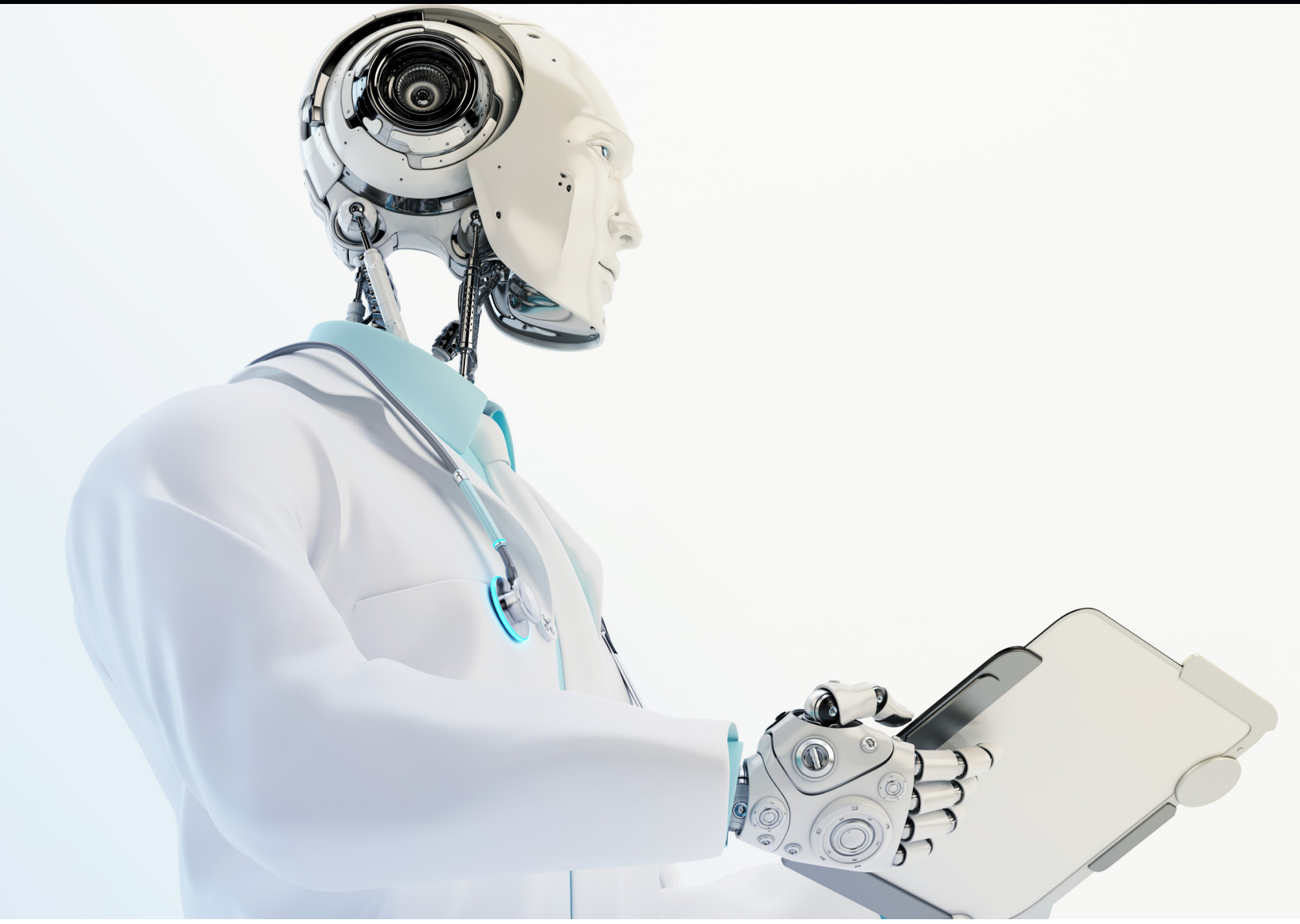
FROM DATA TO KNOWLEDGE IN NEUROSCIENCE: BUILDING TOWARD INDIVIDUALIZED MEDICINE



SYMPOSIUM REPORT

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For further information about this symposium series or reports, please contact the Director of the Center for Neurotechnology Studies, Jennifer Buss, Ph.D. at: jbuss@potomacinstitute.org.

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EXECUTIVE SUMMARY

American innovation has led to some of the world's most inventive and successful medical devices and treatments. However, the medical industry has yet to maximize the potential of the massive amounts of health data offered by new technologies. Medicine is moving into a data-centric era where our ability to anticipate, understand, diagnose, treat, and heal illness and disease will be completely revolutionized. Currently, the field of neuroscience is trying to transform medicine by leveraging the novel opportunity of Big Health Data. To capitalize on this revolutionary opportunity, America must look towards the future – taking advantage of Big Health Data by embracing technological advancements, sharing personal data responsibly, and discovering new health knowledge. Doing so will enable breakthroughs in health innovation, decrease healthcare costs, and help realize the dream of personalized medicine.

This most recent effort by the Potomac Institute's Center for Neurotechnology Studies (CNS) continues its long-standing mission to follow and understand the latest neuroscientific advancements and neurotechologies. In 2013, the Institute's CNS report "Neurotechnology Futures Study" presented a technology investment Roadmap and outlined the key research areas and technologies required to move neurotechnology forward. The Institute's 2015 report "Trends in Neurotechnology" discussed the vast implications of neurotechnology – not only for particular fields such as medicine and defense, but also for society as a whole.

In 2016, the CNS engaged in a year-long effort researching current technology trends and scientific advancements in the field of neuroscience – focusing specifically on how these trends and advancements are building towards more individualized medicine. A comprehensive literature review and market trend analyses were conducted to identify technologies on the forefront of this revolution in medicine. Several months of research and analysis culminated in a CNS seminar highlighting the initial research findings, including discussions of how neuroscience utilizes Big Health Data to improve treatments for neuro-related complications as well as what is needed to truly understand the mind.

