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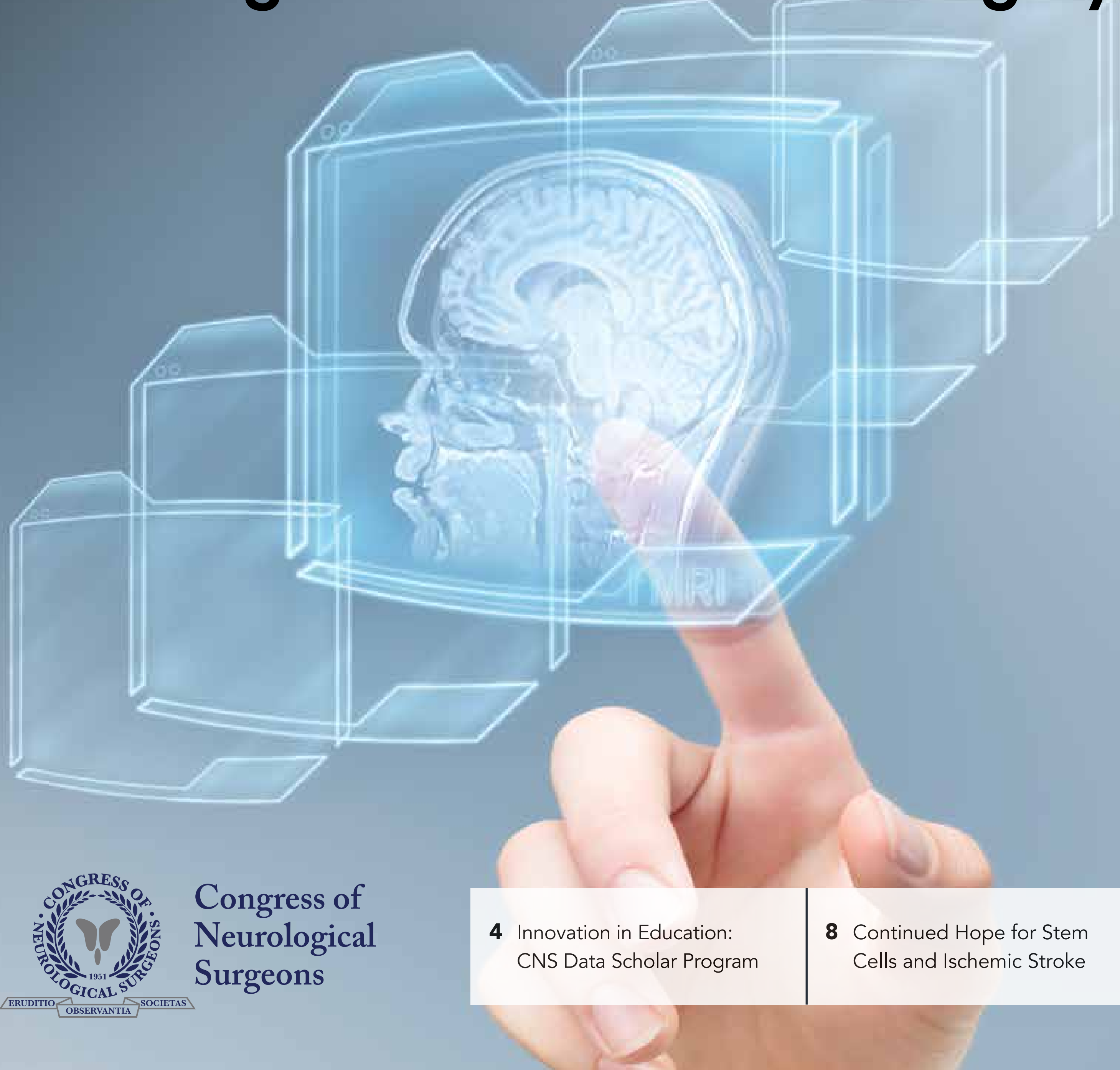
congressquarterly

SPRING 2020

INNOVATION
is Driving the Future of Neurosurgery



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The Congress of Neurological Surgeons exists to enhance health and improve lives through the advancement of neurosurgical education and scientific exchange.

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Congress of Neurological Surgeons

EDITOR'S NOTE

Martina Stippler, MD
2019-20 Editor
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Dear readers:

I hope this issue of the Congress Quarterly finds you safe, well, and sane. As we conceptualized this issue on Innovation in Neurosurgery, we did not anticipate that we would deliver it in a world very much different from the one we knew.

As our day-to-day lives are disrupted, these unprecedented times challenge us to innovate, adapt, and change. Who would have thought that we would be holding our clinics virtually and checking on our patients through videocalls and chat rooms? Some of us have pioneered telemedicine for years, only to have the clinical and regulatory system make implementation cumbersome. As a result, telemedicine was not widely adopted. But within 48 hours of our hospital restricting access, we had a telehealth platform in place, a billing code available, and were seeing most of our patients virtually. You will find a refresher on telehealth and how this innovation could change the care we are providing in this issue.

As schools and universities are closed and large gatherings are banned, we now must conduct all our education virtually. Many neurosurgery programs have acted swiftly and embraced the new platform, as did the CNS, and I want to make all of you aware of the Virtual Visiting Professor activity the CNS has launched with the help of numerous volunteers. In this issue, Drs. Steinberg and Veeravagu, along with their program manager, Diana Antony, also share their team's experience with virtual teaching using the next generation of simulation.

Luckily, neurosurgery does not need a pandemic to institute change. As we show in this issue, innovations in the field of neurosurgery already take place on multiple fronts.

Drs. Lawton and Frisoli present innovative bypass surgery techniques. Doctor Grande et al report on stem cell therapy for stroke. We learn about precision medicine and application outside of cancer diagnosis. Drs. Tso, Rajah, and Dossani discuss the novel idea of remote robotic neuroendovascular surgery, which is most interesting in the current environment.

Big data research and its application to neurosurgery is presented by Drs. Oermann and Caridi, and Dr. Chambless informs us of the CNS Data Scholar Program, a new education model the CNS if offering to stimulate big data research in neurosurgery.

If you have ideas and are interested in becoming an inventor or mentoring people around you, will enjoy the article on how the Barrow Innovation Center mentors future inventors, as well as the article by Dr. Savastano on how to get your start-up off the ground.

Although these are challenging times for so many of us, this crisis brings our priorities into focus and will change us and our specialty. We all can innovate, adapt, and change neurosurgery for the better. Put more directly, in the words of Rahm Emanuel, "*Never let a serious crisis go to waste. And what I mean by that it's an opportunity to do things you think you could not do before.*"

Stay safe!

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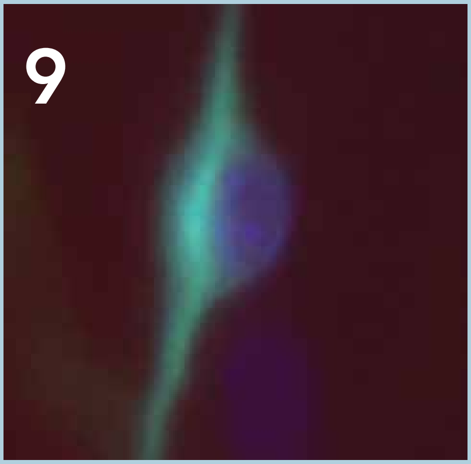
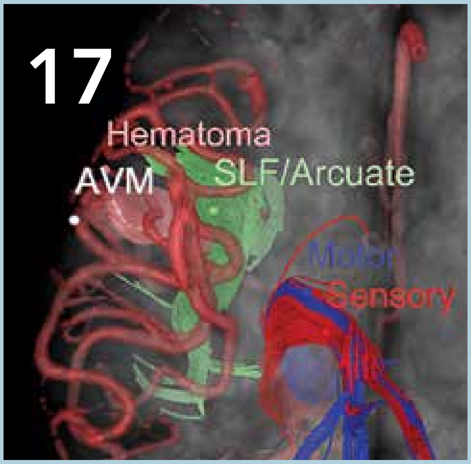
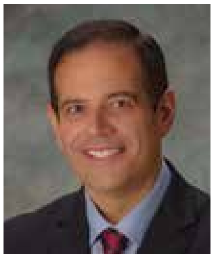




PRESIDENT'S MESSAGE



Steven N. Kalkanis, MD
President, Congress of
Neurological Surgeons

In this unprecedented time of challenge facing our nation, it's important to remember that innovation has always been central to the Congress of Neurological Surgeons' DNA. From the earliest days of our organization, our founding fathers sought to innovate the way surgeons gathered and educated themselves, and provided the best possible care to our patients. Throughout our history, we have welcomed the challenge of being organized neurosurgery's testing ground for new technologies and educational delivery platforms—from 3-D video to surgical simulators to immersive virtual reality.

Even this past month, in the face of the COVID-19 pandemic, our tireless CNS volunteers and staff developed two new programs to help our Resident members stay connected and continue their education in innovative new ways, free of charge. The CNS' robust online catalog of on-demand webinars has been curated and presented as an online residency training curriculum covering all subspecialty areas in an effort to partner with program directors and department chairs around the country in the face of cancellations of in-person didactic sessions, teaching seminars and grand rounds. As an alternative, each week, the CNS Education Team will deliver recommended webinars that will provide at least 2-3 hours of didactic material ranging from subspecialty topics to healthcare economics. We are also launching a new Virtual Visiting Professor activity that will enable one pre-eminent lecturer to present a chosen topic to multiple neurosurgery departments at once via CNS' robust webinar platform. We plan to hold at least four such fully moderated

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> AS ALWAYS, THE CNS REMAINS COMMITTED TO SEEKING NEW WAYS TO CREATE VALUE FOR MEMBERS AND ADVANCE THE SPECIALTY. I ENCOURAGE YOU TO REACH OUT TO ME IF THERE IS ANY WAY CNS CAN BETTER HELP YOU ADVANCE YOUR NEUROSURGICAL CAREER. <

Virtual Visiting Professor lectures, varying by time zone, on a monthly basis to ensure that as many programs as possible can participate.

This fall in Miami, we will extend our great tradition, and take a deep dive into the innovations shaping neurosurgery today and for years to come. Our theme for the Miami meeting *is Neurosurgery 20/20: Vision for the Future*. You can expect to see another amazing lineup of original science presentations, breakthrough developments in the field, and illuminating keynote speakers, who will challenge us to rethink the way we approach our practice. From futurist Adam Gazzaley to pre-eminent leaders like Ambassador Nikki Haley and so many others, we will celebrate our past and plan for a future with neurosurgery leading the way. We are also celebrating the tremendous diversity in our profession, culminating with the celebration of the 30th anniversary of Women in Neurosurgery at our annual meeting. By popular demand, also plan on seeing the integrated, specialty-specific symposia on Saturday and Sunday—including some courses that bridge specialties to benefit from the expertise of a broader faculty beyond neurosurgery from related disciplines —as well as controversial topic debates to give you a broad perspective on topics relevant to your sub-specialty.

This issue of Congress Quarterly celebrates our organization's commitment to innovation, but also broadly explores how innovation impacts our field today and into the future. Throughout the issue, you'll find insight on advances across our specialty, including stroke care, bypass and personalized medicine. You will learn how Stanford University is leveraging new virtual reality technologies to change Residency training, and how the Barrow Neurological Institute is helping foster development of new surgical technologies through their Innovation Center. Dr. Lola Chambless also provides an update on page 4 about CNS' Data Science Scholar program, created to help the next generation of surgeons develop skills to help us filter and integrate advanced data science techniques into applications accessible to the broader neurosurgical community.

I hope you enjoy this issue and I look forward to further exploring innovation with you in Miami this fall. As always, the CNS remains committed to seeking new ways to create value for members and advance the specialty. I encourage you to reach out to me if there is any way CNS can better help you advance your neurosurgical career.

Please stay safe and strong for your families and for your patients during this challenging moment in our history. As always, neurosurgery can and will serve as the tip of the spear to guide our colleagues through this turbulence.

Lola B. Chambless, MD

Innovation in CNS' education

CNS Data Scholar Program

Education is in evolution. Models of learning that were entrenched in our culture for a century are increasingly shown to be a poor fit for the educational environment of the 2020s. Didactic lectures, rote memorization and the Socratic Method were mainstays of most of our medical education. However, the data revolution of the early 21st century has changed the landscape in which we learn. The sheer volume of information at our fingertips is both thrilling and intimidating; it means that today's physicians need to be as good at accessing, interpreting, and judging new information as they are at remembering core medical facts.

This evolution is readily apparent in the medical school of 2020. Today, students increasingly participate in "flipped classroom" environments with an emphasis on finding and interpreting primary scientific literature. Experimental design and critique are emphasized as core competencies in a world where the sheer volume of scientific publications is insurmountable, and the quality is highly variable. While much neurosurgical skill acquisition still happens in the mentored environment of the operating room, it is important to realize that today's trainees enter residency with a different skill set and look at medicine through a modern lens. At the organizational level, the Congress of Neurological Surgeons seeks to map this changing landscape and identify opportunities to support trainees and members in novel ways.

One of the specific challenges we face as physicians today is understanding and harnessing the rapidly changing field of data science. Most physicians were trained with a basic background in statistics and little, if any, exposure to computer science. However, the explosion of "big data" and integration of artificial intelligence into all aspects of our daily lives means that many of us operate with an understanding of analytics that is largely obsolete. Unfortunately, these are complex fields and real understanding requires extensive training in mathematics and programming which is simply not feasibly obtained in the course of most neurosurgical careers.

In 2017, then CNS President-Elect Ashwini Sharan created a new committee on Data Science and Technology. He recognized the data revolution underway in healthcare and hoped to ensure that CNS members were equipped to use these new technologies to improve care for patients with neurosurgical disorders. In our initial efforts we used courses, symposia, and literature reviews to introduce these concepts to the CNS membership. Over time we recognized that moving beyond a superficial exposure to these techniques would require an innovative approach and we developed a new program: the CNS Scholarship in Data Science.

This annual scholarship, co-sponsored by the CNS Foundation (CNSF) and industry leader in deep learning, Viz.Ai, provides one neurosurgery resident annually with $20,000 of financial support and mentorship from leaders in the field of neurosurgical data science. This program is meant to be undertaken during a research/elective year of residency and includes individualized coursework, connection to a research mentor and project, and support for travel for research collaborations and scientific meetings. The Scholar will also join the CNS Data Science Committee to participate in the ongoing development of additional programming for CNS members in this space.

