, has a particular interest in MS that informs his investigations of brain changes in patients with the disease. The imaging center offers OHSU researchers the most advanced technology available for basic science and clinical trials. In one study, Rooney and the MS center team are conducting research on bioenergetic deficiencies in the brains of patients with MS. Additional investigations focus on the effects of bioenergetic deficiencies on disease progression and how risk factors for vascular disease may contribute to accelerated MS progression.

Top: Control subject. Bottom: MS subject.
Despite its unique focus, the Center has not neglected its role in investigating and developing new disease-modifying agents for MS. Currently, Bourdette and biochemist Thomas Scanlan, Ph.D., are developing a drug that promotes remyelination. This research is supported by the Laura Fund for Innovation in MS Research and the National MS Society.
Oregon Health & Science University’s Advanced Imaging Research Center has some of the most powerful magnetic resonance imaging in the United States. The AIRC is home to five research-dedicated MRI instruments used for human and animal investigations across OHSU and in national collaborations. Bill Rooney, Ph.D., director of the AIRC, elaborates about the capabilities.

**Q: What makes the OHSU AIRC such an important resource?**

**Rooney:** Equipment and people. We have some of the most advanced MRI instruments available anywhere in the world, and we make them available to researchers. These are research-dedicated MR instruments, here to satisfy OHSU’s research mission. Our 7-Tesla magnet is a human-sized MRI — that is, the magnet is large enough to fit a person in it. There are not many of these in the world, and we are very fortunate to have one. We use the 7-Tesla MRI to produce sharper images of structures inside the human brain. It provides amazing images.

Thanks to a grant from the National Institutes of Health, we also just upgraded our 3-Tesla MRI to a Siemens 3T Prisma — one of the most capable 3T MRI instruments available anywhere. The AIRC is home to 12 faculty scientists with diverse expertise in MR science. These experts are available to help OHSU investigators advance their research. We also have a close partnership with Siemens, manufacturer of our large MRI instruments, and a Siemens Senior Scientist is resident at the AIRC. Finally, we have a talented scientific, technical and administrative staff that works hard to make the AIRC an efficient and effective center.

**Q: How are these people an asset to the AIRC?**

**Rooney:** For example, we currently have several MRI studies in which the research subjects are young boys, some as young as 4 years old. One of our studies involves young boys with Duchenne muscular dystrophy (DMD), a genetic disease that results in loss of muscle strength. Our group is part of a consortium that is investigating better ways to track muscle involvement in DMD. Our approach samples large amounts of skeletal muscle and is very sensitive to disease progression.
These studies are completely noninvasive and do not use any sedation. To keep a young boy confined within the small space of an MRI and to have this child remain still — since small amounts of motion will destroy image quality — requires a very skilled team of investigators. And it takes the most experienced, caring people to keep a child comfortable in the scanner so we get quality images. We show videos, have them play games — it’s all about distraction. Our team works closely not only with the boys, but also with their families to make their study visit as pleasant and convenient as possible.

Magnetic resonance imaging is highly nuanced, and our team members are highly skilled MRI readers and users. We also have an outstanding team of computer scientists who have created a unique, proprietary system to store the AIRC’s data and processes.

**Q.: How is work at the AIRC advancing care in neurology — the medical aspect of care?**

**Rooney:** To follow up on the example of DMD, we are now using these MR methods and working with Erika Finanger, M.D., and Barry Russman, M.D., pediatric neurologists specializing in neuromuscular disorders and dystrophies, to track if muscles improve following new neuromuscular therapies. We also have a long-standing relationship with Dennis Bourdette, Vijayshree Yadav and Rebecca Spain, who specialize in multiple sclerosis. We are developing quantitative MRI approaches to summarize cerebral metabolic aspects in people with MS.

**Q.: How do you see AIRC research advancing neurosurgical care?**

**Rooney:** We are developing novel ways to measure fluid movement in the brain. Together with Nathan Selden, and colleagues, we look forward to advancing techniques on their new intraoperative MRI instrument in this area.