On September 12, 2016, the Potomac Institute held a seminar titled, "From Data to Knowledge in Neuroscience: Building Toward Individualized Medicine." It featured a panel of three distinguished speakers, including: Dr. Stacy Suskauer, Co-director of the Center for Brain Injury Recovery at the Kennedy Krieger Institute and Associate Professor of Physical Medicine and Rehabilitation at Johns Hopkins School of Medicine; Dr. Mahesh Shenai, a neurosurgeon and Director of Functional and Restorative Neurosurgery at the Inova Neuroscience and Spine Institute; and Dr. Jessica Eisner, a Senior Fellow at the Potomac Institute and former Senior Medical Officer and Clinical Consultant at the FDA.

Following the panel presentations, Dr. Jennifer Buss, Director of the CNS at the Potomac Institute, moderated a question and answer session that led to a series of engaging discussions. A consensus emerged that there is a need for the use of Big Health Data in two different contexts: 1) using Big Health Data to create better physical, as opposed to statistical, models of human health in order to improve our fundamental understanding of human biology, and 2) using Big Health Data to improve the quality of medical practice for the individual, leading to better, more predictive patient outcomes. Additionally, an insightful discussion took place regarding the creation of new incentive structures that promote the kinds of high-risk, high-reward research endeavors needed to capitalize on the potential of personalized medicine. It was determined that unless the liability challenges plaguing the medical profession are overcome, these hurdles will drastically limit the usefulness and progression of the personalized medicine revolution.

The future of neuromedicine needs to leverage data collection capabilities and build better individualized health models so that initiatives like the BRAIN Initiative can inform medicine through the precision of individual health baselines. There are immediate benefits to using Big Health Data with statistical methods to improve our ability to anticipate, diagnose, and predict outcomes for individual patients, as well. However, we must not neglect the goal of creating better physical, mechanistic models of human health, in the forms of generalizable theories of biology, to enhance our fundamental understanding of human health and direct our efforts to developing better medical practices and cures in the future.

FINDINGS, CONCLUSIONS, AND RECOMMENDATIONS

THEME #1: NEUROMEDICINE DATA COLLECTION AND ANALYSIS

FINDINGS:

- **Current health data management systems are largely ineffective.**

  The systems currently being used for searching health data lack integration and interoperability, which hinders the usefulness of the interconnected network of searchable data and literature databases. These systems need to be reimagined and optimized such that searching for health data is streamlined and intuitive. Physicians often get a very limited amount of time with their patients and need health data management systems that can provide them the information they need, precisely when they need it. Improving health data management systems will lead to greater efficiency and efficacy in patient care.

- **Tools to effectively analyze Big Health Data data are missing.**

  More health data is being collected on patients then ever before, but the tools to extract important health information from this data are largely absent from the medical field. This inability to appropriately capitalize on the new influx of health data not only hurts the patients, but it also stymies the Big Health Data industry. With better sharing and analysis tools for health data, the medical field can begin to improve patient outcomes with the realized potential of Big Health Data. Further research and development into such tools will help create integrated knowledge and resource systems that are easy to use, incentivized and interoperable.

- **Multidisciplinary health data management systems do not exist.**

  Multidisciplinary health data management systems are absent in the medical field. This interrupts the analysis of multiple populations and modalities to provide personalized care. Systems that are designed to combine data (health images, biomarkers, genomics, etc.) will begin to demonstrate the usefulness of Big Health Data opportunities. With health data management systems that integrate multidisciplinary types of data, more holistic models of patient health can be developed. This will lead to more individualized data driven approaches to patient care, which is something largely missing from the medical field. Furthermore, patients are now collecting health data about themselves all the time with technologies like wearable devices, yet patients still find it difficult to share this data with their doctors to improve their quality of care.

- **Neuroscience is not the only field in medicine that is lacking health data tools.**

  All medical fields experience some type of delay or obstacle in collecting health data and having the tools to translate that data into useful information. The medical field could use data quality management as well as organizational training to help keep systems up to date and optimized over time. Making improvements regarding the use and development of health data tools in the field of neuroscience will only incrementally improve the entire medical field. Big Health Data promises to revolutionize modern medical practice, but it will not be realized without a comprehensive plan to develop and improve health data tools for all medical fields.

CONCLUSIONS:

- **The ineffectiveness to collect, manage, analyze, and share Big Health Data has severely limited the potential of the personalized medicine movement.**

  The current medical system is severely limited in its ability to capitalize on the personalized medicine movement. This is despite the fact patients today provide their doctors with more data regarding their health then ever before. The medical field is currently failing at collecting, managing, analyzing and sharing patient health data so that it can be translated into more effective and predictable treatments. Doctors are finding it difficult to access the data they need to provide better care for their patients because the tools available to extract the most useful information from that data are inadequate. With better analysis tools and integration of data systems containing multidisciplinary data sets, we can expect to start to achieve the realized potential of personalized medicine. Data contributed from multiple fields of medicine are required for a comprehensive understanding of an individual's health profile. The more information known about a patients baseline health and current medical state will lead to a more timely and personalized treatment that is optimized for their health. Improving these systems will allow for the creation of better patient models, leading to improved patient outcomes, and finally allowing the medical field to capitalize on Big Health Data.

RECOMMENDATIONS:

- **New data collection, management, analysis and sharing systems are needed to capitalize on the large increase in available patient data (i.e., Big Health Data) and bring more personalized treatments to patients.**

  The medical field needs to develop and integrate better Big Health Data systems. Electronic medical records are a great start, but we need better tools to share and analyze the information within. These new systems should be designed to provide the necessary information required to build more complete understandings of patient health. This will lead to more effective treatments and improved patient outcomes.