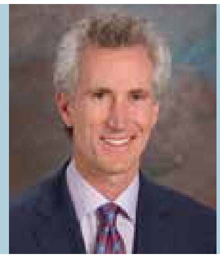
One of the goals of this scholarship is to create a small group of future leaders who are neurosurgeons with true expertise in advanced data science techniques. Our hope is that these scholars will develop skills that they use not only in their own research careers but on an organizational level to help us filter and integrate this knowledge into applications accessible to the broader neurosurgical community. In this way, we are counting on our youngest minds to help us prepare for the future needs of our specialty. This reflects the theory behind the flipped classroom; anyone who has ever tried to teach a concept can recognize that teaching is easily the most effective way to learn.

This scholarship is a unique pilot program in other ways. Through this project we seek to provide trainees with education that is beyond the core competencies of a neurosurgical residency. We offer training that is methodological rather than technical. Importantly, this work is undertaken in parallel with the existing residency curriculum. Conventional fellowships offer additional training beyond residency and bear a significant financial and logistical cost as a result. An important feature of this scholarship is that it is inherently flexible and carefully designed to be accessible as an enfolded opportunity to residents in most training programs. The mentorship model allows us to work with a scholar and their Program Director to ensure their success in the scholarship program while not detracting from their residency responsibilities. Fully protected time is not required, nor is a local research mentor.

Inclusion is also an important goal of this program. We seek to offer a robust academic opportunity to residents who may otherwise not have a research project of this type available to them. We hope to connect enthusiastic, driven trainees with national mentors they might otherwise never meet and to bring them into the CNS Committees where they will have the opportunity to gain experience in organized neurosurgery. In the future, other scholarships of this type may be developed to train future leaders in fields like Quality Improvement, Ethics, Device Development, or others. Administration of such programs by a national organization like the CNS can ensure accessibility of such training regardless of individual residency program site.

Innovative educational programming of this type is impossible without financial support. The CNS Foundation and industry partner Viz.Ai have jointly sponsored this program because of their recognition that the field of neurosurgery is at a critical point where understanding and adopting advanced data science is critical to the mission of improving patient care. Supporting the CNS Foundation is another way neurosurgeons can ensure that our education mission continues to evolve towards better and better patient care.

We received many applications for the inaugural position from residents with backgrounds ideally suited to future leadership in this space, and in February, the CNS awarded the 2020/21 scholarship to Dr. Matthew Pease, a PGY-5 Resident at University of Pittsburgh Medical Center. Applications for next year's position will open in October 2020 – please consider applying or encouraging a trainee to take part in this educational experience. For more information, please visit **cns.org/datascholar**



Fabio Frisoli, MD

Michael T. Lawton, MD

Innovations in Bypass Surgery

Introduction

An issue examining innovations driving the future of neurosurgery would not be complete without including bypass surgery. Unlike many of the deconstructive operations that we perform (like aneurysm clipping, AVM resection, or tumor removal), bypass surgery is constructive, creating connections between donor and recipient arteries not previously in existence to revascularize sacrificed arteries or augment deficient blood flow. Bypasses can be built with conventional extracranial-intracranial (EC-IC) constructs like a superficial temporal artery-to-middle cerebral artery (STA-MCA) low-flow bypass or an external carotid artery-to-middle cerebral artery high-flow bypass. However, bypasses can also be built with more innovative constructs like the intracranial-intracranial (IC-IC) reconstructions that include reimplantation, reanastomosis, in situ bypass, or interpositional bypasses. These six different types of bypasses, plus the combination bypasses for lesions that require revascularization of more than one efferent artery, give us a wide variety of options and opportunities to innovate (**TABLE 1**).

Shifting Toward Intracranial Reconstruction

Conventional EC-IC bypasses are common because of their simplicity, familiarity, and durability. Woringer and Kunlin performed the first common carotid-internal carotid bypass in 1963,[1] and early bypasses were used to treat occlusive disease with extracranial donors such as the STA or common carotid artery with saphenous vein or synthetic interposition grafts.[2,3] The STA-MCA bypass was refined by Yasargil and Donaghy in the 1960s,[4,5] and indications expanded in the 1970s to include moyamoya disease, vertebrobasilar insufficiency, and dolichoectatic aneurysms.[6-9] These 1st generation (low-flow EC-IC bypasses with scalp arteries as donors) and 2nd generation (high-flow EC-IC bypasses with interposition grafts) techniques continue to feature prominently in the armamentarium of the bypass surgeon four decades later. However, the paradigm is shifting towards IC-IC bypass (3rd generation bypasses) because of advantages that include: no extracranial donor harvest; similarity of recipient and donor vessel caliber; protection within the skull; and a single incision/approach.[10] Numerous studies have demonstrated the efficacy and versatility of the IC-IC bypass for aneurysm surgery .[11-13]

TABLE 1. Characteristics of fourth-generation bypasses compared to other bypasses

Bypass	Seven Bypasses No.	Generation (type)	No. of Anastomoses	Anastomosis	Technique
EC-IC bypass	1	1	1	E-S	Conventional
EC-IC interpositional bypass	2	2	2	E-S, E-E	Conventional
Reimplantation	3	3	1	E-S	Conventional
		4A	1	E-S	In situ
		4B	1	E-E	Conventional or in situ
		4B	1	S-S	In situ
In situ bypass	4	3	1	S-S	In situ
Reanastomosis	5	3	1	E-E	Conventional
		4A	1	E-E	In situ
		4B	1	E-S	Conventional or in situ
		4B	1	S-S	Conventional or in situ
IC-IC interpositional bypass	6	3	2	E-S, E-E	Conventional
		4A	2	E-S, E-E	In situ
		4B	2	S-S	In situ
Combination bypass	7	3	≥2	E-S, S-S, E-S	Conventional or in situ

E-E = end to end; E-S = end to side; S-S = side to side.

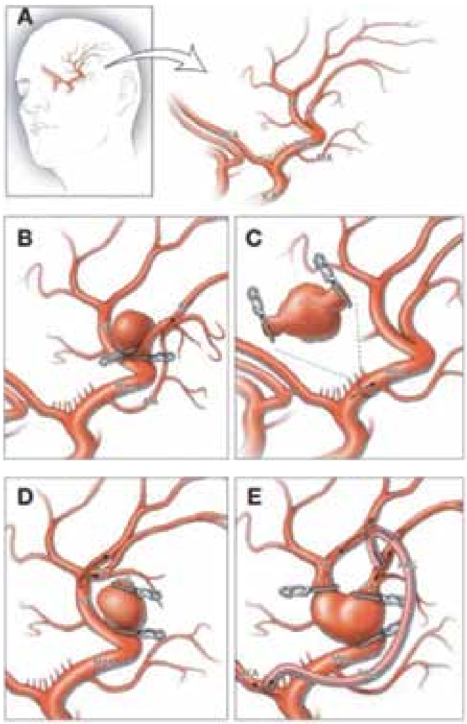


Figure 1: *3rd generation intracranial -intracranial (IC-IC) bypass techniques for MCA aneurysms.* **A)** *conventional MCA anatomy;* **B)** *in situ bypass (ATA-M2 MCA);* **C)** *M1 MCA reanastomosis (end-to-end);* **D)** *M2 MCA reimplantation (end-to-side);* *and* **E)** *intracranial interposition bypass (A1 ACA-RAG-M2 MCA+M2 MCA)*

An in situ bypass uses a communicating side-to-side anastomosis between donor and recipient arteries that run in parallel, without a dedicated donor limb and with bypass flow regulated by intrinsic demand. Examples of parallel arteries joined with in situ bypass include the insular M2 segment of the MCA and the anterior temporal artery (ATA) within the sylvian fissure (**FIGURE 1**), the bilateral anterior cerebral arteries (ACA) within the interhemispheric fissure, the posterior cerebral artery (PCA) and superior cerebellar artery (SCA) within the ambient cistern, bilateral posterior inferior cerebellar arteries (PICA) beneath the cerebellar tonsils, and finally the PICA and anterior inferior cerebellar artery (AICA) within the cerebellopontine angle. When a branch artery is compromised during aneurysm trapping, reimplantation of the efferent artery onto the parent artery can be performed with an end-to-side anastomosis, most often with branches of the MCA, ACA, and PICA. Reanastomosis is an end-to-end reconstruction of the parent artery after excising intervening pathology, with feasibility predicated upon redundancy or slack in the ends after excision and the presence of just one outflow artery. Interposition grafts can be used to join remote intracranial arteries, but unlike EC-IC interpositional bypasses that require long grafts and tunneling, intracranial grafts are shorter and lend themselves to combination bypasses that reconstruct bifurcations. An example would be an A1 ACA-RAG-M2 MCA+M2 MCA double reimplantation bypass for a trapped MCA bifurcation aneurysm. The breadth and diversity of intracranial bypasses allow the neurosurgeon to be creative when improvising or dealing with unexpected intraoperative circumstances.

4th Generation Bypasses

While 3rd generation bypasses mentioned above use conventional anastomoses and conventional suturing techniques, a fourth generation of bypasses emerges when these anastomoses and techniques are mixed and shuffled (**FIGURE 2**). A conventional construct can be created using an unconventional suturing technique (Type 4A), such as a p3 PICA-p3 PICA reanastomosis performed end-to-end with intraluminal suturing for the back wall rather than extraluminal suturing throughout. An unconventional construct can be created with conventional suturing technique (Type 4B), such as an A1 ACA-RAG-M2 MCA+M2 MCA double reimplantation bypass with the graft supplying one of the M2 trunks and the M2 trunks transected from the aneurysm and reimplanted to one another end-to-end (**FIGURE 3**).

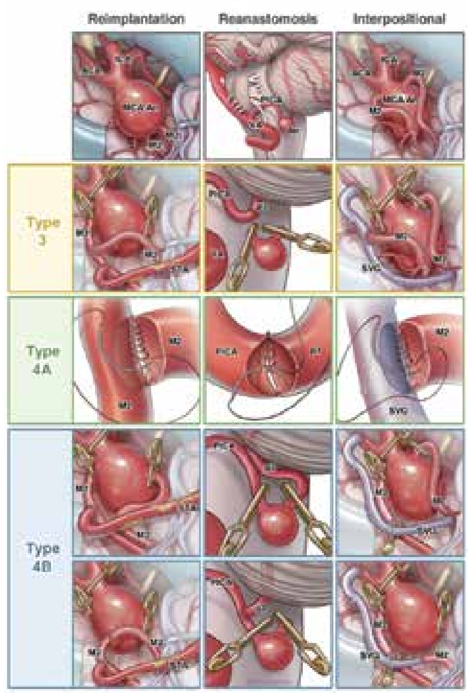


Figure 2: *4th generation bypasses arise from variations in structure or technique of 3rd generation constructs (second row). Type 4A bypasses contain conventional structure but utilize unconventional technique (i.e., intraluminal suturing; third row). Type 4B bypasses couple unconventional structure with conventional or unconventional technique* (fourth and fifth rows). *MCA+M2 MCA)*

This last bypass is an example of a "middle communicating artery" (MCoA). It repurposes the arterial limbs that would have otherwise been "dead-ends," freeing them from the aneurysm and rejoining them to communicate flow from the interposition graft to both M2 trunks originating from the trapped MCA bifurcation aneurysm. Revascularization of two efferent branches usually requires double-barrel STA-MCA bypass or a high-flow EC-IC interposition graft with double reimplantation of the M2 divisions. Both techniques have deficiencies that can be improved upon. For example, with double-barrel STA-MCA bypass, the M2

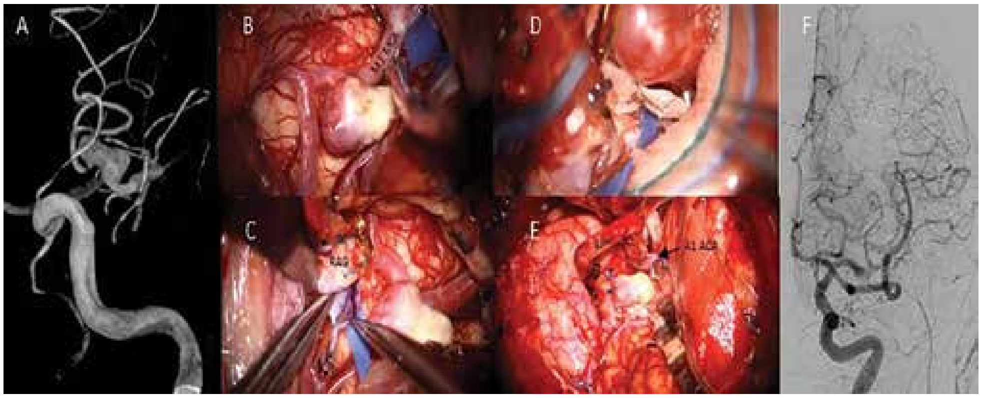


Figure 3: *Case example of a dolichoectatic MCA bifurcation aneurysm treated with bypass (A1 ACA-RAG-M2 MCA+M2 MCA, with a middle communicating artery or MCoA) and distal clip occlusion.* **A)** *3-dimensional reconstruction of internal carotid artery (ICA) angiogram demonstrating the dolichoectatic MCA bifurcation aneurysm involving the origin of both M2 divisions.* **B)** *Intraoperative photograph demonstrating inflow and outflow of the aneurysm.* **C)** *Intraluminal view of the suture line between the radial artery graft (RAG) and the recipient inferior M2 division.* **D)** *End-to-end reimplantation of superior division to the inferior division of the MCA, creating the MCoA.* **E)** *Final construct demonstrating the 3 anastomoses (A1-RAG, RAG-M2 MCA, and M2 MCA-M2 MCA) and distal clip occlusion of the aneurysm.* **F)** *Postoperative ICA angiogram demonstrating patency of the bypass and distal branches, as well as thrombotic occlusion of the aneurysm. with conventional or unconventional technique* (fourth and fifth rows). *MCA+M2 MCA)*

trunks are isolated and a diminutive STA may be inadequate to meet the demands of half the MCA territory. However, fourth generation techniques like end-to-end M2-M2 reimplantation, can create a communicating bypass between the efferent branches that permits bidirectional flow to either trunk as dictated by demand and pressure gradients. In effect, this recapitulates the function of the anterior (ACoA) and posterior (PCoA) communicating arteries. The construction of communicating arteries gives a bypass the capacity to respond immediately to demands created by pressure gradients or arterial occlusions, without compromising native blood flow in parent arteries. Just as the combination of an ACoA and two PCoAs to form the circle of Willis prevents countless strokes, the creation of a MCoA can have protective benefits in the MCA territory. The MCoA bypass is an example of innovative applications of bypass techniques that advance our surgical solutions.

