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Presidential Address to the 2021 Annual Meeting of the Congress of Neurological Surgeons

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My Friends and Colleagues, Welcome to Austin! It has been the honor of my lifetime to serve as your president. The relationships forged in this most amazing of professions, especially at gatherings like these, are what I value the most—which is why I feel blessed that we are here in person to share our innovations for the future. Of course, when we first conceived of the theme for this meeting a few years ago, it was a play on the upcoming year 2020 when we expected to be together in Miami, hoping to share our own "20/20 Vision for the Future."

Well, history taught us that "vision" is not a crystal ball. Although no one could have predicted these unprecedented times, I am not surprised that neurosurgery has found a silver lining through this pandemic to come together in the service of our patients and our profession, to move our frontiers ever forward. Today, as we reimagine our own vision for the future, please join me on a journey through time as we reflect on where we have been, in each of our subspecialties, and how far we have come. Just a few short years ago, the tools and techniques used today in our operating rooms, clinics, and laboratories would have seemed like far-off space age science fiction, yet collectively we made it a reality.

Are we adequately preparing the next generation of neurosurgeons, for what comes next? Together, we need to enhance our educational platform and expand the reach of our profession so that neurosurgery remains at the tip of the spear. Our colleagues desire it. Our trainees need it. Our patients deserve no less.

Before I begin, I must thank my own department, without whose support and camaraderie it would have been impossible to make it through not only this year but also for the past 17 years I have called Henry Ford home. Thank you to Jack Rock for being an amazing interim chair after I took on the chief executive officer (CEO) role, and to Ghaus Malik, Mike Chedid, Mwafa Abdulhak, Ellen Air, Jason Schwalb, Ian Lee, Adam Robin, Asim Mahmood, Don Seyfried, Vic Chang, Max Kole, Tom Mikkelsen, Tobias Walbert, and so many others, for your friendship and mentorship.

To my Congress of Neurological Surgeons (CNS) family—starting with the legacy of passionate volunteers who first gathered in 1951, to my own Executive Committee—our journey over the past 12 years when Elad Levy and I first came on the executive committee together until now has been one of my career's prized experiences… and it is all made possible by the most dedicated staff in all of organized medicine, led by the truly exceptional Regina Shupak and also Deanne Starr, April Martin, David Berg, and their incredible teams.

I am so honored to have called Brian Hoh a close friend ever since we were in residency together 2 decades ago, and he has been a phenomenal leader for this organization.

This year represents a combined extravaganza of the best highlights from our planned 2020 meeting and our 2021 lineup, thanks to the herculean efforts of Nader Pouratian, our scientific program virtuosos Brian Nahed, Ashok Asthagiri, and Lola Chambless—these are impossible jobs in any year—but imagine having to plan, put on hold, cancel, reschedule, replan, and get everything perfect along the way!

The time-honored tradition of selecting luminaries in our field to serve as honored guests is alive and well. Thank you to 2 of my most incredible mentors who so significantly shaped my own career: Bob Carter, my chief resident when I started at Harvard-Massachusetts General Hospital and now the Chair there, Mark Rosenblum, who recruited me to Henry Ford and is now the Chair Emeritus, and of course Brian's 2021 Honored Guest, Bill Friedman, the chair emeritus at the University of Florida.

While it is impossible to thank everyone who has influenced my professional journey, there are several individuals in addition to those I have already mentioned who have made all the difference, and I am forever grateful for your mentorship and your friendship over many years. Neurosurgery is a sport of lifelong learning, and I am so blessed to have learned from all of you.

I took over my role as CEO at Henry Ford just 10 days before the pandemic struck Detroit, which I assure you was not in the fine print of the contract…

But no matter how dark the days became, we learned that in the middle of difficulty lies opportunity, and hope, and that the heroes of health care, and our patients, revealed many silver linings.

Including being able to launch a record number of new educational programs that brought our members together, even as we remained apart—such as the CNS Townhall Experience, Virtual Visiting Professor programs, Virtual Tumor Boards, and the new Future Women Leaders in Neurosurgery Scholarship. Our journals processed a record number of submissions (including 200 related to COVID) and launched our newest publication, *Neurosurgery Open*.