Key to this will be the development of new tools to analyze and integrate diverse health data sets. The equilibrium between these systems will provide the medical field with an interconnected network of data that ranges from various populations and modalities. A complete and effective Big Health Data system will ultimately help improve the individualized care of patients and rapidly change the way we understand human health.

THEME #2: KNOWLEDGE TO PRACTICE

FINDINGS:

- **The regulatory system is failing to keep up with the rate of medical technology advancement.**

  Medical technologies, like neurotechnoogies, are being developed at a rapid pace and the current regulatory process is unable to adequately manage this. There are many stopping points for new technology mandated by safety, efficacy, and evaluation requirements that require months or years to satisfy. The regulatory process for new medical technology is likely to continue to get worse before it gets better since the problem is largely unrecognized within agencies such as the FDA. Additionally, there are technologies attempting to come to market that regulatory bodies are technically ill-equipped to appropriately evaluate. These "knowledge gaps" lead to situations where agencies lack sufficient technical guidelines to appropriately evaluate the safety and efficacy of new technologies.

- **Doctors and patients lack training to effectively use new medical tools and interpret personal health data.**

  New medical technologies allow doctors to incorporate new types of medical data into their processes for evaluating and treating patients. While these tools have great promise to improve patient outcomes, they cannot be effectively utilized if the doctors using them do not understand them or the data the produce. For example, flooding a doctor with new information regarding epigenetic biomarkers is of no real use to the doctor if the doctor is not well trained in interpreting and utilizing epigenetic data. Furthermore, patients are obtaining access to many new devices that offer access to personal health data they did not have before. Everything from wearable technologies to genetic sequencing data are now available to the patient despite the fact the patient is not able to use or understand this information in a meaningful way. Complicating this situation is the reality that patients find it very difficult to share this new, self-collected, health data with their doctors. The patient is left with a lot of data about their health that they do not understand and an inability to get clarity or use out of it from their doctor.

- **Opportunities to be innovative and take risks are lacking in medicine.**

  The medical field tends to focus on streamlining the costs of medical treatments and as such is missing a balance between incremental improvements to the current system and high financial-risk projects that could provide huge innovative leaps in capabilities and understanding. There is a lack of serious incentives for doctors or medical professionals to take on cost and liability factors associated with development or use of the kinds of medical technologies needed to provide patients with more personalized treatments. Insurance agencies are providing the largest hurdles for the medical community to take on the risks and challenges needed to unlock the potential of personalized medicine enabled by Big Health Data.

CONCLUSIONS:

- **There are many obstacles impeding the ability to bring the advantages of Big Health Data to patient's lives.**

  Problems with the regulatory system, doctor and patient education, and the risk incentive structures in medicine are holding back the promise of Big Health Data and personalized medicine. The regulatory system is failing to keep up with the pace of technological medical innovation on both the technical and evaluation front. This is keeping promising technologies off the shelves while at the same time potentially letting bad ones on them. New approaches to efficiently and effectively regulating an industry that is rapidly changing and evolving are desperately needed. At the same time, new training and education initiatives are needed for both doctors and patients. Without this, doctors will be unable to incorporate new breakthroughs into their actual medical practice and patients could end up doing more harm as they attempt to "treat themselves" using personal health data provided by technologies such as wearable devices. Lastly, insurance agencies can kill a revolutionary product by simply thinking that the process is too risky or won't be productive. As a practitioner, the riskier you are, the more your insurance costs, so innovation is limited by the amount of affordable risk. Improvements in these areas will lead to a medical system that more easily translates the knowledge available using Big Health Data into more personalized and effective medical practices.

RECOMMENDATIONS:

- **The medical community needs to incentivize high-risk, high-reward procedures and research to improve patient care.**

  The way we can change this risk-adverse culture is to create policies providing an insurance clause allowing innovative research so the insured are protected against lawsuits, or give people – innovating within certain bounds – a pass. This will bring out

more medical practitioners who will not be scared of, or worse penalized for, testing their risky ideas. Such improved systems might try to learn from failed programs as opposed to shutting them down. Developing a continuous and supportive process for innovation will place value on high-risk, high-reward studies and hopefully enable more medical professionals to bring innovative ideas to the table.

- **The regulatory system should be completely overhauled to deal with the pace of technological innovation and advancement in the medical industry.**

  The Big Health Data movement has caused a range of new challenges associated with the complexities of new technologies and the types of data new health technologies create. Regulations need to be more flexible, deal with variability, and avoid the "culture of no" that stems from the inability to handle many nuanced variations. Policymakers should enact legislation that charges the FDA to modernize and optimize its regulatory process for evaluating the safety and efficacy of medical devices and treatments so that it can accommodate the pace of development and increased technical challenges such advancements cause. Additionally, better, more transparent partnerships between the FDA and companies in the medical industry needs to be encouraged. With a more robust and streamlined regulatory process that is engaged with its community, patients can be ensured of better, more reliable, and more personalized treatments.

EVENT TRANSCRIPT

GENERAL AL GRAY

Introduction

Let me welcome everybody on behalf of the Potomac Institute. I'm particularly proud to welcome our distinguished visitors and we really appreciate you taking the time to be with us.

The topic of neuroscience has grown by leaps and bounds beyond the initial efforts towards medicine and into many ideas from people who study this challenge with respect to society, in general. We at the Potomac Institute are quite involved in the neuroscience issue, and we have been since the late 1990s. We started initially, as we always do, looking at the intersection and interface between science, technology, policy, government, law, and ethics, which continues to be our overarching idea – our theme – as we go forward. In the early 2000s, we put out a number of reports on this topic, many of which were spearheaded by Dr. Jim Giordano, who's sitting here today.

Later on, under the guidance of our chairman, Mike Swetnam, we took interest in whether we could take neuroscience beyond just medicine. We're going to talk about medicine today, but we are also interested in whether we can move beyond that into the broader realm of societal applications, in general. A few years back, we developed a long-range study that laid out two tracks we wanted to take in terms of neuroscience and the future. One had to do with continued research at the intersection of policy, law, science, and government, and trying to move beyond bureaucracy, and all the other challenges we face. The second track had to do more with applications.