Conclusions

In this modern era where innovation is synonymous with technological advancement, it is remarkable what can and has yet to be created with simple suture and meticulous technique. The application of IC-IC reconstructive techniques and 4th generation bypasses allows the bypass surgeon to innovate without high technology. The list of new bypasses conceived but not yet performed is long, and it challenges us to not only maintain competencies in this refined craft, but to push our dexterity further. Even though bypass techniques are decades old, their application in novel ways makes the future of open vascular surgery dynamic and exciting.

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Continued Hope for Stem Cells and Ischemic Stroke: Review and Future Perspectives

An Increasing Need and Potential Opportunities

Can stem cells be used to treat stroke? Ischemic stroke remains a leading cause of death and disability throughout the world. Adjuvant therapies that can be used beyond the restrictive time windows of IV tissue plasminogen activator (tPA) or mechanical thrombectomy are desperately needed in order to prevent death or life-long disability. Throughout the past three decades, the field of stem cell biology, as it relates to stroke, has continued to excite and challenge clinicians and scientists.

Endogenous Neurogenesis from Neural Stem Cells

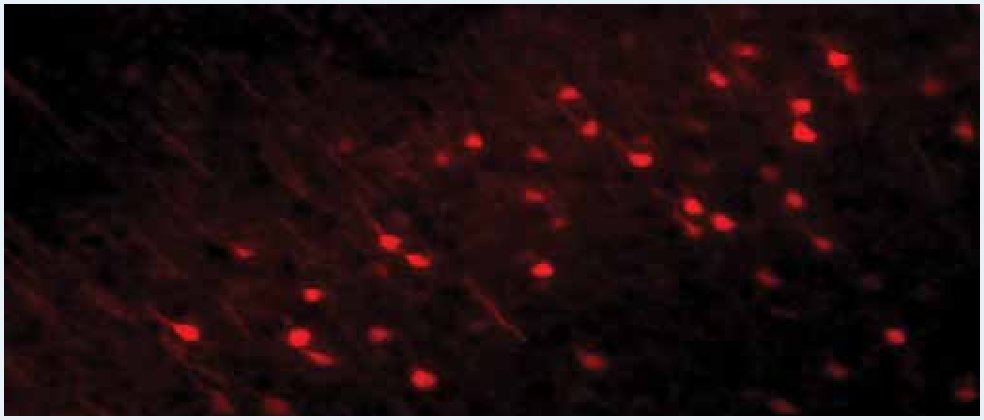
In 1913 Professor Santiago Ramon y Cajal spoke of the post-natal brain's ability to regenerate itself by saying, "In the adult centers, the nerve paths are something fixed, ended and immutable. Everything may die, nothing may be regenerated." It wouldn't be until 80 years later when a series of studies demonstrated the persistence of small populations of neural stem cells (NSCs) in the post-natal rodent subventricular zone (SVZ) thereby disproving this "harsh decree." Subsequent studies expanded upon this finding by demonstrating that neurogenesis may be an ongoing process within the adult mammalian brain in both the SVZ as well as the subgranular zone (SGZ) of the dentate gyrus. From these findings in rodents several questions arose, including whether or not these same populations of NSCs existed within the adult human brain. If they did, then was neurogenesis a lifelong process similar to what had been demonstrated in rodents? In a 1998 study, Eriksson et al. provided one of the first pieces of evidence that dividing cells exist within the human dentate gyrus.[1] Subsequent studies demonstrated that this process occurs throughout adulthood within the SGZ.[2] Further excitement was incurred by Paredes et al. who found that NSCs were also found to reside in the SVZ of human infants, similar to that seen in rodents.[3] Furthermore, the NSCs found in this study demonstrated extensive migration into the frontal lobes, invoking added enthusiasm for the potential of human neurogenesis. Could this endogenous process be harnessed and manipulated to generate new neurons following a stroke? Despite a surge of enthusiasm from these early studies, disappointment was on the horizon. It was subsequently discovered, that the migratory pattern of these NSCs within the SVZ was not evident beyond 2 years of age, indicating that NSCs of the SVZ have limited involvement in the regenerative process within the adult brain.[4] In fact, though cells with NSC-like properties have been isolated and cultured in vitro, the existence of NSCs within the adult SVZ[5] remains in question. Some rodent studies have shown that NSCs can migrate ectopically to the striatum following a stroke in this area, but this has failed to be demonstrated within the cortex. Even with attempted recruitment of NSCs to the site of cortical infarction using various growth factors and cytokines no such migration has been evident. Even though NSCs within the dentate gyrus have been well-demonstrated to generate new neurons throughout adult life within the hippocampus, there is no evidence that they can be recruited to sites of injury following stroke. Despite early excitement, these more

High-magnification images of neurons derived from neural stem cells in vitro. These neurons are expressing Tuj1 (green), a marker of a more differentiated, mature neuron.

recent findings have tempered enthusiasm that endogenous neurogenesis in the human brain can be harnessed for brain repair after stroke. Consequently, alternate avenues for generating new neurons following stroke began being pursued.

Exogenous Stem Cells

Around the turn of the century, as an alternative to manipulating endogenous neurogenesis following stroke, several groups began to wonder whether an exogenously administered source of stem cells could regenerate lost neurons. Pioneers and leaders in the field including Professors Michael Chopp and Walter Low developed strategies to regenerate the brain utilizing allogeneic lines of stem cells from sources such as bone marrow and umbilical cord blood administered intravenously in rodent models of stroke. Initial studies demonstrated a robust benefit in which treated animals had significantly improved neurological function as compared to control animals. These findings generated excitement about the use of exogenous stem cells as a potential stroke therapeutic. The proposed mechanism of these cells was that they would migrate to the damaged brain parenchyma, differentiate into the appropriate neuronal subtype and integrate themselves into the host circuitry thereby effectively replacing lost neurons. Intriguingly, the researchers did not find any evidence that these infused stem cells had differentiated into neurons in the brain. How could there be such an obvious functional benefit without generating new neurons? The answer would be revealed in subsequent studies which found the donor cells provided therapeutic benefit indirectly by modulating the toxic post-stroke milieu, both within the brain and systemically. Within the brain, infused stem cells were found to secrete supportive and protective factors that decreased neuronal apoptosis and increased survival. They were also found to secrete potent pro-angiogenic signals that increased the formation of blood vessels, thereby enabling the development of collateral blood flow pathways to the injured penumbral tissue. Perhaps the most robust mechanism that exogenous stem cells were found to utilize was immunomodulation of the peripheral immune system. By secreting immunoregulatory factors, the damaging intraparenchymal post-stroke inflammatory response could be abated, thereby reducing collateral damage within the brain. With the discovery of these modulatory capabilities and abundant animal studies demonstrating robust efficacy, industrial involvement in stem cell therapies for stroke has increased significantly. Indeed, several clinical trials have been completed and many are currently ongoing. Thus far, data from these trials has not been as exciting as pre-clinical animal models: Though they have been shown to be safe, their efficacy has, in contrast to animal models, been rather variable. This contrast has inevitably posed the question as to why such strong data was observed in the laboratory but not in the clinic. The The multipotent adult progenitor cells in acute ischaemic stroke (MASTERS) phase 2 trial funded by Athersys Inc. (Cleveland, OH, USA) found that IV administration of multipotent adult progenitor cells between 24-48 hours after symptoms onset was safe, although there was no significant improvement in 90 day neurological outcome between treatment and control groups.[6] One hypothesis for the disappointing results posed by the authors is that cells were administered too late, and it was suggested that a future study should utilize a shorter time window after symptom onset. Multiple theories have been generated for the failed clinical translation such as that seen in MASTERS. One such theory is that rodent and human immune systems carry many significant differences. Given the primary immunomodulatory mechanism of exogenous stem cells, one can see how this could lead to varying results between the two species. As such, the importance of testing these potential therapies in models that are more evolutionarily similar to humans, such as non-human primates, has been emphasized in order to improve translation. Could route of administration play a role? Besides IV infusion, other routes of stem cell administration have also been utilized including injecting directly into the peri-infarct area.[7] Areas for potential improvement of exogenous stem cell treatment for stroke continue to be addressed, though other stem cell-related therapies may be more attractive to some.



Section of mouse brain showing neurons that have been transduced by a viral vector to express mRuby2 (red). Such viral vectors represent a potential method of reprogramming non-neuronal cells to adopt a neuronal phenotype in vivo.

Cellular Reprogramming and Stroke

In two groundbreaking papers published in 2006 and 2007, Professor Shinya Yamanaka described how both mouse and human fibroblasts were able to be induced to form pluripotent stem cells in vitro by using only four critical transcription factors.[8,9] With this discovery, the field of induced pluripotent stem cell (iPSC) biology was born. With this new technology, the question for developmental neuroscientists was whether or not cells such as fibroblasts or astrocytes could be induced to form neurons in vitro via a similar mechanism. Several subsequent studies demonstrated that not only was this possible, but that with the correct culture recipe distinct subtypes of neurons could be specified. These findings lead to the question that, if grown correctly in culture, could iPSC-derived neurons be transplanted into a brain that had undergone a stroke? Indeed this has since been accomplished.[10] However, several issues with this method arose: Can the correct, complex mosaic of neuronal subtypes that were lost in a stroke be regenerated in culture and subsequently transplanted effectively? How long would developing this complex neuronal phenotype in vitro take? Given these challenges, researchers began to wonder whether or not abundant supporting cell types in the brain, (astrocytes or pericytes, for example) could be reprogrammed in vivo. Several subsequent papers demonstrated that in vivo reprogramming of non-neuronal cells was not only possible, but that, based on locoregional and other environmental cues within the brain, multiple distinct neuronal subtypes could be generated from non-neuronal cells, via a reprogramming approach.[11] These findings indicate that the environment within specific brain regions may direct the formation of subtype-appropriate neurons, and all that needs to be applied on our part is the correct reprogramming signal. Currently direct in vivo reprogramming is thought to represent a much more efficient method of generating new, subtype-specific neurons as opposed to in vitro reprogramming of iPSCs to neurons with subsequent transplantation. Though this approach represents an exciting avenue to potentially generate new neurons after stroke, this methodology remains in its infancy, and much work remains to produce a safe and efficacious treatment modality.

What lies ahead?

Stem cells have been and continue to be a promising treatment modality for stroke. Despite mixed results in early clinical trials, the use of exogenously-administered stem cells to dampen post-stroke inflammation, induce angiogenesis, inhibit apoptosis and provide neuroprotection continues to be an attractive adjuvant option for stroke patients. With the help of improved animal modeling, rigorous pre-clinical study design and proper administration timepoints, exogenous administration of stem cells remains an exciting therapeutic avenue. Indeed, several clinical trials are ongoing, some of which include variations such as surgically placing stem cells directly into the peri-infarct area, which may represent a more efficacious administration strategy. The introduction of iPSC technology has revolutionized the field of regenerative neurobiology and several lines of evidence have shown that new neurons can be generated in vitro. However, advances in the areas of direct in vivo reprogramming of non-neuronal cells may be a more efficient and efficacious method of generating new neurons after a stroke, though a long road remains to be traveled in this regard. With these myriad potential options, stem cells remain steadfast in their promise to make an ever-improving impact on stroke treatment and in the lives of stroke patients.

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Ellen L. Air, MD, PhD

Precision Medicine

More than 70 years ago, the Framingham Heart Study (FHS) began the audacious task of following more than 5,000 men and women in Framingham, Massachusetts to identify risk factors for cardiovascular disease.[1] Following the scourge of infectious disease coming under control in the 1940s, nearly 50% died of heart disease. Typical approaches to determine the causes continued to fail. Hard to imagine now, but the FHS approach, and insights gained, initiated a dramatic shift in biomedical research and disease management.

In this age of 'Big Data', it is again time to rethink our approach and accelerate medical breakthroughs. This is exactly what precision medicine aims to do. While the FHS investigators recognized the likely interaction between "host and environment," ongoing discovery is revealing the importance of epigenetics (as one among a number of molecular 'layers' which can modulate gene expression) in disease development and treatment. This is particularly true for cancer. Yet, obtaining genetic information, not to mention interpreting and applying it to an individual's disease, is a formidable task.

Precision medicine meets this challenge by combining a detailed analysis of a patient's genetics and environment with the insights gained from data sourced from large numbers of diverse individuals. As CNS President and CEO of Henry Ford Medical Group, Steve Kalkanis, describes, "discovering a unique and clinically relevant mutation in a patient who had failed second-line brain tumor therapy, allowed the patient to be enrolled in a clinical trial targeting that mutation, even though that treatment was originally intended for a different disease. Beating the odds, the patient responded to the treatment devised through crowd-sourced bioinformatics."

The Henry Ford Cancer Institute (HFCI) in Detroit, MI implements precision medicine by incorporating experts of a Molecular Tumor Board into the traditional tumor board process. In addition, as part of the Cancer Moonshot^{SM} Initiative[2], HFCI has partnered with Syapse, Inc. to share de-identified data across health systems so the right information can be accessed to solve specific problems.

While cancer is at the leading edge of precision medicine, it is an approach increasingly applied to other diseases. The NIH is doing just that through its Precision Medicine Initiative (PMI) and the All of Us Research Program[3] by gathering genetic, biometric, environmental and other data from a minimum of one million people. With more than 300,000 individuals already enrolled, the number of data points generated already dwarfs that of the FHS.

> IN THIS AGE OF 'BIG DATA', IT IS AGAIN TIME TO RETHINK OUR APPROACH AND ACCELERATE MEDICAL BREAKTHROUGHS. THIS IS EXACTLY WHAT PRECISION MEDICINE AIMS TO DO. <

Combining such a large data set with an ever-expanding capacity for analysis promises new insights into long-standing medical mysteries. Furthermore, the ability for any approved researcher to use the data in testing new hypotheses, opens the door to innovation and cross-fertilization. The results have the potential to change the way healthcare is delivered.