**Q.: As an expert, what do you see in the future of imaging?**

**Rooney:** The future of imaging lies in developing quantitative approaches focused on specific patient needs. This will be achieved through smart imaging devices that adapt and correct acquisition problems in real time, leading to more reliable diagnoses and more cost-effective imaging.
Center for Radiochemistry Research

OHSU recently joined the select group of research universities in the nation with a Center for Radiochemistry Research. The core asset of the facility is a cyclotron with cleanrooms and specialized automated systems to develop radiotracers to address specific research questions using positron emission tomography (PET) imaging. Combining advanced diagnostic techniques with strong research programs in the neurosciences will lead to groundbreaking work, says Jeanne Link, Ph.D., the director of the Center for Radiochemistry Research. “Our team will work with researchers to select and develop the best probes to be used for their studies,” she says. “Then we can assist with protocols, regulatory requirements and data analysis.”

Fresh is best with isotopes

PET isotopes have a very short half-life. “Having the ability to synthesize the isotopes on-site is a need for researchers,” says Link. “We have the ability to work with researchers to find the molecule that will best probe their target.”

Also, because the isotopes decay quickly, OHSU can do imaging studies at baseline and after giving a treatment in one session.

Following brain functions

The Center for Radiochemistry Research opened in September 2016, but already is assisting researchers and clinicians in a variety of brain-related studies. Link says OHSU clinicians and basic scientists are using or developing radiochemistry to study hypoxia in brain tumors, inflammatory response in MS therapies, circadian rhythm and glutamate pathways in addiction and Parkinson’s disease.

Future applications immense

A noninvasive technique and one of the only tools for investigating functionality, radiochemistry’s contribution to understanding the mechanisms of disease is significant. One application that is advancing is using radiochemistry to determine if tumors are reoccurring or in pseudoprogression. “With functional imaging, we will be able to get more specific about whether the tumor is proliferating or if inflammatory cells are doing their work,” says Link.

Having access to the latest radiochemistry technology and techniques will provide a tremendous opportunity for research into brain processes and disease progression, as well as a superior evaluative
tool for therapies. “We are just starting,” says Link. “With the strength of the neuroscience research here at OHSU, it’s an exciting time to be on campus.”

**Coming soon: An imaging deep-dive**

PET imaging is incredibly sensitive at the functional level, able to measure infinitesimal signals in vivo and time duration. MR imaging produces beautiful structural images. When combined, the two capabilities provide a very powerful technique for brain research and require about one-tenth the radiation of PET/CT, so pediatric patients can be imaged. OHSU will be adding a PET/MR scanner in the near future, one of less than 50 in the United States. The combination of radiochemistry and this advanced imaging equipment provide powerful tools for discovery and disease treatment.

**Preclinical support**

The Center for Radiochemistry Research will also use PET imaging and other nuclear medicine diagnostic techniques at OHSU’s Small Animal Research Imaging Center (SARIC) to bridge preclinical and clinical research.
From leading the charge in developing new drugs to better identifying small adrenocorticotropic hormone tumors in patients with Cushing’s syndrome, the OHSU Northwest Pituitary Center is on the forefront of improving the lives of those with pituitary disorders.

The Center, led by internationally recognized pituitary expert Maria Fleseriu, M.D., F.A.C.E., has participated in or led more than 15 major research studies in the past five years, including landmark trials of the first two drugs approved for Cushing’s syndrome and a second-generation acromegaly agent.

**Developing global treatment guidelines**

Team members contribute significantly to neuroendocrine treatment guidelines and disease state reviews, including:

- **Hormonal Replacement in Hypopituitarism in Adults:** An Endocrine Society Clinical Practice Guideline — *Journal of Clinical Endocrinology & Metabolism*.

- **Pretreatment Endocrine Evaluation of Patients With Nonfunctioning Pituitary Adenomas** — *Congress of Neurological Surgeons*.

- **American Association of Clinical Endocrinologists and American College of Endocrinology Disease State Clinical Reviews on acromegaly and Cushing’s** — *Endocrine Practice*.

**Leading the way in discovery**

OHSU’s single-center studies provide data:

- Demonstrating in patients with acromegaly that determining tumor type based on growth hormone staining provides information essential to selecting the correct medical therapy and avoiding delays in instituting biochemical control that can have detrimental effects on patient survival.

- Showing, for the first time in a U.S. population, that:
  - Patients with acromegaly have a higher risk of vertebral fractures than healthy subjects, despite normal bone density.
  - Medical therapy with dopamine agonists can reverse adrenal insufficiency in patients with prolactinomas, avoiding the risks of long-term glucocorticoid exposure.
The team collaborates with neuroradiology and neuropathology colleagues on several ongoing retrospective studies based on a large pituitary disease database. These include:

- Investigation of pituitary dysfunction before and after surgery.
- Predictive value of weight gain in patients with acromegaly after treatment.
- Hormonal tumor staining and imaging characteristics in determining recurrence risk for pituitary tumors.
- MRI to detect acromegaly tumor type, potentially predicting treatment response before surgery.