Finally, the topic of neuroscience has taken off. The number of publications over the last four to five years is huge, even compared to what it was at the turn of the century. Innovation is another area which is really growing – patents have exploded to several times as many innovative patents now as there were five years ago.

With that, I'm going to turn it over to Kathryn, who's going to take it from here.

KATHRYN SCHILLER-WUSTER

Opening Remarks

Thank you, sir. I'm Kathryn Schiller Wurster. I'm the Director of the Center for Revolutionary Scientific Thought at the Potomac Institute, standing in for Dr. Jen Buss, who's the Director of the Center for Neurotechnology Studies, who will be making closing remarks. I want to thank

General Gray for kicking it off, and thank you to all our speakers for being here. Like General Gray said, this is a topic we've been looking at for over ten years. What we try to do at Potomac is to anticipate new, emerging technologies, to help push the development of technology in a positive way for society, and to predict some of the policy challenges that may emerge in light of these developments.

Today we're going to talk about Big Data, and how we can use data to help make medicine even better. One of our important topics for this year is examining the future of medicine and how emerging technologies will shape this future. We try to look at the field of medicine not only in the sense of Big Data, but even further out to the future – at things like personalized medicine, sensors, genomics, brain machine interfaces, and apps. All these things are emerging, and the regulatory frameworks are lagging behind. So what can you do to help develop those things in a way that's beneficial and overcome some of the apparent challenges?

I'm going to let the experts continue the discussion. First, we have Dr. Stacy Suskauer. Dr. Suskauer is with the Center for Brain Injury Recovery at the Kennedy Krieger Institute, and is an Associate Professor at the Johns Hopkins University School of Medicine. She works on understanding outcomes after childhood brain injury. The Kennedy Krieger Institute has been a great partner in studying these emerging technologies and some of their applications. Then we have Dr. Jessica Eisner, a Senior Fellow at the Potomac Institute, who has an incredibly broad array of experience – most recently, and most applicably here I think, working at the FDA as a Senior Medical Officer and helping review some of the issues that we are talking about. She also works with AAAS, which is a great partner to us, as well, in looking at science and technology policy. And, Dr. Mahesh Shenai is a neurosurgeon and Director of Functional and Restorative Neurosurgery at the Inova Neuroscience and Spine Institute, and he's an expert in deep brain stimulation. We're recruiting him to help with some of these topics as well. When we first started all this work, deep brain stimulation was a very new, rough, primitive technology, but it's come such a long way the last few years. The applications of that are really mindboggling – what we can do with it today. I'd like to thank you all for being here with us today, and we'll get started.

PANEL

With expertise spanning research, clinical care, and government regulation, the speakers discussed the vision of how healthcare could be transformed with integration of Big Data and cutting-edge devices, as well as the challenges standing in the way of that future. Rapid technology advancement, with the ability to collect abundant data through genome sequencing, neuroimaging, and wearable or implantable devices, makes possible a world in which physicians can use personalized patient data to make specific diagnoses, predict the outcomes of potential treatments, follow up on patient status in real time, and even predict the development of a neurological condition before

symptoms appear. However, realizing this vision will require a true paradigm shift: developing the tools and incentives to integrate multi-modal data into usable knowledge ecosystems, updating regulatory policies that have not kept pace with technological change, creating policy strategies to enable high-risk innovations in healthcare and technology, and balancing data-driven individualized care with the quest to build better models of neurological and biological systems that can inform medicine for all people.

STACY SUSKAUER

From Data to Knowledge in Neuroscience: Building Toward Individualized Neuromedicine

What I would like to do today is help describe how we need to use existing data to help guide us towards using emerging technologies to help us practice better medicine. From a clinical and research perspective, my specialty is across the spectrum of brain injury – from concussions, which I am not going to talk about in my slides but we can talk about during the discussion period, to more severe brain injury. Here, I will specifically talk about traumatic brain injury (or TBI) – injury caused by some sort of external force to the brain – as opposed to other forms of brain injury, such as those caused by stroke.

Severe brain injury is less common that milder brain injury, such as concussion; however, the morbidity and mortality are much greater with the more severe injuries compared to milder injuries. Traumatic brain injury is the most frequent cause of disability or death in childhood. Children with severe TBI go on to require a great deal of care from society. We strive for better care that will help them experience more complete recovery and thereby decrease that burden on society as well.

There is actually a clinical scenario that drove my interests in brain injury, and part of what I will discuss with you today is how little progress we have made in the 15 years since I was in residency and first encountered this scenario. For example, if we have a teenager who is in the intensive care unit after a traumatic brain injury, the rehabilitation consultants are often called to the bedside, and the question for us is what we anticipate the long-term outcome to be. There are a lot of people who want answers to that question. Certainly families want to know what to expect and plan for. The family needs to know if they need adapt their home to be ready for a wheelchair. They need to know if their teenager will be physically reliant on a parent when they get back home.

It's also a really important question for medical providers who may be counseling families related to whether or not to continue life support. While in adult ICUs that discussion typically happens in the first week after a severe injury, in many cases those discussions may not occur on the same timeline in a pediatric ICU. Today, there are real questions about whether these decisions are being made too quickly. Critical decisions ride on early prognosis of the long-term outcome after injury.

In addition to families and medical providers, insurers want to know what the outcome will be to determine what additional care they should provide. For example, how will a child's function change if they go to inpatient rehabilitation after a severe brain injury?

We also need this information on prognosis to prepare the school and the child's broader community. Will this child be able to return to her prior typical high school schedule? Will a special school setting be needed?