"It's all about tailoring medicine and prevention to the individual – treating patients based on genetics, immunology, metabolism, diet, and all kinds of personalized things," states Christine Cole Johnson, Ph.D., MPH, Chair of Public Health Sciences. Dr. Johnson, along with Brian Ahmedani, PhD, Director of Research for Behavioral Health Medicine, are the Principal Investigators for the Trans-American Consortium for the Health Care System Research Network, led by Henry Ford Health System (HFHS). HFHS is one of seven sites in the country working to sequence those million-plus Americans and working the expand the diversity and reach of the PMI. If the FHS, with 5,000 patients dramatically changed the way we addressed heart disease and risk factors like cholesterol, hypertension, etc., imagine what might be in store for us with the new molecular genetic tools we now have to analyze this new treasure trove of data.

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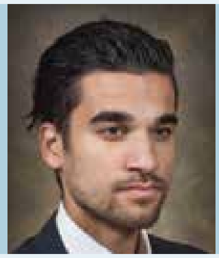
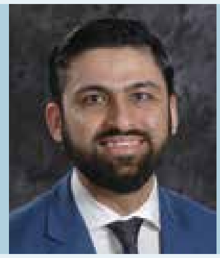

Michael K Tso, MD, PhD, FRCSC   **Gary B Rajah, MD**   **Rimal H Dossani, MD**

Robotics in Neuroendovascular Surgery: The Future is Now

An endovascular robotic platform was first developed for interventional cardiac procedures. The first percutaneous coronary intervention (PCI) robotic system was the RNS (NaviCath, Haifa, Israel), which was a table-mounted, joystick-controlled apparatus.[1] Subsequently, an initial robotic platform called the CorPath 2012 (Corindus Vascular Robotics, Waltham, MA, USA now recently acquired by Siemens Healthineers, Erlangen, Germany), was approved by the FDA in 2012 for PCI.[1] This was followed by a next generation CorPath GRX (Corindus Vascular Robotics, Waltham, MA, USA), which was approved by the FDA in 2016 for PCI.[1] The set-up involved a robotic arm mounted to the table with a disposable cassette and three slots used to place the guide catheter, rapid exchange catheter, and 014" microwire. The interventionalist, who sits at a workstation remote from the angio table, has the ability to advance and retract as well as rotate each of the three component slots. The CorPath GRX has also been successfully used in peripheral vascular interventions such as angioplasty for below-the-knee peripheral artery disease.[2] In preclinical studies, the CorPath GRX was also used to navigate into intracranial arteries of animal models.[3]

On November 1, 2019, a team at the Toronto Western Hospital in Toronto, Ontario, led by interventional neurosurgeon Dr. Vitor Pereira, performed the world's first robotic intracranial neurovascular intervention. The patient was a 64-year-old female with a large unruptured left superior cerebellar artery (SCA) aneurysm undergoing elective stent-assisted coiling. Interventional neuroradiologists Dr. Timo Krings and Dr. Patrick Nicholson provided endovascular support at the bedside and Ms. Nicole Cancelliere, the radiation technologist, provided assistance with the CorPath robot itself. There were no intraprocedural complications and the patient was discharged the next day. The team at Toronto Western Hospital had acquired the robotic platform several months prior and trialed its use with a reconstructed flow model of the patient's aneurysm. As of February 2020, the CorPath GRX has not yet been FDA approved for intracranial work. However, it has been used for diagnostic cerebral angiography and placement of extracranial stents. It is only a matter of time before the CorPath GRX will be approved for use in treating patients with intracranial vascular diseases in the US.

The CorPath GRX platform has the potential to address several issues relevant to the endovascular treatment of patients with cerebrovascular diseases. With the neurointerventionalist in close proximity to the radiation source of the angio apparatus, there is still significant radiation exposure despite appropriate radiation hygiene (including lead apron, lead glasses, ceiling-mounted shield and floor shields, and possibly head shield). Repeated radiation exposure can result in stochastic (e.g. cancer) and deterministic effects (e.g. cataracts).[4] By controlling the CorPath GRX from a remote shielded workstation, it possible to significantly reduce overall radiation exposure to the neurointerventionalist. Also, taking one step forward and using wireless technology, the interventionalist can be stationed in one location with the actual procedure being performed in a remote location, whether in another city or another state. This would help expand access to endovascular treatment for stroke to patients in remote areas and provide sufficient procedural case volume for neurointerventionalists to maintain expertise. There has been a trend toward decreasing case volume per hospital for mechanical thrombectomy, with better outcomes in high-volume hospitals.[5] In addition, there is opportunity for provide education and mentoring at remote locations. Finally, the robotic platform has the potential to provide a greater degree of precision in neuroendovascular procedures, especially with placement of stents.

The CorPath GRX platform was originally developed for PCI and is the first version to be used for intracranial pathology. There are significant limitations currently with this platform. There is still a considerable amount of work required for the angiography team at the patient's bedside including obtaining arterial access, loading the catheters and wires, and deploying stents with a push-pull delivery system. There is a loss of tactile feedback when using the robotic platform. Wire and catheter exchanges can be cumbersome. Finally, there will be a learning curve with this new technology for not only the neurointerventionalist but for the entire neurointerventional team.

Although we are still at the beginning of the early adoption phase of the innovation curve, robotics will have an increasing role in neuroendovascular procedures. The future is now.

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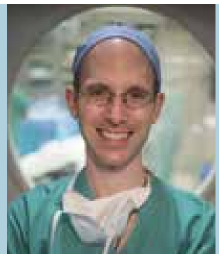

Eric K. Oermann, MD

John Caridi, MD

Innovations in Big Data for Neurosurgery

Modern existence is increasingly defined by big data – our ability to capture, store, and analyze large datasets. These capabilities are driven largely by technical innovations in digital storage and networking, as well as innovations in data analysis and artificial intelligence (AI). Neurological Surgery is one of the most technology focused medical disciplines, and is on the path to directly benefiting from several innovations in the big data space. While the areas where big data most directly impacts neurosurgery tend to be technical, we are increasingly seeing actual clinical innovations emerge as the field of big data matures.

Technical Innovations

Over the past decade, technologies like Hadoop and Spark seemed to promise the creation of monolithic data storage environments often built around relational databases and operated as "data warehouses". However, increasingly we are learning that the radically different storage needs of different data types: images, time series, knowledge graphs, etc, still favors siloing data into distinct storage systems. Uniting these systems in a "data lake" consisting of non-relational databases tied together by a common application programming interface (API) is beginning to fulfill the promise of a single interface to access all available organizational or clinical data. The Fast Healthcare Interoperability Resources (FHIR) offers a standard for accomplishing this in healthcare, and all medical fields but particularly neurosurgery are able to benefit from the increased ease of access to a broad range of health data. Other than FHIR, it is increasingly easy for big data to be mobilized using custom extract, transfer, and load (ETL) pipelines built on rapidly maturing data science libraries in Python, R, and in some cases Julia and C++. For follow-up analytics work, Kubernetes and Docker have revolutionized the provisioning of high performance computing resources and deployment of microservices. It has never been a better or more exciting time to exist as a developer in the big data space.

The other major area of technical innovations in big data is in the realm of algorithms. Over the past few years deep learning and AI techniques have begun to tackle the problem of learning models from less data. More data efficient algorithms are critical for allowing neurosurgery to harness the benefits of "big data" despite smaller datasets and patient populations. These techniques include: weakly supervised learning, generative adversarial networks, simulated data, and transfer learning. One of the most exciting that bears special mention is generative adversarial networks (GANs), whereby two deep neural networks compete in (typically) a zero sum game involving one forging data and the other guessing whether the data it sees is real or one of the forgeries. This technique can be used to augment smaller datasets with simulated examples that radically decrease the required amount of data for developing algorithms. When trying to classify animals, for example, the synthetic images from the corgi lead to the GAN model requiring substantially fewer images to have improved performance relative to a benchmark model (**Figure 1A-B**).

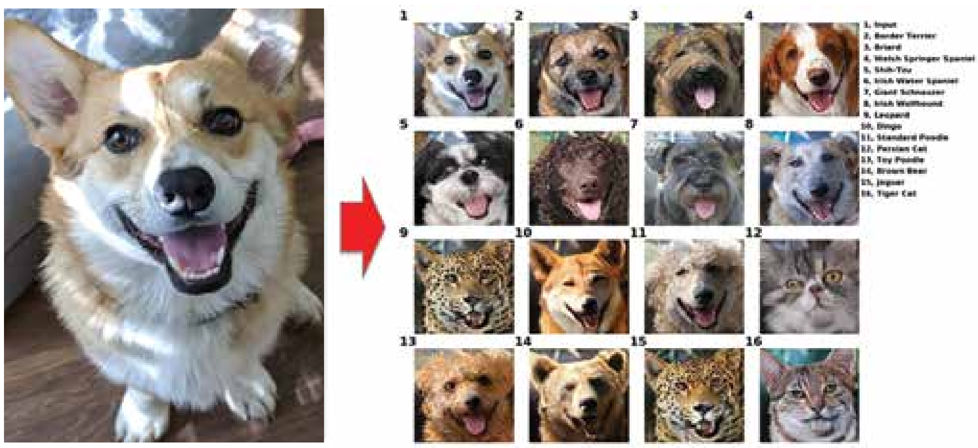

Figure 1A: *Demonstration of synthetic image generation by a generative adversarial network (GAN) that preserves key semantic properties of the original image while generating novel examples with novel features.*

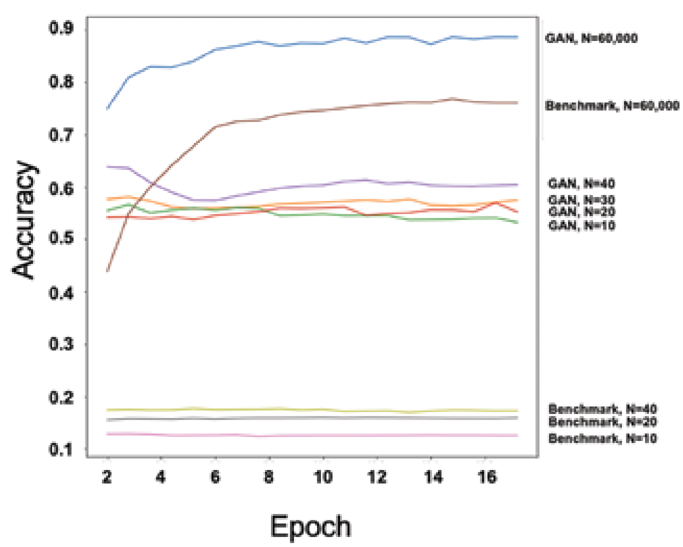

Figure 1B: *Training deep neural networks utilizing synthetic images can yield significant performance gains with regards to data efficiency. GANS with 10-40 original images significantly outperform standard convolutional neural networks (CNNs) on classification for the CIFAR-10 dataset.*

Clinical Innovations

With regards to clinical innovations in big data impacting neurosurgery, the rise of large multicenter registries for neurosurgical care is one of the foremost innovations.[1] Prospective registries such as NeuroPoint's Quality and Outcomes Database (QOD) offer the possibility of answering clinical questions that can't be addressed with randomized controlled trials, and aids in moving the field towards more data driven practices. Prospective registries have had a massive impact in Orthopedics in the form of joint registries, and it is reasonable to expect that, as neurosurgical registries accumulate more data, they too will have an impact on neurosurgical practice and outcomes.

Similarly, large claims databases are increasingly being harnessed to provide insight into neurosurgical diseases and populations. Databases such as the National Surgical Quality Improvement Program (NSQIP), National Inpatient Sample (NIS), and others can give researchers the ability to analyze neurosurgical disease at the population, local, and, in some cases, institutional level. These large analyses can give us a better understanding of outcomes, the natural history of diseases, and the broader impact of neurosurgical care on the population.

On a more granular level, the most impacted field by big data and machine learning in medicine is Radiology, and neuro-radiology is at the forefront of these changes. The ability to store large numbers of images and analyze them at scale has enormous promise for the use of big data in neurosurgery. AI driven analyses of these large datasets have begun to explore the possibility of radical new technologies for neurological surgery including: imaging gene expression, predicting clinical and radiographic outcomes, and providing rapid decision support.[2–6] Other imaging technologies involve the use of surgical video and its analysis, with the promise of automated case tracking, improved intraoperative imaging, and intraoperative decision support. Radiogenomics, the ability to use imaging to predict gene expression, is particularly promising as it offers a potential alternative to invasive biopsy and for monitoring treatment response.

Conclusion

Perhaps the most critical innovation in big data is that we're starting to learn what the right questions are. Technology is only as useful as the problems it solves, and as a field we're just starting to learn what constitute good questions to tackle with big data based approaches. As we better understand the questions in neurosurgery that big data and machine learning can answer, we will increasingly see the major gains in outcomes and performance from big data that have already been realized in other fields.