Optimizing patient quality of life

The Center’s advanced practice nurse-researcher, Chris Yedinak, D.N.P., developed a tool measuring quality of life in patients with pituitary disorders. This tool allows researchers to gather data on the effectiveness of current treatments. The team continues to study and refine this valuable tool for assessing care needs and optimizing outcomes.

The OHSU Northwest Pituitary Center is an international leader in caring for pituitary disorders and one of the largest centers in the United States. The team cares for more than 500 patients a year, including more than 200 with acromegaly and 100 with Cushing’s syndrome—a higher volume than any other West Coast center.

Game-changing new drugs

Maria Fleseriu, M.D., F.A.C.E., is global principal investigator of the first study of oral octreotide for acromegaly, at 43 sites worldwide. Oral octreotide holds the promise of improving quality of life for pituitary patients now depending on a lifetime of drug injections.
Neuroimaging

OHSU neurosurgeon Justin Cetas, M.D., Ph.D., performs more than 100 surgeries annually for pituitary disorders, as well as for additional skull base and vascular conditions. Cetas and Fleseriu are collaborating with neuro-oncologists using a novel contrast agent to better identify small adrenocorticotropic hormone tumors in patients with Cushing’s disease.
Transformative spine care

Spine care at OHSU is led by a team of highly trained subspecialty neurological and orthopedic surgical experts, working with specialists from neurology, anesthesia and neurosurgery pain medicine, physical medicine and rehabilitation, and physical and occupational therapy. OHSU’s integrated spine center has advanced recently in leaps and bounds, including:

- A newly constructed and dedicated outpatient spine care clinic in OHSU’s Center for Health & Healing (a LEED Platinum award-winning medical care facility).
- Clinical outcomes data collection for every spine surgery patient, with integration into the electronic health record to ensure the clearest understanding of treatment choice and response for both patient and physician.
- Six world-class spine surgeons trained in the most innovative approaches including adult deformity correction and minimally invasive spinal surgery.
- Sophisticated real-time electrophysiological monitoring provided by the Department of Neurology for all complex spinal surgery, providing the highest degree of safety possible.

Jason Chang, M.D., and Joanna Adams, P.A.-C., with patient.
When minutes count to survival and outcome, OHSU delivers some of the most sophisticated interdisciplinary stroke care in the country. OHSU has focused on very early adoption of broad regional networks for 24/7 stroke care, cutting-edge interventional techniques and continual research and innovation.

**Bringing the medical center to the patient**

The OHSU Stroke Program serves nine hospitals and health systems around the state of Oregon via secure video link. Some hospitals have made OHSU telestroke care part of their stroke protocols. One, Rogue Regional Medical Center in Medford, Oregon, is able to treat 80 percent of stroke patients locally through routine telemedicine stroke consults. This means more than faster treatment in a relatively familiar, convenient setting — it represents a substantial reduction in health care costs by reducing helicopter and ground emergency transports.

Patients who truly need transfer to a comprehensive stroke center are also identified as quickly as possible by telemedicine — essential to treating such a time-sensitive condition. The specialist who provided the telemedicine consult meets the patient and family on arrival to OHSU and remains the attending physician during their stay, providing continuity of care and helping mitigate stress.

Since the telestroke program’s inception in 2010, OHSU specialists have performed more than 1,200 telestroke consults. On average, 60 percent of patients remain in their home communities, and an estimated $11 million has been saved from averted patient transports.
An expanding role for telestroke care

• **Virtual stroke clinics.** The OHSU Stroke Program has several satellite telehealth centers for follow-up care and research studies. Patients meet with OHSU specialists virtually at local clinics while the clinic staff provides information to OHSU.

• **Telestroke house calls.** Many stroke patients are immobile, so OHSU stroke specialists make virtual house calls. Through a secure internet link, patients or caregivers connect with the physician for follow-up or clinical trial visits. The goal is to provide the full resources of an academic medical center to every patient and make care as convenient as possible.