Now, with this in-person meeting, as we gather as a neurosurgery family from across the globe, it is hoped that we can return to our regularly scheduled program—innovating for the future.

When we think about innovation, we often think of Steve Jobs and the modern digital revolution…but there are many lessons to be learned from our own rich history in neurosurgery. In footage from 100 years ago, Harvey Cushing can be seen laying the groundwork for the future. In his day, 65% of patients died after surgery. Through his meticulous techniques and discoveries, mortality plummeted to 11% by the end of his career, allowing neurosurgery to go beyond just palliative decompression to more definitive surgery. Today, with surgical case mortality rates near zero, our patients can expect a personalized, targeted approach to care through the wonders of precision medicine, 3-dimensional (3D) imaging, and navigation guidance. By examining how we got here, we can better prepare for a future that is happening now. Indeed, the possibilities are endless…

Let us examine each of our specialties to see how far we have come and what we need to ensure future advances.

Beginning with my own field of tumors, we learned yesterday from Dr Rosenblum that electricity was believed to cure disease and that applying current might dissolve tumors.

The first operations for malignant glioma occurred in the 1880s, but all the patients at that time died of complications from the surgery and not the disease itself.

As recently as the 1960s, this Elsberg cannula was used to probe the brain blindly to allow the surgeon to "feel" where a more rigid tumor might be located—which gives a whole new perspective to the term "navigation probe."

Today, of course, we have rocketed light-years ahead. We have the luxury of real-time imaging with fiber tracking and functional navigation to ensure safe and effective outcomes, allowing neurosurgeons access to parts of the brain previously deemed inoperable.

The future of brain tumor therapy will be driven by next-generation navigation, minimally invasive and targeted techniques, and molecular innovations like liquid biopsy.

Four years ago, I was honored to accompany Dr Hadjipanayis and a great team to secure Food and Drug Administration approval for 5-aminolevulinic acid (5-ALA), an oral prodrug that takes advantage of the protoporphyrin-9 synthesis pathways to form fluorescent molecules, which selectively accumulate in tumor cells and not normal brain.

The views from our first case amazingly matched almost exactly an artist's stylized rendering.

After excitation with blue light, the tumor cells emit a red-violet color, enabling surgeons to visualize tumor remnants that might otherwise be left behind, allowing for a more complete resection and thereby enhanced survival. Today, 5-ALA and intraoperative MRI are just 2 of several intraoperative techniques pushing our frontiers forward.

Raman spectroscopy, first developed 100 years ago, was mainly used in wartime battlefields by the military to detect radiation matter emitted by improvised explosive devices. Neurosurgeons adapted this technology to human tissue after discovering that Raman could detect brain tumor cells with 99% sensitivity.

We used a 1000 samples from our Henry Ford tissue bank to develop a machine learning paradigm capable of distinguishing normal vs glioma vs necrotic tissue within a fraction of a second, linking it to a standard navigation probe, and a robotic arm, to help make real-time resection decisions during surgery.

In the future, we might eliminate the half hour or more that we spend waiting for frozen section results, with near-instant results instead, including insight into molecular biomarkers like IDH1 in real time.

In thinking about the next frontier of liquid biopsy, the author Steven Johnson writes about innovation in his book, "Where good ideas come from," that massive breakthroughs do not just happen in 1 step. Rather, you need to go through several doors like interconnected rooms in a house to reach your destination. So, from Cushing to the Elsburg cannula, to early navigation efforts to 5-ALA and Raman, the future of molecular genetic wonders is now on us.

We all know what a glioblastoma multiforme looks like, but imaging has its limitations. Right now, obtaining an actual tissue diagnosis is still the standard of care. But what if all you needed was an $8 blood test to detect circulating biomarkers within minutes? In our laboratory, we compared 15 molecular markers between matched blood and tissue samples and found that the blood analysis predicted the correct tissue diagnosis with 100% accuracy. In tumor boards of the future, we may soon have a quick, accurate way of distinguishing true vs pseudotumor progression, with the hope of dramatically changing the trajectory of this dreaded disease.