Part of the reason these questions are so challenging is that after severe TBI there is a very wide range of possible outcomes, ranging from "this child will pretty much be the child you knew before, with perhaps mild changes in attention but no significant long-term changes in the child's educational and life path..." to "this child is going to be physically disabled and be dependent on others for all daily needs..." to "this child may be able to walk, but he/she will have difficulty regulating their behavior which will impact their success in school and independent living..." While these scenarios have vastly different impacts on a family and require varying medical needs, unfortunately, today – just like 15 years ago – the answer to the question "what will this child be like..." is still, "we really can't predict." We add to that, "as a rehabilitation team, we will be there every step of the way and will do our best to help your child get the best outcome, but we can't say for sure what that will be."

When faced with this scenario, we often say how we wish we had a crystal ball. I think the crystal ball is out there, but we need to figure out the best way to assemble it, so that we can improve prediction in this scenario. Until we know what outcome to expect for an individual, it's really hard to personalize intervention to improve outcomes and to be able to measure how much benefit the intervention provided.

I'm going to talk a little bit about bedside clinical data points, which is usually the best data we have for clinical care today. We'll touch on imaging, biomarkers, and genetics, which are some of the pieces of the crystal ball which are out there being used in different ways and different places. What we really need to do is figure out how to combine these pieces, and I believe this is where some of the Big Data opportunities exist. Assembling those Big Data has the potential to help us create this crystal ball which will allow families and providers to know what to expect. When we think about what we want to get out of Big Data, we need to remember that we have to be able to boil the data down to apply to an individual patient in a clinical scenario.

Here I'll discuss some of the data we have published. We have examined the outcomes of children with severe TBI who came through our inpatient rehabilitation unit and retrospectively examined variables that predict their outcome. The bottom line is that we have shown that the number of days from injury until a child can follow commands is somewhat predictive of the later outcome. As simple as this is, it did add to prior knowledge and allows us to be a little better with prediction than we were 10 years ago. Interestingly, we are best at predicting who is going to have the worst outcome. From a common sense perspective, it is not surprisingly that

children who cannot follow commands until almost a month after injury show worse outcomes than children who achieve that milestone earlier after injury. What I think is far more surprising is that even within the group of children who can follow commands within the first couple of days after injury, the range of outcomes is large, and we can't promise that they are going to do well.

Some of our data come from an outcome measure called the WeeFIM which is the child version of the Functional Independence Measure, which is the measure most frequently used to track progress during inpatient rehabilitation. The WeeFIM and FIM are heavily weighted toward motor outcomes, whereas the most frequent lasting problem after TBI relates to cognitive and behavioral function. When we move to a different outcome measure, the Glasgow Outcome Scale-Extended, revised for Pediatrics, which better captures the range of changes in daily functioning after TBI, while we have some ability to predict who will have a good versus poor outcome on this measure, though these clinical data points only account for 35% in the variance of outcomes. Even then, we still face a large range of functioning within the "poor" outcome range. On this measure, a child classified as having a "poor" outcome could be independent from a motor functioning perspective but with cognitive and behavioral changes, or could be severely disabled from a motor perspective and reliant on others for physical needs. I hope this example makes it clear that we have a long way to go to be able to provide better prognostication in order to respond accordingly with selection and evaluation of interventions.

Just a brief word on neuroimaging: I am showing here clinical images. There are a number of more advanced imaging techniques, which are being used, mostly for research and to a lesser extent in clinical practice, but overall, the same premise holds. Imaging findings do not allow us to predict specific outcomes and will likely only be one piece of the puzzle. We can expect that to create our crystal ball, we will need to be able to synthesize many pieces of data.

Thank you all and I look forward to answering questions in the Q&A session.

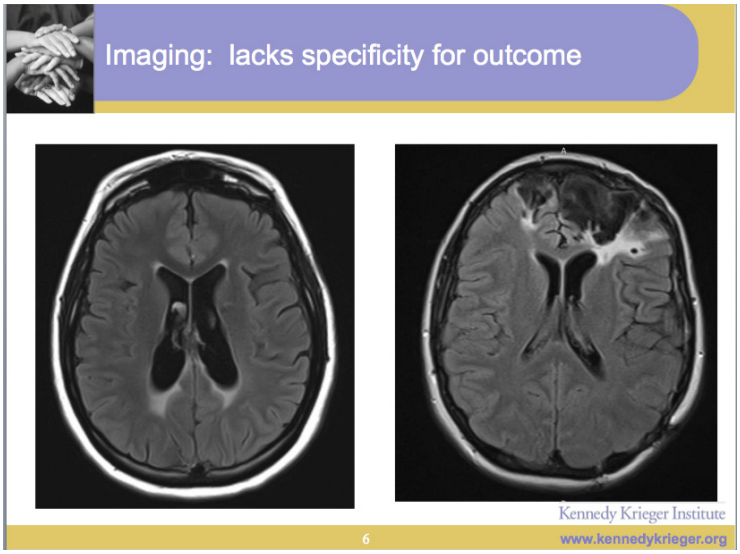

Image courtesy Stacy Suskauer.

MAHESH SHENAI

Personalized "NeuroHealth": A Challenge of Scope and Scale

I am going to talk today about going from data to knowledge, and knowledge to practice – and that clinical practice gives us an opportunity to study our results and go back to create new data and new knowledge and practices. Deep Brain Stimulation (DBS) is also a story of continued innovation. The device was FDA approved in 1994, and we are now routinely treating patients with essential tremor (ET), Parkinson's disease (PD) and dystonia. There are multiple new indications that are currently being investigated, such as Alzheimer's, epilepsy, depression, and obsessive compulsive disorder (OCD). We have new methods such as better visualization tools that are changing how we put DBS into the brain. There are some new devices that have just been commercially released that are increasing what we can do to treat patients.