• **Telestroke follow-up for long-term care and skilled nursing facilities.** Neurology and neurosurgery specialists care for stroke patients even at their long-term care facility using the OHSU Telehealth Network. Secure Telehealth video links bring OHSU stroke and other experts directly to recovering patients at Vibra Specialty Hospital, Oregon’s largest long-term acute care facility, and numerous skilled nursing facilities around the state.

Neurology and neurological surgery come together in the OHSU Stroke Program to provide the resources of an academic medical center to every corner of the state. OHSU’s early adoption and embrace of telemedicine makes the state of Oregon a national example for high-quality stroke care.

**Beyond tPA: Advanced endovascular care**

OHSU is a leading clinical trial center for neuro-endovascular therapy, with 25 years of experience. The OHSU Stroke Program, in collaboration with the neurointerventional team, has also been in the forefront of testing the newest stent clot retriever and thrombectomy devices. Success rates for opening up blocked arteries using thrombectomy are approximately 90 percent, with a 65 to 70 percent rate of good neurological recovery. Although the traditional time window for thrombectomy is less than eight hours, OHSU has extended this precious window of opportunity for some patients by using advanced perfusion imaging to identify a subset of patients with brains at risk who can safely undergo thrombectomy even after eight hours.

**Cerebrovascular leaders**

Wayne Clark, M.D., director of the OHSU Stroke Program (left) with Aclan Dogan, M.D., head of OHSU’s Division of Skull Base and Cerebrovascular Surgery (right).
As one of 31 NIH Alzheimer’s disease centers in the United States and the only one in Oregon, the Layton Aging & Alzheimer’s Research Center at OHSU pilots projects on several fronts, from patient quality of life to tracking disease progression. For example, Layton Center researchers are putting well-known technology to new uses in assessing and monitoring patients with Alzheimer’s disease and other dementias.

Creating a template for cognitive evaluation via telemedicine

Layton Center researchers developed the ACT-ON study of telemedicine for dementia care to “meet families where they are,” says principal investigator Alison Lindauer, Ph.D., N.P. Funded by the National Institute on Aging and the Oregon Health Authority, this two-phase study aims to establish the reliability of measures commonly used in dementia interventions (phase 1) and assess the feasibility of performing standard clinical evaluations by telemedicine (phase 2).

ACT-ON was the first study to compare the reliability of a common tool, the Montreal Cognitive Assessment, administered in clinic and by telemedicine. Results indicate that practitioners can confidently use it remotely. The team also assessed the reliability of measuring caregiver strain by telemedicine, with similarly encouraging results. Researchers can provide a template for telemedicine dementia care anywhere in the United States, for use by anyone with a computer and Internet access.

Home-based assessment, 24/7

While telemedicine is highly promising, patients with Alzheimer’s and other dementias cannot use computers, at least not without assistance. A further complication is that 800,000 U.S. residents with Alzheimer’s disease live alone, notes the Layton Center director Jeffrey Kaye, M.D., the immediate past chair of the Alzheimer’s Association’s International Society to Advance Alzheimer’s Research and Treatment (ISTAART).

In the past year, Kaye and his team have begun investigating new technologies to meet these challenges. Wearable technology can be a reliable, low-stress way of gathering information on people with dementia. With the Oregon Center for Aging and Technology (ORCATECH), Layton Center researchers are trialing alternatives to the standard face-to-face clinical assessment. Sensors similar to those used in automatic doors are placed around a patient’s home to gather
information on sleep, gait and even social engagement as measured by computer use. Sensors on pillboxes track patients’ adherence to medication regimens.

The aggregate data give Layton Center clinicians a sense of their patients’ overall trajectory of change. “It’s a new way of following patients with cognitive decline,” says Lindauer.

**Does video chat have cognitive benefits?**

The Layton Center conducted the first clinical trial to improve social engagement in isolated older adults with mild cognitive impairment. The study, led by Hiroko Dodge, Ph.D., tracked participants’ daily video chats with a trained conversationalist. “It was the most successful trial in terms of compliance that we’ve ever had,” says Kaye. Audio analysis of study participants will reveal signs of cognitive change via language and speech patterns.

An active participant in national and international efforts to understand and develop treatments for Alzheimer’s disease, the Layton Center is at the leading edge, conducting studies of promising treatments, technology for patient support, genetics, neuroimaging and pathology.

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**Understanding aquaporin-4 protein may be useful for treating or preventing Alzheimer’s**

OHSU researchers found that the brains of those without Alzheimer’s or a history of neurological disease had well-organized aquaporin-4. However, Alzheimer’s patients appeared to have disorganized aquaporin-4 protein, which perhaps may reflect the inability of these brains to efficiently clear away wastes like amyloid beta.