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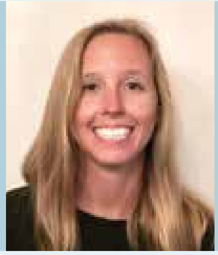

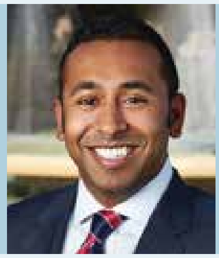

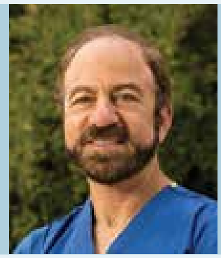

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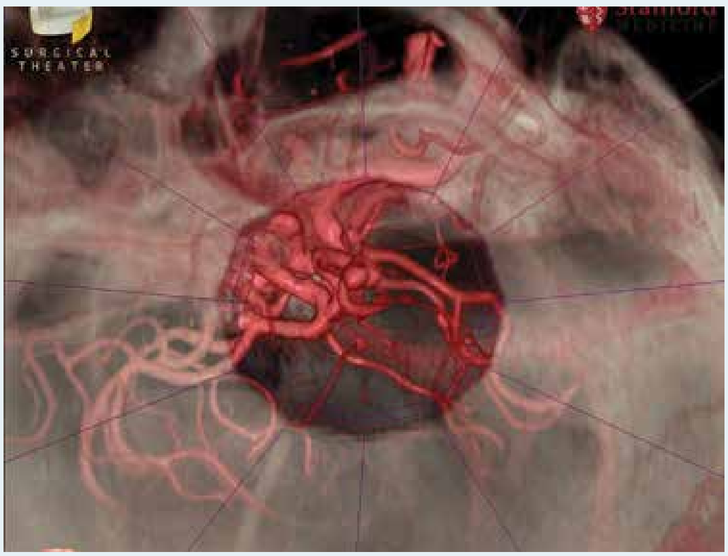
Gary K Steinberg, MD

Next Generation Simulation: Teaching in a Virtual Environment

"Practice makes perfect", or so they say. When it comes to neurosurgery, many would agree that perfection is what we strive for. Years of experience in the operating room, meeting hundreds of patients and discussing their symptoms, countless hours shadowing other physicians, and working in cadaver labs are all assembled together in the experience of a neurosurgeon, giving him/her continuous practice throughout his/her entire career. However, all the combined information that one acquires through these experiences leaves the surgeon with a collection of knowledge from different patients, each with different outcomes. We can draw parallels and make educated assumptions about each new patient we see, but one patient's experience can never be directly translated to the next. With recent developments in the field of Simulation, neurosurgeons can take advantage of a new tool that allows them to practice their skill on patient specific data. Never before has medical training been available in such a targeted and focused way. An exciting, new advanced tool, Virtual Reality, is responsible for this innovation.

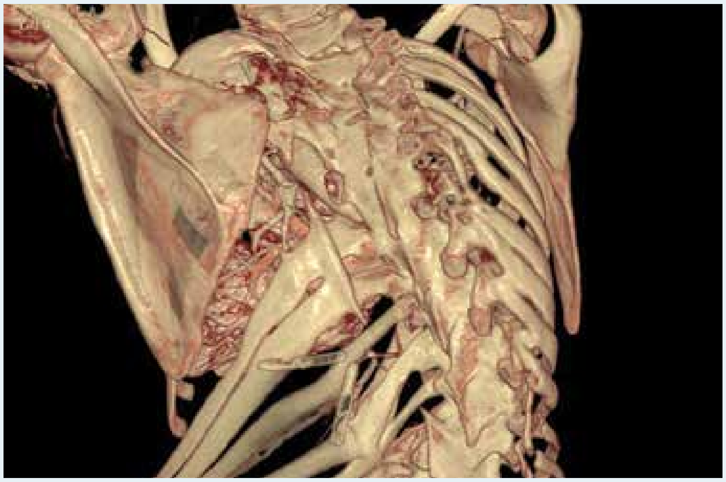


This 360VR rendering of an aneurysm allows Dr. Steinberg to view the pathology from his planned surgical corridor, rather than being restricted to radiology views.

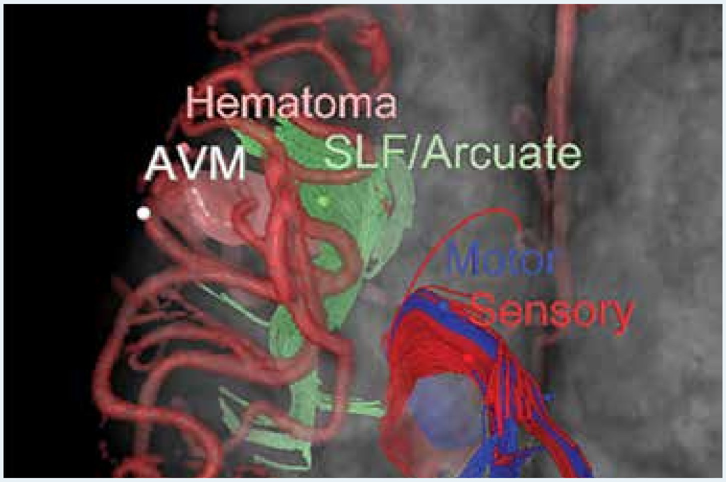
Virtual Reality (VR) is an artificial environment created with a computer program that people can experience in a way that makes the user feel or believe that the environment is actually real. The premise for a neurosurgical application of virtual reality is this: imagine shrinking to the size of an ant and immersing yourself in the anatomy of your patient. While conventional CT and MR scans capture a tremendous amount of information, they are not presented to the viewer in an intuitive format. The images can only be viewed in three separate planes, and a volumetric understanding must be constructed mentally, which can be difficult for small, unusual pathologies. Another drawback to conventional imaging is that you can only view one scan at time using the raw data, even though we need different scans to visualize different tissues. Creating a virtual reality environment overcomes this drawback. The virtual reality environment we use can fuse multiple distinct imaging modalities together to be viewed simultaneously, which represents a more realistic training environment. This technology has been adapted for clinical use, to enable our surgeons to experience their patient's own unique anatomy to prepare for and use as guidance during surgery. Our goal of producing safer surgeries with higher accuracy is becoming more attainable, since the preoperative VR rehearsal creates confidence that the surgeon is not operating on this particular patient for the first time.

Stanford University saw the value in this technology immediately, and has been developing a program through its Neurosurgical Simulation and Virtual Reality Center since its inception in 2016. Our Program Manager allocates our resources to interface with the various stages of patient care in a four-point program discussed in the following paragraphs: those are Patient Engagement in the clinic, Surgical Planning, Intraoperative Support, and Teaching/Research.

In the clinic, individualized cases are constructed based on the raw data DICOM images via an interface to the hospital's own PACS system. The raw data is uploaded into the PrecisionVR visualization platform (Surgical Theater, Inc., Cleveland, Ohio), and the clinical engineer (in our case this is the program manager) works on various segmentations, fusions, and color-coding in order to construct the



A 360VR rendering of this patient's spine was used in their clinic visit to help them and their family understand what kinds of surgery this patient had already undergone, and what procedure Dr. Veeravagu planned to do.



This enhanced 360VR model shows relevant functional structures and pathways surrounding this AVM and was used intraoperatively as part of the navigational guidance.

final case. Then, the case, on a mobile computer cart, is wheeled into the patient's consult room for an enhanced visit. We often use the model to explain not only what the pathology is, but also what kind of surgical treatment plan is recommended. Often, the pathology is not clearly visible until it is viewed as a 360VR case, during which times, the surgical treatment can be confirmed or modified. Having 360VR renderings of a patient's own body present for them while they are being asked to make a critical decision regarding their health is crucial to engaging them fully in the discussion. We have found that that patients often have their first "Aha!" moment when they see their scans in this way. It inspires both patient confidence in their provider, and provider confidence when they commence the surgery.

In surgical cases, the 360VR model can be used in a few different ways. Sometimes, we like to sit down in the virtual world and explore the pathology from every angle, observing its interactions with the surrounding anatomy. Often, this is done in the company of the supporting surgical care team, who uses this tool to learn what each surgeon looks for, what they notice, and what the options are. At the Stanford Neurosurgical Simulation VR Studio, attendings and residents can explore the virtual world of their patient together, at the same time. The experience can be awe-inspiring for both patients and doctors alike, and there is also a detailed dialogue taking place between teacher and student.

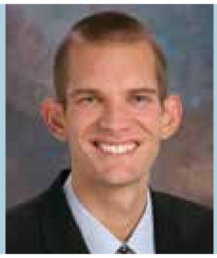
When the time for surgery comes, both the patient and surgeon feel confident in the plan. The 360VR model is brought into the OR on one of the intraoperative mobile carts, and is often connected to the cranial navigation system and microscope, in our recent cases, the newest Medtronic Stealth System S8 and Zeiss Kinevo. This allows real time guidance of microscope and/or probe position, and the ability to track the surgical location in any view. Examples of further enhancement features to the case include adding "invisible" functional data to the brain and displaying distance to the target.

Apart from this functionality of using 360VR models in the OR, we find that they naturally facilitate teaching in the OR as well. For example, attendings utilize the 360VR model to rehearse the craniotomy they want to perform, based on the tumor location and parenchyma of the surrounding brain. We find that 360VR models of patients are much more intuitive for understanding unique anatomy, and we are currently pursuing two different projects that will allow our models to help engage youth across the nation and Stanford's own first year medical school students with the importance of neuroanatomy and function.

There is already tremendous value in all of these features, which is why to date, over 1,300 patients at Stanford Hospitals have used 360VR models in their treatment, and five neurosurgeons are using the tool regularly. The most exciting part is that it only continues to improve. Looking to the future, one of the newest features about to be integrated with virtual reality in the patient care continuum is Augmented Reality. Augmented reality addresses the issue with virtual reality, which is that in a virtual environment you must first exit the real world to place yourself in the virtual world. Augmented reality enhances the real world by combining it with an artificial environment, created just for that purpose. This allows us to upgrade our view of the real world with information that can be pre-calculated, planned, chosen and rendered with the help of a computer to become visible to the human eye. Clinically, Stanford has been successful in testing the use of augmented reality in features such as including location of functional information (such as DTI pathways in the brainstem for a cavernous malformation resection), location of anatomical landmarks obscured from view by something else (such as the M2 vessel coming out of the 'back' of the aneurysm), measurements, markers, colors, etc. These features are pushed from the 360VR computer through the eyepiece of the microscope, so that they can act as a real time visual guide during surgery, or in the future, during regular examinations.

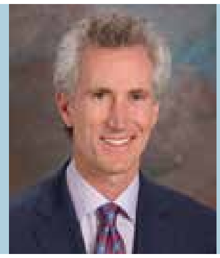
To conclude, we'd like to share a few words from our Program Manager to comment on her role in facilitating the work of our VR Center. "I find my job creative, exciting, and innovative. The role of virtual and augmented reality in healthcare is so robust that the field encompasses many backgrounds: those of engineering, medicine, operations, education, outreach, to name a few. It is an honor to work in a field that touches so many, and to be a part of the team that is driving the innovation forward, shaping the way virtual reality is sure to be used in every hospital and in every field, in the coming future.

DISCLOSURE: Dr. Gary Steinberg and Dr. Anand Veeravagu are consultants for Surgical Theater, Inc



Michael A. Bohl, MD

Michael J. Donovan, JD



Michael T. Lawton, MD

The Barrow Innovation Center: A Model for Training Neurosurgical Innovators

Introduction

Neurosurgery has a long and proud history of innovators who pioneered our field and modernized medicine. From the development of electrocautery and magnetic resonance imaging to the introduction of the operating microscope and microsurgical instruments, neurosurgeons have advanced surgical and engineering technologies to better diagnose and treat patients facing all types of diseases.[1-4] Innovation is not easy: "the act or process of introducing new ideas, devices, or methods" inherently runs against "the gradient of the status quo and frequently seems self-destructive."[5,6] Successful innovators must therefore identify unmet needs in clinical practice, and in addition they must be scientists in their approach to understanding an unmet need, artists in their design of potential new solutions, master clinicians in their application of novel devices or procedures, and stubborn optimists willing to "self-destruct" their work in search of better understanding or more effective solutions. Krummel once wrote, "A scientist seeks understanding, an inventor seeks a solution, an innovator seeks an application."[6] Innovation is therefore the practical application of scientific knowledge and creative problem-solving towards the betterment of the human condition. In short, innovation is what it means to be a neurosurgeon.

Given the importance of innovation to our field, and a hunger for educational opportunities in medical innovation, residents at the Barrow Neurological Institute created a center that gave residents the opportunity to pursue their inventions while training to become effective innovators capable of driving meaningful change in our field. This center, the Barrow Innovation Center (BIC), broadly defines innovation as the development of novel surgical procedures, devices, treatments, and diagnostic modalities. The following report provides an overview of BIC's structure, the program's productivity during its first four years, and its impact on the neurosurgical residency at the BNI.

BIC Structure

The BIC was developed first and foremost as an educational program focused on training interested individuals how to take their ideas from napkin drawings to marketable products. Three core principles underlie the BIC structure: 1) innovation should be a part of the day-to-day education of residents and other healthcare providers; 2) barriers to entry for new innovators should be eliminated to the farthest extent possible; and 3) a spirit of collaboration to realize an inventive idea must be an accepted norm. By focusing primarily on education and a collaborative environment where inventors can grow their ideas, we think we can accomplish our secondary mission of advancing patient care and self-funding the BIC through the invention, prototyping, and marketing of novel medical devices.

Legal and Financial Structure

As hospital employees, resident innovators assign the intellectual property rights of their inventions to the hospital. In exchange, the hospital incentivizes resident innovation through a 40-40-20 sharing agreement (40% of generated revenue to the inventor, 40% to the BIC, and 20% to the hospital). The hospital covers all up-front financial risk by funding BIC operations and legal fees for drafting and filing both provisional and non-provisional patent applications. For a standard non-provisional patent application, fees range from $10,000 to $20,000, which poses a barrier to entry for most residents. Eliminating this barrier is critical to a successful innovation education program for resident physicians.

In addition to the legal and financial support provided by the hospital, BIC collaborates with the Lisa Family Patent Law Clinic at the Arizona State University (ASU) Law School. ASU law students interested in patent law can receive credit for working with residents on drafting and filing provisional patent applications for their ideas. These law students also teach residents basic patent law at monthly conferences, which can help guide their future inventions. This collaboration has inspired additional support from both the hospital and ASU, as well as collaborations with the engineering school.

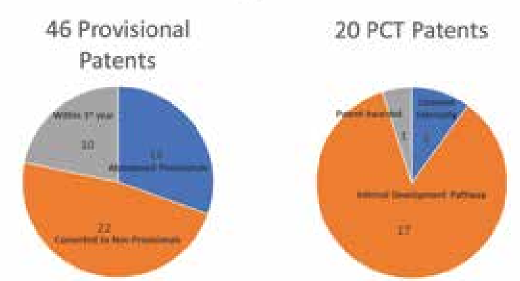
Engineering Support

Most residents lack the requisite engineering skills to fully develop their ideas for new medical devices. BIC established strategic partnerships with engineering schools at ASU and California Polytechnic State University. Residents who require this additional engineering support to develop their ideas first file a provisional patent application (with law student assistance), then present their idea to biomedical engineering students, and recruit their participation in the form of additional course credit or as a capstone project in their final year of undergraduate curriculum. Productive partnerships with engineering students have resulted in the hiring of a full-time BIC prototyping laboratory engineer as well as other engineering students whom are available, as hospital employees, to assist with prototyping.