But how do we get there? By prioritizing innovation. Like many institutions around the world, we are using thousands of clinically annotated and serum-matched tissue samples to create animal model avatars of our actual patients, in real time, to determine which targeted therapies can best help a particular patient. We then link these results with others globally to learn from, and contribute to, real-world evidence. Our patients deserve no less, and slowly but surely the frontiers are being moved.

To be more relevant for our patients, precision medicine innovations will need to be greatly refined. We know that the historical way of naming tumors based on their cell of origin no longer tells the full story. We also know that distinguishing tumors by key molecular markers, such as isocitrate dehydrogenase

(IDH) wild type, which confers a poor prognosis, can signal the need for more advanced therapy. In the future, pharmacogenomics can analyze these markers in the clinic to stratify a seemingly homogeneous group of patients into different treatment groups, with the goal of personalizing precision immunotherapy for the best results. That is the lofty goal of many real-world evidence trials—so that the experience of a patient in Tokyo or London can be relevant in real time for a patient with a similar profile in Detroit or San Diego, and in the days before science became so politicized, many of our leaders with a personal experience with brain tumors encouraged exactly this type of innovation.

So what is next? The global bioinformatic crowdsourcing of massive data might identify—and cure—patients before they even develop a disease—a so-called previvor, or a survivor of a predisposition…

But we know that our journey has only just begun. Today, we have many tools at our disposal, like evidence-based guidelines that seek to ensure a high standard of care, literally at the fingertips now of every neurosurgeon in the world. The history of neurosurgical innovation guides each of our subspecialties.

For vascular neurosurgery and stroke in particular, tissue plasminogen activator (tPA) was developed in the 1970s and used widely for treatment in the mid-1990s, but the revolution continued with the advent of thrombectomy. Recent stroke trials made the impossible possible by extending the window that patients could be treated for potentially devastating strokes, from 3 to 24 hours. The synergistic interplay between endovascular device design and real-time imaging allows clots deep within the brain to be removed, and function restored.

The progress in open vascular surgery has been equally stunning. From the early preoperative planning sketches by William Osler a century ago to today's instant, preoperative 3D imaging guidance, vascular surgery is safer and better controlled, and even when ruptures occur, 3D imaging guidance and pre-op anatomic planning software prepare the surgeon to handle almost any eventuality.

After we almost lost the ability to perform instrumentation in the 1990s, spine is now rightfully a neurosurgical endeavor, with better and better quality safeguards. Cushing himself performed the first intraspinal tumor surgery in 1900, and in the decades that followed, advanced wiring and screw fixation systems were developed. Some innovations, such as the anterior cervical plating construct developed almost 60 years ago, are still used with great success today: from early fixation devices to the modern era, including minimally invasive techniques and advanced real-time imaging navigation. Preplanning software now allows surgeons to perform, based on real anatomic landmarks, the most complex spinal reconstructions in a safe, robotically assisted manner, with impressive outcomes.

To address concerns of value, appropriateness of surgery, and outcomes, we have looked to data to secure our future. One example is the Michigan Spine Surgery Improvement Collaborative analyzing 71 000 detailed patient journeys from more than 30 hospitals, as a statewide platform to improve outcomes. By promoting transparency and sharing best practices, this initiative has already resulted in decreased infections, cost, and post-op complications, while also improving return to work rates and other outcomes. We must invest in similar efforts globally.

Innovation has also helped our youngest and most vulnerable patients. We have come a long way from the need for multiple, repeated shunt surgeries to now the routine use of endoscopic surgeries for pediatric hydrocephalus, and many other conditions.

In epilepsy, traditional grids and strips paved the way for precision robotics and the use of 3D printing and minimally invasive repair at very early ages have revolutionized the treatment and outcomes for complex craniofacial congenital anomalies.