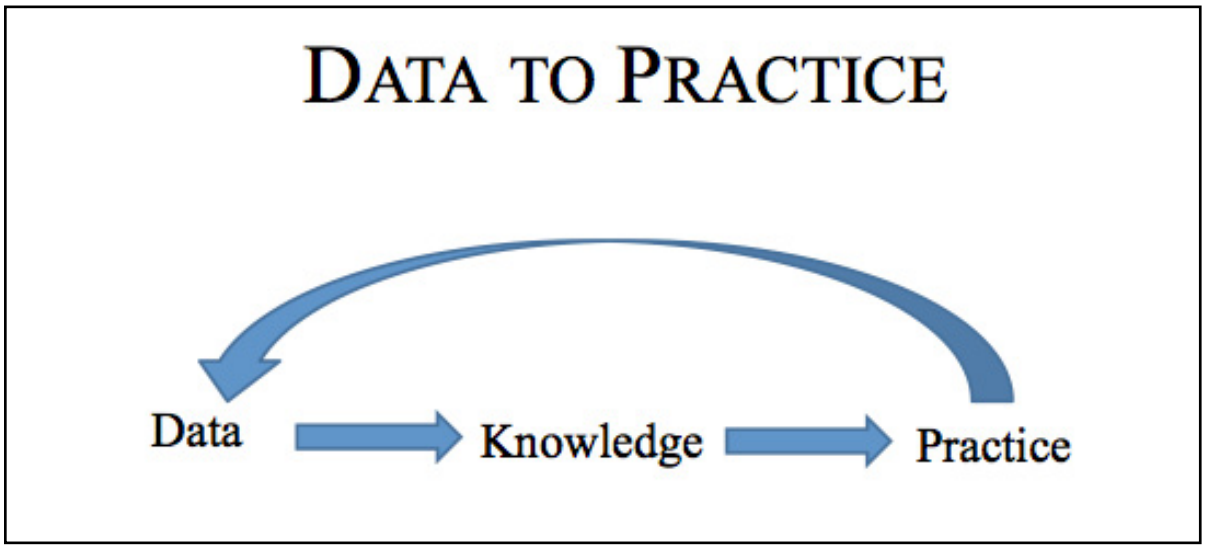

Image courtesy Mahesh Shenai.

We have a few new Big Data approaches that allow us to use results from 100,000 patients to assist us in treating the next patient. These data driven practices are creating an evolution in DBS therapy. When looking at the "data to knowledge to practice" process, you want to focus on the knowledge and practice. If you start with knowledge, you need to come up with novel ideas to test, which usually leads to development and prototypes, creating a process of finding time and money to do such a thing. That leads to the initial hurdles of IRBs, safety trials, and FDA approval. Early adopters are needed to champion initial clinical studies to demonstrate comparative effectiveness. Eventually, the field reaches a point of sufficient study, where experts can provide "guideline level" strategies and the entire field can sit down and agree on specific standards of care.

The Inova Center for Personalized Health integrates all of these topics into one center and brings together research, data, best practices, cutting edge technologies, expedited processes,

and people. It's more than just an abstract notion. As many of you know, Inova purchased the ExxonMobile campus about a year ago. One of the largest corporate headquarters in the world is now being converted towards personalized health – so that is a very big opportunity. When finished, it will house a patient-centered process that provides a patient access to multidisciplinary provider teams that includes entire teams of doctors, instead of just one. The Inova Center for Personalized Health also provides cutting-edge technologies, clinical trials, and quality and safety initiatives. Patient navigation is also provided because it is a complex system. Personalized medicine isn't just a medicine but it's being able to navigate patients through that system. Data analysis and action is what you do once you study patients through treatments and analysis and more importantly the action of what you do from that data. This all comes down to the patient.

I want to tell you a story about one of my patients. He was diagnosed with Parkinson's disease many years ago and came in for a DBS consultation. We talked about doing the "awake" surgery with him but he wasn't comfortable, so we staged a mock operating room for him to see if he could tolerate the situation. He could not handle the situation. Meanwhile, we had introduced a new process at Inova that utilized MR-guided DBS insertion. This is when we convert our diagnostic MRI scanner into an operating room. It was a long process because of certain hurdles but we were able to get him from being significantly symptomatic, to a restoration of function with his gait. We applied cutting edge technology but we did it in a very specific way and that is through individualized analysis and application of new technology – which is patient centered and personalized.

To use this as a case study for the future, we want to introduce what he went through before he got to the point where we could do this type of treatment. Before we met him, he went around the system a lot, saw multiple doctors, and underwent multiple treatments – usually empirically based – and most of his therapies were sub optimal. Initially, he presented to his primary care doctor with symptoms such as difficulty holding a frying pan and inability to handle the basic skills of cooking. In today's day and age, we don't have a screening process for Parkinson's disease patients. Quite frankly, patients will visit their primary care doctor and may experience difficulty walking or notice some functional decline that makes them visit their doctor. In the future, this will be a streamlined systematic process that will have genetic screening tests that you would take early on and it will predict if you will have Parkinson's disease. Parkinson's disease is a very visual diagnosis. You can imagine using all the security cameras to analyze and predict who may develop Parkinson's disease. Our smartphones have sensors in them as we hold them and we may be able to analyze microscopic movements that are Parkinson's predicting. Every day things such as a spoon may be able to sense or screen if we have Parkinson's disease.

Once they are screened, how do we evaluate patients? Right now, we go to see a single doctor in an examination room and that doctor may have you go take a few tests several miles away with a specialist and a sub specialist. That is a lot of churn for the process of evaluation. In the future, we are going to have integrated, multidisciplinary networks where patients come to one

place. Telemedicine will be used as well where you will have access to world experts directly from your home. Also the use of social media such as Facebook and Twitter will be used to help evaluate and navigate through the system.

How is our diagnosis going to change? We will use multiple technologies so this is where the hard science and the basic sciences come in. Right now, the way we diagnose Parkinson's disease is clinical because we don't have a very specific test for it. We test patients frequently over time and then decide if they have Parkinson's disease. In the future, we are going to be able to apply these scientific tests and come up with something very specific, not just idiopathic Parkinson's disease but subtypes of X and Y, so this will be very specific to that person based on their type of disease.