Bic Productivity: First 4 Years

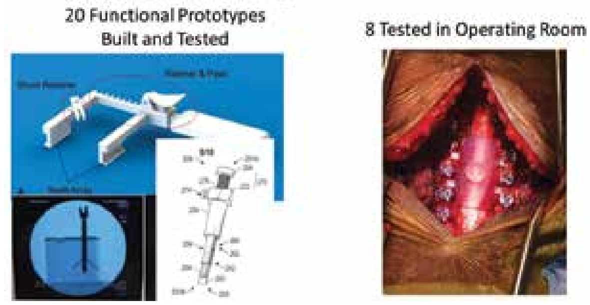
In its four years of operation, BIC has generated intellectual property, academic output, and several products currently on the market. Nearly 50 provisional patents have been filed to date, of which 48% have been converted to non-provisional patent applications, 22% are within the first year of filing, and 30% were abandoned at the conclusion of the 1-year provisional term without a feasible pathway forward. Twenty non-provisional patents have been filed, of which one has completed review by the USPTO and has been issued as a United States patent, and two have been licensed to third-party companies (**Figure 1**). A third patent is currently being considered by industry as a potential commercialization partnership. One non-provisional patent filing was licensed to a new company that is currently utilizing this technology to create surgical training models around the world. This company, Spine STUD, LLC, uses the profits from the sale of surgical training models to fund 80% of the operations of the BIC Prototyping Laboratory, moving BIC closer to the goal of financial solvency through the licensing and sale of successful new products from BIC.[7]

Figure 1



The BIC Prototyping Laboratory has developed and tested 20 functional prototypes in its first four years of operation, eight of which have been tested in the operating room. These devices include shields that protect the spinal cord from iatrogenic injury during spinal instrumentation, new retractors that are compatible with electromagnetic image guidance systems, and devices to improve spinal fixation and arthrodesis (**Figure 2**).[8-10] In addition to these medical devices, 10 new surgical procedures have been described and performed on over 40 patients in three institutions

Figure 2



and resulted in peer-reviewed journal publications.[12-18] This work furthermore inspired a new annual meeting between spine surgeons and plastic surgeons where inter-disciplinary solutions are discussed and studied for patients with challenging spine disorders.[11] Finally and most importantly, the BIC has prepared resident neurosurgeons to innovate in their careers. Their early innovation has produced over 20 peer-reviewed publications, numerous national and international meeting presentations, several awards, and professional contacts that will serve them as they invent and solve the problems in our day-to-day clinical practices.[8-10,12-31]

Conclusion

Supportive environments for innovation like BIC have enormous potential to impact future generations of neurosurgeons and the patients they will care for. William Halsted said, "The art of surgery is not yet perfect and advancements now unimaginable are still to come." To realize these advancements, we must invest in the education of a new generation of neurosurgical innovators, which is best done during neurosurgical residency when minds are open to new ideas and hearts are eager to disrupt the status quo. A commitment to educational programs like the BIC is a commitment to the future of our field and the patients who entrust us with advancing neurosurgical care.

DISCLOSURES: Michael Bohl, MD is the founder of the Barrow Innovation Center, and is the inventor of several patents mentioned in this article. He is also a co-owner of Spine STUD, LLC and has financial interests in this company and the products that it sells.

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Luis Emilio Savastano, MD, PhD

How to Get a Start-up Off the Ground as an Academic/neurosurgeon

A start-up is a "company initiated by one or more entrepreneurs to seek, effectively develop, and validate a scalable business model." From the view of a neurosurgeon, a start-up is a challenging, exciting, and completely foreign journey in a roller coaster to transform a vision into a product that can help patients. A start-up is a venue that enables innovative thinking to become innovative doing and is generally accompanied by irrational optimism, faith in a dubious technology, and eagerness to commit time and resources despite the unlikeliness of success.

A successful startup requires an acceptable technology, hard work, good timing, a great team, and luck. Even with this, more than half of all spinouts fail in their first year. The following are basic elements that should be taken into consideration when deciding if a start-up is worthwhile:

Intellectual property

Intellectual property (IP) includes patents and "know-how" and is the most important asset for an early start-up. Therefore, it needs to be identified, protected, and expanded. In a very early start-up, IP will be a strong driver for the valuation of the company. For inventors in academic centers, the process starts by submitting an invention disclosure to the Office of Technology Transfer (OTT) or Venture Office, which are fantastic resources that generally conduct, free of charge, a preliminary due-diligence. This includes the scope and status of the invention, a previous art search, and a rapid commercial feasibility. As these offices generally have limited budgets that are self-supported by eventual returns from licenses (through royalties, milestones payments, and equity), the patentability landscape and potential business opportunities are critical to decide whether to invest large time and economic resources in IP legal counseling and patent filing. Generally speaking, most of the disclosed ideas are rapidly killed by a rapid previous art search. If OTT is in support of submitting a patent, inventors are teamed up with IP counsel to draft and submit a preliminary patent followed by a full utility patent within 12 months. These 12 months are critical, as they enable the inventors to continue developing the technology and patent claiming a priority date from the submission of the preliminary patent. It is important to understand that the patent search performed by OTT and inventors is not the same as a 'formal' freedom-to-operate (FTO) search, which are conducted by expert patent attorneys and can be very expensive (often $30k to $70k). FTOs are generally conducted by the company during fundraising or by professional investors during the due-diligence process (discussed later).

Market opportunity + unmet clinical need

While IP is critical and resolving an unmet clinical need is the final goal, new technology has to be adopted to generate a return of investments (ROI). If a ROI is unlikely, it is unlikely that the company will be funded. Exciting technologies do not sell themselves, and therefore ROI is not guaranteed. Before you embark on your spinout journey, a thorough market research effort, including interviews to potential customers, should be conducted to really understand whether the market environment and the technology lifecycle are favorable. The technology lifecycle has four distinct stages: research and development, ascent, maturity, and decline. Generally speaking, fundraising efforts and the start-up launch are more likely to succeed and eventually exit (be acquired or go public) in the ascent and early stages of a technology, especially if can be used in a large volume of patients and are well compensated interventions (i.e. high probability of high ROI makes a "hot market").

Proof-of-concept prototype and feasibility test

A proof-of-concept (POC) prototype is a device built to demonstrate feasibility of the technology or technique. POC tests are generally done using early prototypes both ex-vivo in phantoms and in-vivo in translational animal models. POC tests are critical as they provide a tangible demonstration of how the technology works and a glimpse of the value proposition over the competence. Demonstrating feasibility of a prototype is important to "de-risk" a technology and will likely draw more attention from possible investors. Academic institutions generally have internal funding mechanisms (or manage funding from foundations or state-dependent economic development grants) to support the constructions of prototypes and "de-risking" experiments. Many of these activities can be done at a relatively low cost in the same institutions and are very important to enhance the IP and to generate critical data for fundraising.

Team

Although a start-up is a part of the continuum process of "vision to product," by itself it is a separate entity from the academic institution with very different needs and tasks. Therefore, it is natural that the team involved in the conception of the idea and early translational efforts will significantly change from spin-out through evolution. The team members that decide to join a start-up must bring value to the table through clinical and technical expertise (including "know-how"), hard work, and must be willing to continuously learn new skills and adapt to a changing role within the company as it grows and expands. In exchange, they are founder members and fairly compensated. Founders will have the opportunity to learn new skills, possibly have a financial gain through equity (although statistically unlikely), and will be required to dedicate major effort, time, and resources to the venture. The fundamental "core team" of a viable medical device company generally consists of an inventor of the technology, who comes from the academic team, and a business lead with previous successful experience with start-ups, who is recruited from the marketplace. A skilled and experienced CEO-leader, who can complement the founder's knowledge gap and manage the day-to-day business, is "the most" important hire and is generally required by professional investors. In the medical device arena, early start-up business leads are generally engineers with experience in product development (many were "Vice President of Research and Development" in medtech companies) and ideally already an expert in the same area that the company will operate. It is important to seek quality advice from mentors/advisers and discuss what profile of business lead is the more likely to succeed to raise capital, manage the day-to-day activities, and bring the product to market.

Money

The company will require money to develop and grow, and it will not be forthcoming without the four points discussed above. In addition, the stronger the above four points, the higher the valuation of a start-up (i.e. less dilution of founder's ownership at equal amount of money raised). Fundraising is probably the most challenging requirement for a viable start-up and is a full-time job. Although entrepreneurs may be in a position to provide some financial backing themselves or from family and friends, very quickly and almost certainly they will need to turn to external sources of funding. In addition to Small Business Innovation Research and Small Business Technology Transfer grants, which are great NIH sources of non-dilutions funding, the two major sources of money for a start-up include:

- Angels: Successful, wealthy individuals who generally invest in very early stages (e.g., pre-seed and seed) in exchange of equity or convertible notes (that will be transformed into equity at a later date when the company is valuated).
- Venture Capitalists (VCs): Professional private equity investors who provide capital to companies exhibiting high growth potential in exchange for an equity stake. Despite the low chance of success, VCs are willing to risk investing in early companies because they can earn a massive return on their investments if these companies are a success. VCs will conduct a deep dive in the company named "due-diligence," that includes external validation of the technology and a stringent examination of the status of IP rights. If VCs decide to invest, they generally do so for several millions, which is negotiated in a "term sheet." They exercise control by seats on the Board of Directors and bring in experienced management talent to help guide and grow the company. Therefore, good VCs bring money, knowledge, and a well-established network to help the company succeed. VCs can sometimes invest in several rounds of funding and are part of a larger consortium of investors in the company (known as "syndicates"). Generally, investors plan to recoup their investments via exit strategies (sell their equity in a portfolio company within 3-10 years or in an initial public offering).

The above-mentioned five points are generally required to get a start-up off the ground. The company formation process per se follows these steps:

1. Selection and appointment by the founder/s of a corporate lawyer to act on behalf of the company (not the founders). Great attorneys are usually expensive but they are a good investment and many will defer their payments until a significant fundraising milestone is achieved. Corporate attorneys will take care of all steps needed for forming a company (stated below).
2. Incorporation of the company
3. Issue of shares to founders
4. Licensing of IP to the company
5. Take investment into the company

At this stage, the start-up work has just begun. **Good luck!**

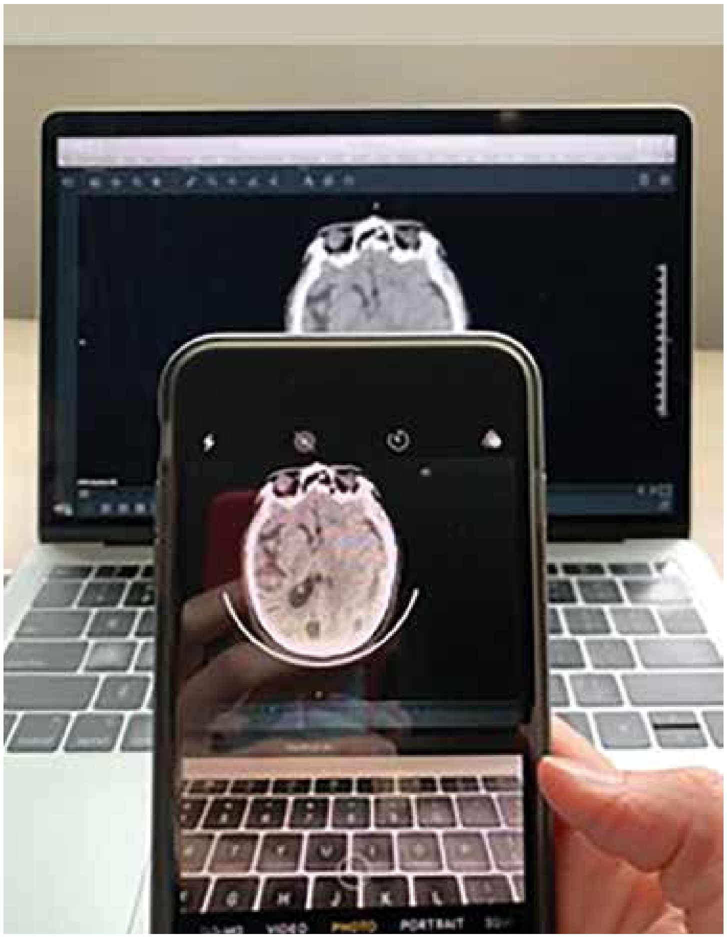
Howard Yonas, MD

Peter L. Steinberg, MD

Martina Stippler, MD, FACS, FAANS

Tele-Neurosurgery Can Play a Role, not only in Rural America

The play and movie *The Music Man* includes a song titled "Ya got trouble right here in River City," and though the problem in River City was simply boys playing pool, we have a real problem in neurosurgery—there are not enough of us. We are located primarily in urban communities and we are aging as a subspecialty. As a result, there is a proportionately decreasing number of providers willing to be engaged in emergency care. Too often, the result, even in major cities, is a lack of 24/7 coverage, which has led to the discussion of whether neurosurgical trauma care should be provided by general trauma surgeons.



Although the problem for urban communities is significant, the problem for rural communities is far worse. Hence, healthcare systems that serve rural areas have often been more likely to embrace telehealth consults. One good example is the ACCESS Telemedicine initiative at the University of New Mexico. The neurosurgery department received a CMS grant to develop an optimal telemedicine system for providing neuro-emergency care. The ACCESS (Access to Critical Emergent Support Services) program provides audio- and visual-enhanced consultations and provides the consultant rapid access to all available imaging data for integration into the consultation. The audio/visual and image data transmit via the cloud to any modern laptop computer, thus removing the need for a provider to be in a fixed location.

From 2015 to the present, the ACCESS program has responded to 4,500 neurological consultations and 500 neurosurgical consultations. Using six months of clinical behavior from our first 12 hospitals for control data, we learned that prior to ACCESS, tPA was delivered to fewer than 2% of potential candidates. We also observed that well over 90% of patients who were neurosurgical cases were being transferred. Included in the program was an aggressive education program for ER physicians and nurses as well as the hospitalists. The education program included on-site training by ACCESS educators, who provided recurring on-site education, in addition to bimonthly telemedicine education.