Our commitment to innovation has led to countless more patients surviving and even thriving, after catastrophic traumatic injury, from the earliest known trephination of skulls in prehistoric times to the first craniotomies performed for trauma by Cushing for wounded soldiers in World War 1. The 20th century brought intracranial pressure monitoring, mechanical ventilation, America's 911 system, and the Glasgow Coma Scale. From the first computed tomography scan in 1972 to more than 30 000 available in almost every corner of the world today, the mantra of "time is brain" has led to novel therapies and better outcomes, from the earliest images unlocking the secrets of the brain to modern precision images available on portable scanners within seconds.

It is incumbent on us to develop more powerful treatments for devastating strokes and neural injury…Exosomes, the "Fed Ex" delivery agents for precise genetic instructions to cells, hold great promise. In the near future—even for human beings, the most genetically diverse organisms—we should be able to unlock the secrets of this exosome-mediated "master switch," of microribonucleic acid transport of key proteins, to restore brain and spinal cord function. But we must invest now in that future.

Finally, the wonders of functional neurosurgery are boundless, from Victor Horsley's first ablation of the motor cortex for movement disorders in the 1890s to the development of the stereotactic frame. The innovation of 3D grids addressed the challenge of 70% of the cortex being located in sulcal folds. With robotic electrode placement, all-day cases can now be performed in an hour. In thinking about depression, our pioneering colleagues have even adapted the learnings from epilepsy monitoring to a new approach for deep brain stimulation for depression, which afflicts millions of people worldwide. At the same time, traditional deep brain stimulation leads are implanted, so are monitoring leads, which can elucidate how brain networks are altered in depression and which parameters can best help individual patients. A monkey playing MindPong without a joystick shows an amazing concept of decoding patterns of neural activity used in every day movement. Soon, paralyzed patients might recreate the same functions with their mind, not their muscles, through a greater understanding of neural networks.

There is perhaps no greater imperative for *visioning* the future than helping blind people see. With new visual cortical implants,

the future is, quite literally, very bright. Here, cortical implants allow a blind man to correctly identify colored shapes with 100% accuracy. In the future, artificial intelligence and virtual reality will push the envelope even further. In 1 example from Dr Pouratian's team, 1 man never dreamed that he would see light or movement again, after losing his sight in a car accident, but with the flick of a switch, his world suddenly grew. A groundbreaking implant converts images from a tiny video camera on a pair of sunglasses into a series of electrical pulses that the brain perceives as visual cues. These flickers of light can signal where a sidewalk begins or ends, or when a person enters a room, enhancing functional independence with daily tasks such as sorting laundry by distinguishing light from dark and safely crossing a street. The future is now.

But so is our imperative to invest in and nurture that future vision. With this tour de force of our collective history, I hope that I have convinced you that innovation is really one of the main cornerstones of our neurosurgical profession. But innovation requires an expanding talent pool and a commitment to include the best and brightest from all aspects of society if we are to set the pace of future discoveries.

Even as we celebrate the 30th anniversary of women in neurosurgery and nearly a century of female neurosurgeons, we know that our journey has only just begun.

But we have great examples from history as to how to proceed. I believe that it all starts with mentorship, as so eloquently stated by Osler a century ago when he noted that the successful teacher is no longer on a height, pumping knowledge into passive receptacles, but rather together on equal footing, making the student feel that he or she has joined a family whose interests are the mentor's first consideration.

My most esteemed colleagues, the future is now. But it will require all of us to prioritize the emerging promise of precision medicine, and minimally invasive technology, and machine learning and big data, to develop cures and treatments beyond our current capabilities. As we pivot to the future, these new skills should be placed on equal footing with traditional bedrock principles of anatomy, neurophysiology, surgical technique, and the patient history and physical examination. We have to do this now. Why? Because the trajectory of our digital, device, molecular genetic, and technological moonshot is about to become vertical. I believe that we can accomplish all this and more by reimagining what I call the 3 axes of neurosurgery.