Left image of individual with AD and right image of cognitively healthy individual. The red fluorescence is the membrane protein aquaporin-4. The cognitively healthy individual has relatively even aquaporin-4 expression throughout the tissue and a stark enhancement of expression around the blood vessel, whereas the individual with Alzheimer’s has uneven, “patchy” expression of aquaporin-4. (OHSU)
Lynne Shinto, N.D., M.P.H., collaborating with OHSU’s Advanced Imaging Research Center, has shown that omega-3 fatty acids are associated with beneficial effects over time on normal brain imaging obtained during advanced aging.

Lisa Silbert, M.D., M.C.R., directs the Neuroimaging Lab at the Oregon Aging and Alzheimer’s Disease Center. She uses OHSU’s high-field MRI and diffusion tensor imaging capabilities to study the different intensities of white matter signaling in the brain. Hyperintensity, more common in older age, can be associated with increased risk of neurological problems and is common in Alzheimer’s disease. Silbert also uses arterial spin labeling to study and characterize brain blood flow related to aging and Alzheimer’s.

Areas of normal-appearing white matter (colored blue and green) are examined as layers around abnormal white matter (colored red) to demonstrate that lower blood flow in normal-appearing white matter increases risk of progressive white matter damage over time.
The Layton Center at OHSU has one of the world’s largest longitudinal MRI databases of normal aging brains; data are readily available to non-Center researchers at adresearch@ohsu.edu.
The future of world-class brain and spine care

For nearly a decade, OHSU has led advances in neurosurgical education, many of which have changed training around the United States and even around the world. Highlights include:

- **The surgical “boot camp” movement began at OHSU.** Since 2010, every neurosurgery trainee in the U.S. takes courses in introductory skills and professionalism first taught at OHSU. Boot camps have since been held in neurosurgery as far away as Great Britain and Pakistan, and in other specialties around the U.S.

- **Curriculum and outcomes measures.** OHSU neurosurgeons led creation of the “matrix” curriculum used to train all U.S. neurosurgeons, as well as the national milestones from the Accreditation Council for Graduate Medical Education used to measure outcomes.

- **Strength in diversity.** OHSU’s highly ranked neurosurgical training program attracts more women at one time — nine — than any other program in history. OHSU trainees reflect strong diversity in ethnicity, educational background and school of origin.

- **Standard in functional neurosurgery education.** In 2015, OHSU pioneered a national course for young functional neurosurgeons from around the world. Taking place at OHSU’s advanced surgical simulation facility, VIRTUOHSU, is the most comprehensive and technologically sophisticated course of its kind.

- **Efficiency and safety in surgical training.** OHSU neurosurgeon Ahmed Raslan, M.D., developed a tool to measure the timing and efficiency of each step in a complex surgical procedure. This tool promises to advance operating room quality and safety.

- **National leadership and recognition.** OHSU’s John Raaf Professor, Kim Burchiel, M.D., F.A.C.S., served as president of neurosurgery’s national residency directors’ society and chair of the Neurosurgical Residency Review Committee. Campagna Professor and Chair of the Department of Neurological Surgery, Nathan Selden, M.D., Ph.D., received the national Parker Palmer Courage to Teach Award.

The OHSU neurosurgical faculty recognizes that caring for each patient and ensuring the progress of the field both depend on innovative, high-quality education. The Department of Neurological Surgery is proud to lead the way in the science of surgical education.
Advanced fellowships

Neurology
The OHSU Department of Neurology has a highly regarded residency program that includes the option of a research track. There are funded adult fellowship programs, most of which include advanced training in clinical research that leverages OHSU’s Human Investigations Program:

- Movement disorders
- Multiple Sclerosis and Neuroimmunology
- Aging and Alzheimer’s/Geriatric Neurology
- Stroke/Vascular Neurology
- Epilepsy
- Neurocritical Care
- Neuromuscular Medicine
- CAM Research Training in Neuroscience and Stress

Neurosurgery
Neurosurgeons come to OHSU for specialty training in the most advanced areas of care:

- Skull base and cerebrovascular surgery
- Endovascular neurosurgery
- Functional neurosurgery (epilepsy and movement disorders)
- Pediatric neurosurgery (the Campagna Endowed Fellowship)
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