A careful monitoring and review of the care received by all patients revealed that the use of tPA had increased from less than 2% to 20% of candidates and that the percentage of neurosurgery patients who were transferred fell from 90% to 17%. The impact upon the "neurosurgical" patients, their families, and the rural hospital was significant.

Limiting over-triage of complicated mild TBI patients can have a positive impact on all stakeholders. This helps keep the ER and ICU beds for patients who indeed need tertiary care. Allowing the community hospital to care for these mild TBI patients significantly improved patient satisfaction. What we have encountered often is that by the time the families arrive at the urban hospital, having driven for many hours to be with their loved ones, the patient is ready for discharge.

The worst part of this story is that the cost of an unnecessary air transport often falls upon the patient and his or her family to the tune

> AS WE SIT IN THE MIDST OF THE COVID-19 PANDEMIC, THE VERY WAY MEDICINE IS PRACTICED HAS CHANGED. PERHAPS THE MOST WIDESPREAD CHANGE HAS BEEN THE NECESSITY TO USE TELEMEDICINE PLATFORMS TO CONTINUE PRACTICING. WHETHER USING THE TELEPHONE TO CONDUCT OUTPATIENT VISITS OR VIRTUALLY "SEEING" CONSULTS IN THE HOSPITAL WITH A SECURE VIDEOCONFERENCING PLATFORM, WE HAVE BEEN THRUST INTO A NEW PARADIGM FOR CARE DELIVERY. <

of tens of thousands of dollars. Another perspective of this all-too-common problem is the loss of potential income to rural hospitals that could have retained the charges for the clinical admission. The number of retained admissions in some of our New Mexico hospitals was the difference between staying open and having to close.

Despite the success of this and many other telehealth programs, it is astonishing that across the United States, telehealth has not become part of routine neurosurgical care. Clinic infrastructure and billing regulations do not reward—and instead punish—the providers who want to offer patient-friendly telehealth for TBI transfer triage, postoperative follow-up, or new patient consultations. In addition, the current system of state licensure and individual hospital credentialing is archaic for this digital age and a real barrier to the implementation of nationwide telehealth consultations.

This was all true until mid-March, when because of the Covid-19 pandemic, nonurgent hospital patients were discharged and suddenly U.S. many specialties—including neurosurgery—discovered telehealth.

As we sit in the midst of the COVID-19 pandemic, the very way medicine is practiced has changed. Perhaps the most widespread change has been the necessity to use telemedicine platforms to continue practicing. Whether using the telephone to conduct outpatient visits or virtually "seeing" consults in the hospital with a secure videoconferencing platform, we have been thrust into a new paradigm for care delivery. Very few US centers were adopting this already, while others were caught sleeping and now must play catch-up. Providers should use this precious time to determine who is best served by a virtual visit, who still needs to come in, and which visit types and diagnoses are best suited to these platforms.

As surgeons, we need to determine how virtual visits will best integrate into our practices. A good starting point is to decide whether new patients will be offered telemedicine visits. The next steps are to review diagnoses you see normally and then clarify which would be acceptable for a telemedicine visit. Some of this will be iterative, and that diagnosis list may expand or contract as you gain experience. Will physician extenders also see virtual visits? How about post-op patients?

Focus on virtual visits where the history, imaging, or other objective data inform most of the decision-making and the physical examination is of minimal utility or can be conducted via videoconference. Telemedicine will not replace examining patients and performing procedures; however, it will make routine office visits to discuss lab results, normal imaging tests, and even post-op visits less frequent. Perhaps telemedicine's newfound role in our practices will emerge as the true silver lining of this pandemic.

Yes, we have a problem "here in River City," but with the aid of modern technology we might be able to provide a partial solution.

SECTION UPDATE

ASSFN Update

Robert Gross

In these modern times, we marvel and féte "disruptive technologies"—no less so in our technology-driven specialty of stereotactic and functional neurosurgery. Robotics, frameless surgery, gene and cell therapy, optogenetics....DBS, even. Such positive disruptions are facilitated by the globalization of economies, products, people, and their ideas, leading to rapid spread of disruptive technologies, and rapid change. Hijacking these same highways and pathways, as always, are forces that lead to negative disruptions. Whether positive or negative, frequent and seismic disruptions lead to a highly unpredictable world (see *The Three Body Problem*, by Cixen Liu, the award-winning Chinese science fiction writer). It has always been "difficult to make predictions, especially about the future," as the saying goes—now more so than ever.

Against this backdrop, a mere month ago I was asked to write this update, to be a fairly straightforward and ardent promotion of our scintillating upcoming biennial meeting planned for Boston from June 20 - 23. Turning on a dime, our priorities as physicians and scientists, parents and spouses have been forced into turmoil. At this writing, while our meeting in late June has not been cancelled, any reasonable person's interpretation of the models of COVID-19 spread can't admit to its being very likely. And though its cancellation would be a tremendous disappointment to our membership—which comes together every other year to celebrate our progress in caring for our patients and our advances in understanding the underlying science—and to the tireless conference chair and scientific program committee, that disappointment pales in the shadow of the tremendous suffering and loss being experienced throughout our nation and our world.

We are allowed to grieve these losses: for our loved ones, our friends, our colleagues, our patients whose surgeries have been postponed for an indefinite period of time, and for all the people and faces we don't know but see on the news every day, and those who we don't see but who suffer as much or more. And we are allowed to grieve for our livelihoods in jeopardy and our lifestyles that have, in many ways yet to be seen, been irrevocably changed. But we are also allowed, I would argue even obligated, to acknowledge that in the shadow of this suffering there WILL be some positive changes, too. We didn't ask for this type of disruptive change but we got it, so—as my dear friend and longtime colleague Mahlon Delong, MD has said to me countless times—"when you fall, pick up a stone."

We see positive changes already, and we need to point them out and honor them, so the great losses suffered are not in vain. Communities coming together to support their health care system

> > WE SEE POSITIVE CHANGES ALREADY, AND WE NEED TO POINT THEM OUT AND HONOR THEM, SO THE GREAT LOSSES SUFFERED ARE NOT IN VAIN. COMMUNITIES COMING TOGETHER TO SUPPORT THEIR HEALTH CARE SYSTEM AND PROVIDERS. INCREASED ATTENTION, RESPECT FOR AND UNDERSTANDING OF PUBLIC HEALTH WORKERS AND EPIDEMIOLOGISTS. AWARENESS OF THE FRAGILITY OF OUR HEALTHCARE SYSTEM. AND TELEHEALTH! <

and providers. Increased attention, respect for and understanding of public health workers and epidemiologists. Awareness of the fragility of our healthcare system. And Telehealth! At my institution we tried for years to implement this, but constantly ran up against obstacles; now, in one week's time, it is being used in our clinics, and to great effect. No longer does a patient need to drive for hours each direction, perhaps with an intervening hotel stay, against economic hardship, for a one-hour psychiatry clearance. Pollution is down across the globe in just a few months: a feat that the Paris Accords—US or no—could perhaps never accomplish. How much impact will there be to know that it can be done?! Fear is even driving people to eat (or at least purchase) more beans, another boon for our environment, not to mention their personal health. For my own part, I was succumbing to my addiction to attending conferences across the globe (I had no fewer than five international trips planned in 2020), even knowing the impact on the environment of the jet fuel I personally was consuming. Now I am at home, and even a bit relieved. Although we are in the middle of teleconferencing boom, it is a good thing, and it turns out that it works far better than we were willing to admit, or even take a chance on! Decreased travel for meetings and conferences, decreased eco-footprint, and more time with our families: these are good things to look forward to keeping from this turbulent time. And then there is the new technology that any time of strife (or "war") unleashes, that we are already seeing. Take the good with the bad seems overly trite: but we are obligated to do it.

So, what of the 2020 ASSFN Biennial Meeting in Boston? We are continuing to plan for all contingencies depending on developments: it happens as planned, we postpone it, or—heaven forbid—it must be outright canceled. It is too early to tell. In any event, I couldn't be more proud of the tireless and creative efforts of meeting chairman and past-president Emad Eskandar and the chair of the scientific program committee Sameer Sheth. They have organized a dynamic conference, showcasing the latest developments (some of them disruptive!) in stereotactic and functional neurosurgery, including clinical innovations and research advances. The content covers the range of our specialty, from the clinical areas of movement disorders, epilepsy, psychiatric neurosurgery, pain, and radiosurgery, to the research arenas of neuromodulation, functional neuroscience, and neuroengineering. To highlight the interdependency and to strengthen ties between ASSFN and our sister societies and membership, the ASSFN Biennial Meeting is, for the first time, being organized in partnership with a neurological organization. We have chosen to partner with the American Epilepsy Society (AES) to enhance content related to epilepsy surgery and related translational neuroscience and encourage cross-disciplinary exchange between our memberships. We expect this partnership to serve as a model for future meetings, which can in turn highlight relationships with other related societies.

In keeping with this theme, the meeting's Honored Guest is Dennis Spencer, MD, FAANS, Kate Cushing Professor in the Department of Neurosurgery, Yale University. As nearly everyone knows, Dr. Spencer is a pre-eminent leader in neurosurgery, and epilepsy surgery in particular, and a mentor to many of us (myself included). Hopefully he will deliver the traditional Honored Guest luncheon lecture on Monday of the meeting. The scientific program includes invited talks and case discussions from over 100 faculty in neurosurgery, neurology, psychiatry, and neuroscience. We received over 200 abstract submissions of very high quality, more than 50 of which have been selected as talks throughout the program. Another 108 abstracts will populate the poster session, which has become a very popular and well-attended feature of our last few Biennial Meetings, under the leadership of Zelma Kiss, MD, PhD, FRCS-C. The ASSFN scientific program committee, the executive committee and our Board of Directors are very excited for this meeting, and we encourage anyone with an interest in this vibrant field of neurosurgery to attend, whether in 2020 or thereafter (more information and the registration page can be found at http://www.assfn.org/biennial.html).

As we all know, we will come through the other side of the pandemical disruption. Many have and will be hurt, affected, disrupted, die. All of our lives will be changed irrevocably. Our first and foremost obligation is to limit these unfortunate and negative effects. But we are equally obligated to balance these with positive disruptions; this is the time most of all when we must have equanimity. Our own society recently began our first strategic planning process, to provide ballast and long-term direction to better fulfill our society's vision and execute on our mission. We did not plan on COVID-19, but true to the aforementioned we will have our final meetings by teleconference rather than in person. ASSFN will be stronger as a result of this process. It has been my honor to serve as president of ASSFN for the last nearly two years, and as I turn over the reins to our president-elect Joseph Neimat, MD at the business meeting in June (be it in person or by web), I know that the future, as always, will be brighter than the past. And I know that our society at large and our world will be stronger as a result of the present crisis.

INSIDE THE CNS

Washington Committee Report

Katie O. Orrico, Esq

COVID-19

CMS Issues Guidance for Elective Surgery During COVID-19 Crisis

Building on guidelines developed by the American College of Surgeons, on March 18, the Centers for Medicare & Medicaid Services (CMS) issued recommendations on CMS adult elective surgery and procedures during the COVID-19 crisis. The agency's guidelines urge health care providers to limit all non-essential planned surgeries and procedures, including dental, until further notice.

CNS and AANS Urge Congress to Provide COVID-19 Relief for Surgeons

Facing steep Medicare payment cuts and economic strains due to the COVID-19 pandemic, on March 20, the Congress of Neurological Surgeons (CNS) and the American Association of Neurological Surgeons (AANS) asked Congress to take action "to fortify the long-term financial stability of physician and non-physician practices across the health care delivery system." In the letter, the groups urged Congress to waive the budget neutrality requirements stipulated in the Medicare law to prevent payment cuts to global surgery codes resulting from the changes to the office and outpatient visit codes. Without relief, neurosurgeons face a minimum 6% pay cut on Jan. 1, 2021.

In addition, on March 19, the CNS and the AANS joined 20 national surgical organizations in urging Congress to help stave off the extreme challenges created by the crisis by providing the following relief:

- Ensure that physicians have the equipment they need;
- Adopt medical liability protections for physicians who volunteer to provide care during the COVID-19 pandemic;
- Relieve unnecessary prior authorization requirements;
- Ensure physician practices are treated like other small businesses receiving financial assistance;
- Suspend Medicare physician pay cuts, including the annual 2% budget sequester and pending cuts to global surgery codes; and
- Pause Medicare Quality Payment Program reporting requirements.

Click here to read the letter.

Legislative Affairs

Year-end Spending Legislation Reflects Neurosurgery's Priorities

On Dec. 20, President **Donald J. Trump** signed the fiscal year 2020 domestic spending bill (Further Consolidated Appropriations Act, 2020, H.R. 1865), which was previously approved by the U.S. Senate by a vote of 71-23 and the House of Representatives by a vote of 297-120. The new law (P.L. 116-94) includes several provisions of interest to neurosurgery:

- Provides $41.68 billion to the **National Institutes of Health**. Funds include $500 million for the **Brain Research through Application of Innovative Neurotechnologies** (BRAIN) Initiative to map the human brain; $818 million for research on opioid addiction, development of **opioids alternatives**, **pain management** and addiction treatment; $12.6 million for research on **childhood cancer** and **structural birth defects**; and funding for research on the deadliest cancers, which include **anaplastic astrocytoma**, **diffuse intrinsic pontine glioma, glioblastoma** and high-risk **neuroblastoma**.
- Provides $68 million for injury prevention activities at the **Centers for Disease Control and Prevention**, including $12.5 million to support **firearm injury and mortality prevention research**; funds to investigate the establishment of a national surveillance system to determine the incidence of **sports- and recreation-related concussions** among youth aged 5 to 21 years; and $6.7 million for **traumatic brain injury** activities.
- Encourages the **Centers for Medicare & Medicaid Services** (CMS) to collaborate with the Food and Drug Administration and consider approved devices and therapies for unique post-surgery patient populations for effective **pain management**; ensure that payment changes do not further exacerbate workforce shortages; and not make payment changes to **robotic stereotactic radiosurgery** and robotic stereotactic body radiation therapy in the freestanding or hospital outpatient settings.

In addition to discretionary spending items, the legislation incorporates other health care policy matters of interest to neurosurgery, including:

- Extending the **work geographic practice cost index** floor, which increases reimbursement for physicians practicing in certain rural areas through May 22, 2020;
- Extending funding for the **Patient-Centered Outcomes Research Institute** for 10 years through September 2029; and
- Permanently **repealing the 2.3% medical device excise tax**, an CNS priority since 2010.