How does that help us with therapy? Well, if we know the subtype then we can use large outcome databases to provide a customized solution for that patient. We can also do outcome prediction to predict how that patient is going to respond to a particular type of therapy. After therapy is initiated, how do we survey that patient? Currently, they show up every three months to our office and we meet with patients for about 30 minutes. In the not too far future, we are going to use wearables – some of these already exist today – where patients are wearing sensors that are connected to personal dashboards that are connected to our office. This way we will know that a patient has a specific issue or if they are doing well or not well based upon wearable sensors. Again, this may include things such as social media and interconnectivity to help us do that.

The challenge of personalized health is more than technology. If you look at the patient that I just described, it started with a screening, evaluation, diagnosis, treatments, surveillance and outcomes. There are a wide variety of technologies that can be applied to this such as basic science, neuroimaging, Internet technologies, pharmacology, and surgical and restorative therapies. I am trying to emphasize that this is not only a technology challenge, but also a system and strategy challenge – because it is a challenge of scope and scale. For example, if you take Parkinson's disease and you look at the various touch points of the patient (screening, validation, diagnosis, treatments, surveillance and outcomes), each step requires a detailed solution, and that is a problem of scope. If we look at the problem of scale, Parkinson's is only one form of disease. If we start expanding that to include other neurological disorders and all their medical diagnosis (the ICD says that if you take 70,000 diagnosis and multiply that by the number of people who could have a different nuance diagnosis), we are talking about a massive scale – so that is really the challenge of personalized health. We need the technology, Big Data, personalized medicine, precision health, and implementation.

The point I want to make today is that to achieve truly "personalized" medicine, we need to have an ecosystem that supports Big Data. The policy consideration for personalized health is that there is a need for a process and consistency in our policies, so I have a few considerations. First, we need to redefine value. The way that we define value today is based on volume and procedures which is a good dimension of it, but I think we need to include how we are being innovative, personalized, and incorporating new practices into patient care. We also need to

vertically integrate across multiple domains, not just for a patient visit for one day but in a multidisciplinary fashion for the entire course of the treatment. We look at information technology and a lot of these solutions are going to involve mobile devices but the information technology bureaucracy that is present right now is looking more at the security perspective. The potential for mobile information creates a sense of fear but it is also driving a lot of initiatives and security measures. Finally, I think we need a system that fully involves physicians in the process of creating policies. I think there is a feeling among us that the way healthcare is going, a physician can be marginalized in the overall development of institutional strategy. You have to understand that the issue of scope means that you need to understand the very basic levels of each disease that we treat. In coming up with a scale strategy, we need to involve the experts of scope, which are the healthcare providers. Thank you for allowing me to speak today and I will gladly answer questions at the end of the forum.

JESSICA EISNER

Addressing Neuroscience and Neurotechnology Challenges as a Regulatory and Policy Issue

Good afternoon. My understanding of my role here today is to address neuroscience technology challenge as a regulatory and policy issue. I am a physician but I have not seen a patient in about eight years. I have been working in clinical trials and product development for almost 20 years – four of those years were with the FDA. Unlike my colleagues beside me, I am going to focus more on the regulatory, device, therapeutic aspects versus treatment. I will say that the healthcare infrastructure pieces that my colleagues mentioned are their own major challenges for policy and regulation. Translating data into valid practices that are both accepted by practitioners and endorsed by organizations is its own arch of research and policy. When you go from data to knowledge to practice and you want to include a new device or product, that is where I come in with my expertise.

I was a former senior medical officer at the FDA so I don't represent their views but I can give you some insight into what goes on there. The pace of policy and regulatory innovation just has not kept up with technological innovation and having been in both CDER and CDRH, it became very clear to me that innovation outpaced regulations before I got there. People on the regulatory side cannot keep up with this pace because there are so many stopping points that are mandated by safety, efficacy, evaluation, and regulations. In the current scheme of how things are being conducted now, I think that it is going to continue to get worse.

I will give you an example of a device that has used data and how that looks for potential patient care. I was at the FDA as early as 2015 when the Ebola outbreak occurred. I worked in the general hospital device branch, which people didn't think would have to do with the Ebola response. Most people thought about diagnostics and getting a better, more rapid diagnostics for Ebola as well as antivirals and vaccines. The hospital device branch deals with gloves, gowns and thermometers that are all potentially regulated medical devices and we had problems with all three of these. I am going to focus on thermometers because that turned out to be one of the more critical

issues that we came across as far as data goes. As the outbreak started spreading throughout nations, there were initiatives to set up fever monitors in certain airports and it came to pass that people were getting different readings from the same thermometer and eventually this issue came to the FDA to our division. Thermometers are a Class 2 device meaning it is a device that is used for medical utility and its use poses minimal risk. Historically, thermometers were a Class 2 device and weren't highly regulated. If a manufacturer wanted to manufacture a new thermometer or a new version of one then all they needed to do was show that this new thermometer is substantially equivalent to the thermometer that exists on the market. All you would need to do is register on the FDA website and there is really no other follow up except for periodically registering.

Image courtesy Jessica Eisner.

When the Ebola outbreak hit, people really became aware of the fact that there was a great inconsistency in thermometers. When it came to the FDA that people wanted a recommendation for the best thermometer to use, the FDA had to look at this problem. We found that thermometers are all sort of clumped up into one thermometer category so we didn't differentiate between thermometers that are suited to predict ovulation, baby thermometers and new thermometers like the ones used in the airport that scans your forehead were not reliably reproducing results. Generally, people didn't think this would be important in impacting the Ebola outbreak but it turned out to be very important because you could not trust this data from the thermometers. This resulted in a slightly more regulated process for the thermometers. In July of last year, the FDA decided that people will have to submit a application for any thermometer. I bring this up because these are the types of things that the FDA deals with but it shows the quality of data that comes through the FDA door. We were getting data from Africa using two different thermometers and giving two completely different profiles for the same patient. There are about 800 thermometers that are registered on the FDA website.