The first is redefining all the skills needed to perform well in the profession itself. Understanding that, despite our small size, neurosurgery is the tip of the spear. Our ability to unlock the secrets of one of the last remaining black boxes in medicine—the wonders of the brain and all of neuroscience—will have an outsized impact on the future of health care globally. Second, we must seek out, and hone, those personality traits most likely to predict success for future generations of neurosurgeons. I submit that those who embrace innovation and who are willing to jump right into the arena, as Teddy Roosevelt stated, with great devotion for a worthy cause and not fearing failure, are the rightful heirs of all those who worked tirelessly over the past century to make ours the greatest profession imaginable. Finally, we must refresh our educational paradigm. Abraham Flexner established a model in 1910 that successfully improved the quality of medical training, allowing medicine to grow into the most respected profession, by increasing prerequisites to enter medical school, limiting the number of medical schools to those practicing in a scientific manner with engaged faculty in research, and strengthening state license regulations. While these core tenets rightfully endure today, we have newer imperatives too.

Henry Ford, perhaps one of the greatest of all innovators, intimated that we have the power within each of us to effect change. In Flexner and Cushing's day, the focus on quality control for basic survival transitioned us from homeopathic remedies to a modern age of scientific rigor. Now, well into the space age, we need to aim for restoration of neurological function and molecular cures by embracing the information age. While Flexner paved the way for biological breakthroughs, we now can translate more and more of those into actual clinical benefits—from rescue to restoration and transforming lethal into chronic disease.

A century ago, Rockefeller gave $100M to revolutionize health care. As we enhance neurosurgical education as a model for all of medicine, our contributions should imbue new core elements into training. First, we need to teach data science, statistical analytics, and machine learning skills—not just facts. We need to highlight the intricacies of healthcare policy and finances to better equip leaders of the future, and we should consider rotations at places such as Google, Apple, and innovation laboratories around the world, making room for new content in our ever-changing world. We need to nurture teachers who teach and foster team building and communication skills with more leadership courses like the 1 pictured here. My own residents, including now 4 women in our program who are taking neurosurgery by storm, continue to inspire and teach me every single day.

For our generation of neurosurgeons, our time is now. Although the journey is long, what we do today will set the course for generations to come. Of course, it is hard. But it is not like amazing transformations that have not happened before. Because I am from Detroit, I like to retell the story of when Henry Ford was asked about innovation, he said that if he had just asked people what was easiest to imagine next, they would have wanted a faster horse. In 1900, this image of fifth Avenue shows just 1 automobile amid hundreds of horse-drawn carriages. In a little over a decade, cars became the norm, and the world was forever transformed. Data are the currency powering our future much like oil did in the past century. Think what neurosurgery can do now, with our arsenal of space age tools at our fingertips.

If we act today, our vision will become a reality. On this journey, I am forever indebted to, and inspired by, my mentors at Harvard and Henry Ford, and my neurosurgery family around the world.

My journey simply would not have been possible without the unconditional love and support of my own family, and they are my greatest blessing. I have had many titles in my career, but the

ones that I value most are dad, husband, and son. To Nicholas, Connor, and Grace, I am incredibly proud of you and all you have accomplished in your young lives so far, and you give me the greatest hope that our future is indeed in phenomenal hands. To my amazing mother Grace, I will always be grateful for your incredible sacrifices so that I could pursue my dreams. To Laurel, who first captured my heart at the age of 14 and now after 23 years of marriage, you are the love of my life and the heart and soul of our family.

To my colleagues, thank you for this incredible honor to serve our profession. I know that together, we truly can shape our vision for the future. As we contemplate these next steps in the incredible journey of neurosurgery, my wish for all of us and our profession is that the future of neurosurgery is *As wise as it is smart*, *As restless as it is proud*, *As bold as it is thoughtful*, *As new as it is old*…

In the service of our patients, *as good as it is great*. Thank you.

Watch Dr Kalkanis' full Presidential Address on the Congress of Neurological Surgeons YouTube channel at http://youtu.be/KvPv6NO1T4c.

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