Neurosurgery Joins Alliance in Calling on Congress to Provide Positive Medicare Update

On Dec. 23, the CNS and the AANS joined the Alliance of Specialty Medicine in calling on Congress to quickly address the unresolved need to provide positive Medicare payment updates. Per the Medicare Access and CHIP Reauthorization Act (P.L. 114-10), beginning in 2020, physicians face a pay freeze for six years. Neurosurgeons also face a 2% pay cut from budget sequestration and additional cuts related to changes in office visit code values. The letter notes that other Medicare providers, including hospitals and skilled nursing facilities, will receive positive payment updates for 2020, while physician payments continue to fall to keep pace with inflation.

Neurosurgery Offers Suggestions for Cures 2.0 Legislation

Recently, Reps. **Diana DeGette** (D-Colo.) and **Fred Upton** (R-Mich.) released their initial vision for their Cures 2.0 legislation, calling on experts and stakeholders to submit their ideas and feedback on the plan — which aims to modernize coverage and access to life-saving cures. Cures 2.0 would build on the original 21st Century Cures Act (P.L. 114-255), which aspires to advance medical research and foster a new era of medical innovations.

In our Dec. 16 comment letter, the CNS and the AANS urged Reps. DeGette and Upton to strengthen the use of clinical registry data to speed innovation and device approval as well as for use in post-market surveillance. The letter also recommends improving coverage and reimbursement policies to ensure that patients have access to innovative therapies.

Neurosurgery Leads Effort on Surprise Medical Bills

Led by the CNS and the AANS, on March 4, a coalition of 19 national and state medical associations, sent a letter to congressional leaders outlining medicine's recommendations on surprise billing legislation. The letter, which was sent to the chairs and ranking members of the House Committees on Energy and Commerce, Education and Labor, and Ways and Means, outlines key components for a fair and effective solution to address surprise medical bills. At present, Congress continues to work on final compromise legislation that could be included in a broader health care package later this spring.

Good Samaritan Health Professionals Act Introduced in the House

On March 13, Reps. **Raul Ruiz**, MD, (D-Calif.) and **Larry Bucshon**, MD, (R-Ind.) introduced H.R. 6283, the Good Samaritan Health Professionals Act. This legislation will ensure that health professionals who provide voluntary care in response to a federally declared disaster are protected from unwarranted lawsuits. The bill specifically applies to health care providers who cross state lines to aid disaster victims. The CNS and the AANS sent a letter to Reps. Ruiz and Bucshon supporting this bill. Companion legislation (S. 1350) was introduced in the U.S. Senate by Sens. **Bill Cassidy**, MD, (R-La.) and **Angus King** (I-Maine) on May 7, 2019.

Coding and Reimbursement

Neurosurgery Urges CMS to Reverse Course on Global Surgery Payment Rules

On Dec. 6, the CNS and the AANS joined the Alliance of Specialty Medicine in submitting additional comments to the CMS regarding the 2020 Medicare Physician Fee Schedule. In the letter, the groups urged CMS to reverse course on the agency's plan not to increase global surgery payments to reflect increases in the evaluation and management (E/M) visit codes. In the final rule, CMS announced plans to revise the documentation requirements for office visit codes. As part of this initiative, the agency is also adopting increased values for the newly revised evaluation and management E/M codes. Unfortunately, despite support from nearly all medical organizations, CMS does not plan to increase values for E/M services delivered as part of the global surgery codes. CMS justifies its decision by pointing to its ongoing study of global surgery services that aims to determine the number and level of E/M services delivered in the global period.

The CNS and the AANS also submitted comments to CMS, echoing the points raised in the Alliance letter. In a Dec. 26 letter, the groups reiterated that by failing to increase the global surgery code values, CMS is violating the law, which prohibits Medicare from paying physicians differently for the same work. By not incorporating E/M code increases into the global surgical codes, CMS is effectively paying surgeons less for the same E/M services. The CNS and the AANS will continue to work to reverse this new policy.

Neurosurgery Comments on Proposed Coverage for Vertebral Augmentation

On Jan. 28, the CNS and the AANS joined 10 specialty society members of the Multispecialty Pain Workgroup (MPW) in submitting comments to Medicare Administrative Contractors (MACs) regarding proposed Local Coverage Determinations (LCDs) for Percutaneous Vertebral Augmentation (PVA) for Osteoporotic Vertebral Compression Fracture. The letters express concerns regarding the LCDs' exclusion of all fractures over six weeks old and the requirement for a four-physician multidisciplinary team to determine treatment by consensus. Click here for the Novitas letter and here for the First Coast letter.

Neurosurgery Comments on MRI Guided Focused Ultrasound for Essential Tremor

On Feb. 8, the CNS, the AANS and the American Society for Stereotactic and Functional Neurosurgery (ASSFN), sent letters to Novitas and First Coast, thanking them for proposing positive draft Local Coverage Determinations (LCDs) for MRI Guided Focused Ultrasound (MRgFUS) for Essential Tremor (ET). The draft LCDs specifically cite an ASSFN position statement. The paper titled, "MR-guided Focused Ultrasound for the Management of Essential Tremor," includes a robust review of the literature for the procedure.

Regulatory Affairs

Neurosurgical Practices Need to Prepare for New CMS Imaging Rules

Starting Jan. 1, CMS will implement the appropriate use criteria (AUC) for advanced diagnostic imaging program. Under this program — which was established by the Protecting Access to Medicare Act (P.L. 113-93) — when an advanced imaging service is ordered for a Medicare beneficiary, the ordering professional must first consult AUC using a qualified clinical decision support mechanism (CDSM). Professionals who furnish these tests must document the ordering professional's consultation of AUC to be paid for the service. During this initial education and testing phase, CMS will address technical coding and billing concerns, and the agency will not deny claims if they do not contain the proper AUC consultation information.

The Medical Group Management Association has published information on how practices can prepare for the program. Click here to access the toolkit.

Quality Improvement

HHS Issues Strategy for Reducing HIT and EHR Burdens

On Feb. 21, the U.S. Department of Health and Human Services (HHS) issued a report titled, "Strategy on Reducing Regulatory and Administrative Burden Relating to the Use of Health IT and EHRs." The report identifies regulatory and administrative burdens relating to the use of health information technology (HIT) and electronic health records (EHRs), while also outlining strategies and recommendations that can be used to help clinicians focus their attention on patients rather than paperwork. As required by the 21st Century Cures Act, the report was led by the Office of the National Coordinator for Health Information Technology (ONC) in conjunction with CMS. The report outlines three primary goals and offers recommendations to:

- Reduce the effort and time required to record information in EHRs for health care providers when they are seeing patients;
- Reduce the effort and time needed to meet regulatory reporting requirements for clinicians, hospitals, and health care organizations; and
- Improve the functionality and intuitiveness (ease of use) of EHRs.

In related news, the CNS and the AANS joined the Alliance of Specialty Medicine in commenting on HHS' draft "2020-2025 Federal Health IT Strategic Plan."

CMS and ONC Release Final Rules to Advance the Interoperability of Health Information

On March 9, HHS announced the release of their long-awaited final rules implementing the 21st Century Cures Act requirements to enhance interoperability and patient access to data. The final rule issued by CMS focuses on driving interoperability and patient access to health information by implementing policies that will help patient data flow freely and securely between payors, providers, and patients. The ONC rule aims to provide additional opportunities for innovation through secure access to health data and new tools to help patients shop for and coordinate their own care. The ONC rule also prohibits HIT vendors and providers from engaging in information blocking.

Click here a fact sheet on the CMS final rule and here for information on the ONC rule.

JOIN THE CONVERSATION ON SOCIAL MEDIA

Connect with the Washington Committee and Washington Office on various social media platforms to keep up with the many health policy activities happening in the nation's capital and beyond the Beltway.

- Neurosurgery Blog: More Than Just Brain Surgery
- Neurosurgery's Twitter Feed: @Neurosurgery
- Neurosurgery's Facebook Page
- Neurosurgery's Instagram Page
- Neurosurgery's LinkedIn Group
- Neurosurgery's YouTube Channel
- Neurosurgery's Tumblr Page

IMAGES IN NEUROSURGERY

Rupture Resemblance Score

A 60-year-old man was referred to our clinic for evaluation of unruptured bilateral middle cerebral artery (MCA) aneurysms. Digital Subtraction Angiography (DSA) demonstrated bilateral MCA bifurcation aneurysms measuring 12.1 x 7.5 mm and 10.1 x 5.9 mm on the right and left, respectively. The Rupture Resemblance Score (RRS) is a risk stratification tool evaluating an unruptured aneurysm's similarity in morphology and hemodynamics to previously ruptured aneurysms treated at the University at Buffalo. The RRS model incorporates high risk factors predicting aneurysm rupture, such as relative residence time (a measure of flow stasis) and size ratio (aneurysm height divided by mean parent vessel diameter), among others (**Figure 1**). The faculty at our weekly case conference recommended treating both aneurysms, starting with the left-sided aneurysm. After the conference, the RRS model was applied in a blinded manner, demonstrating that the left-sided aneurysm had a higher RRS score, i.e. greater similarity to previously ruptured aneurysms and therefore higher theoretical risk of rupture, than the right-sided aneurysm. We treated the left-sided aneurysm with stent-assisted coiling (**Figure 2**) followed by stent-assisted coiling of the right-sided aneurysm two weeks later (**Figure 3**). 6-month follow-up DSA demonstrated no significant recurrence of either aneurysm.

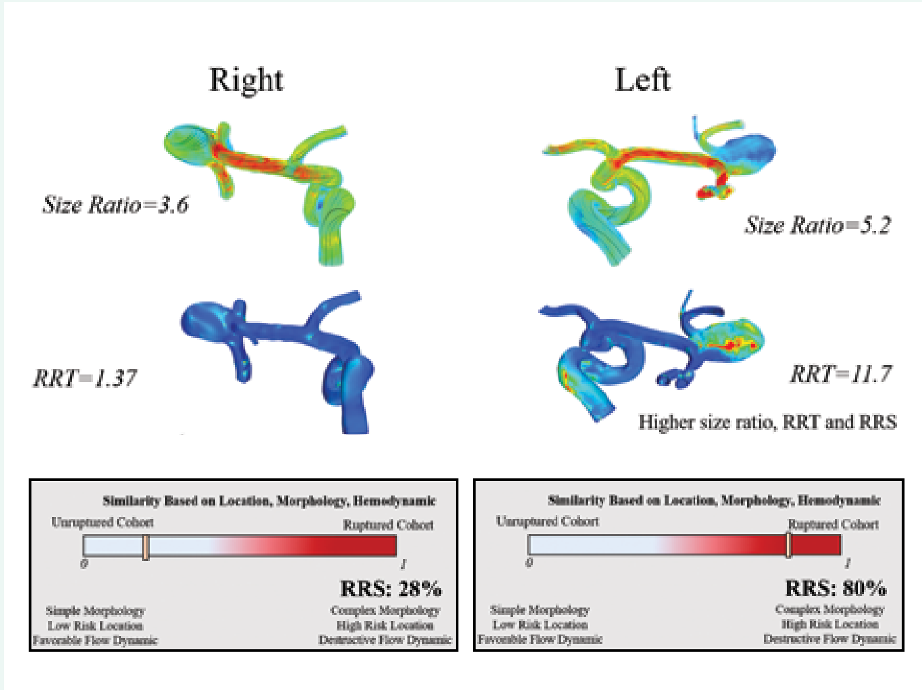


Figure 1: 3-dimensional morphological analysis and computational flow dynamics for bilateral middle cerebral artery (MCA) bifurcation aneurysms. The left-sided aneurysm had a higher size ratio, higher relative residence time (RRT) and higher rupture resemblance score (RRS) than the right-sided aneurysm. The higher RRS predicts a higher theoretical risk of rupture for the left-sided aneurysm.

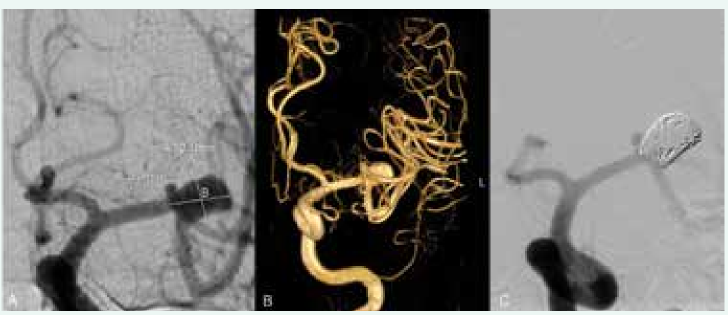


Figure 2: Left internal carotid artery AP projection demonstrating left-sided MCA bifurcation aneurysm (**A**). 3D reconstruction of the aneurysm is presented in (**B**). The aneurysm was treated with LVIS Blue jr stent-assisted coiling (**C**).

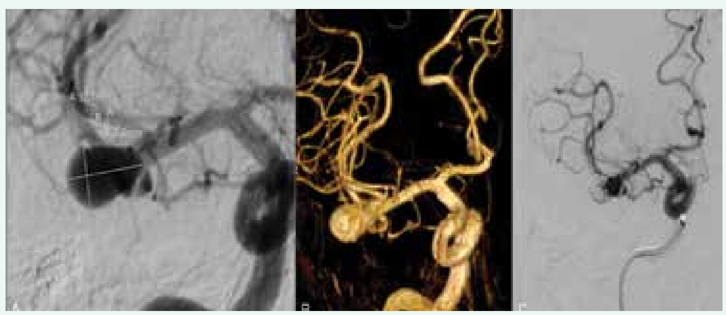


Figure 3: Right internal carotid artery AP projection demonstrating right-sided MCA bifurcation aneurysm (**A**). 3D reconstruction of the aneurysm is presented in (**B**). The aneurysm was treated with Neuroform Atlas stent-assisted coiling (**C**).

Reference:

1 Xiang J, Yu J, Choi H, Fox JM, Snyder KV, Levy EI, Siddiqui AH, Meng H. Rupture Resemblance Score (RRS): toward risk stratification of unruptured intracranial aneurysms using hemodynamic–morphological discriminants. *Journal of neurointerventional surgery*. 2015 Jul 1;7(7):490-5.

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