I am going to switch over from the quality and quantity of data to the current situations with neurotechnologies. I am not a neurologist but I have worked on a few neurologic devices and

a lot of these have integrated software and circuit boards in them. Some of the devices take any data that they have and transmit it to a remote computer or vice versa where the remote computer will transmit data to the device itself. In the age of smartphones, people don't think twice about issues involving cybersecurity, what kind of device it is, and whether it transmits data without being manipulated? The other two main aspects of data are mobile medical app data and hospital software system data. Currently, these are all data issues that the FDA is dealing with in a way and in a volume that they have never had to deal with before. The FDA infrastructure has been there for a while but the explosion of these systems has overwhelmed the FDA. My colleague mentioned wearables earlier – that subject in particular has become a controversial medical device area because event though it is patient generated data and it may be feeding into something like an app on your phone, the data still may be getting manipulated. An example is if an app on your phone tells you what to do when a certain number of data points meet a certain threshold. This has the potential for health and legal implications – specifically, the liability of the manufacturer and the FDA if they cleared it. In the overview, I provided a few examples of the way data comes into the FDA, how people ask us to deal with data at the FDA and some of the issues that are yet to be resolved within the FDA. I will be available to answer questions as well during the Q&A.

PANEL Q&A SUMMARY

The panelist discussion explored principal challenges and critical opportunities involved in translating neuroscience data into medical knowledge and clinical treatments by improving data sharing and analysis practices. The conversation also included policy considerations for utilizing neuroscientific data for nationwide advancements in mental and neurological health and dialogue regarding liability issues related to innovation in research and practice.

PANEL DISCUSSION

MODERATED BY JENNIFER BUSS

Jennifer Buss
First, I want to thank everyone for being so patient with me, as my last meeting ran a little long. I do want to open the floor to the conversation in the room, to ask questions to our speakers.

James Giordano
Really good presentations from all of you, as always. Thanks for being here. Work we did here a few years ago demonstrates that a lot of these disorders – certainly brain trauma as well

as stroke and a lot of neurodegenerative disorders and neuropsychiatric pathologies – exist along a spectrum; in other words, they are spectrum disorders. So the only way you can really approach that is to use Big Data – to enable a fully individualized depiction of contributory and expressive factors, with particular attention paid to attribute-treatment interactions, by asking where along the spectrum an individual falls and how this is relevant to their care. This can be a problem for the FDA, specifically when you speak about how and when to use certain neurotechnologies, for example deep brain stimulation. As you know, the second and soon to be third generation of these devices are available and developing a precision approach to their use – and what their use demonstrates – will be crucial and highly reliant on massive, multimodal data. This is important to the FDA because much of the work being done with these devices is as IIR, Investigator-Initiated Research. The issue is, at what point, and to what extent do you have enough and enough types of data to either move into or obviate a clinical trial, and how would you make these data broadly available, sustain provenance, and deal with liability issues?

So, the specific questions I have for you are: In the main, if we could untie your hands – in other words, if t we asked not what we can do for better regulation, but rather what should regulation do to allow viable translation. Specifically, what kind of policy would you like to see enacted, to allow safety and efficacy that translates to effectiveness in practice?

Mahesh Shenai
I think the overriding thing is probably transparency in the conversation between the FDA and the investigators. Often if you look at the way some of the studies are done and the results, a lot of the idiosyncrasies can be discussed, and usually logic can prevail. But many times, we are on different wavelengths. If we had the ability to enhance that conversation, rather than have a very competitive standing point and a very linear process, I think that would improve it.

James Giordano
Are you comfortable with the current state of the IIR device exemptions and regulations? In terms of what you're able to do in your practice?

Mahesh Shenai
With deep brain stimulation, basically there are three FDA approved indications: Parkinson's, essential tremor, and dystonia. But we recognize there are a wide variety of other indications that we could use DBS to treat. At which point are you doing something that is scientifically motivated, as opposed to trying something out of the blue? The device exemptions are fine internally – within our institutions. We have multiple processes, but there's a lot of variation from institution to institution in terms of how you move through that process to try something that's off-label. So, I would say more guidance in terms of how you can use those device exemptions would be helpful. I think a more community-based or evidence-based approach would be best so that there is less variability from institution to institution and more governance-based organization.

Stacy Suskauer
Regarding moving from an investigation to clinically available treatments, my response comes less from the research perspective and more from my clinical experience. Within Pediatrics, currently a lot of the medications we use are not actually studied for use in children. I mention this to suggest that one factor to consider is how to make sure that research specific to pediatrics is encouraged. And there is another issue, not with deep brain stimulation but with transcranial magnetic stimulation: it looks very promising in a number of studies, and patients are clamoring for it, but it is not clinically available. I think identifying how to cross that gap from research to clinic sooner is an important piece, although I'm missing expertise to talk about the processes along that way. And when a treatment is adopted as approved clinical care by insurance companies it's not necessarily a universal decision, so another issue to address is how to improve universal access to new treatments?

Jessica Eisner
And also the biomarkers that you mentioned – getting those to be covered over researched.

Mike Swetnam
I wonder if we're asking the FDA, and in turn the medical profession, things that we shouldn't be asking them to make decisions on. For instance, the accuracy of thermometers. Of course, doctors will look at it through the lens of medical science, which is often empirical and based on a limited number of trials, whereas physicists look at a thermometer and say, this is something we can know very precisely. And we can set standards asserting that if it doesn't measure within one tenth of a degree 99% of the time then we don't consider it a viable instrument and therefore throw it away, and a NIST standard instead of an FDA ruling might have been more appropriate. Maybe we're doing the same thing when we ask questions about whether the computing devices in a hospital should be talking to each other, the effect of one computing device on another is something that software engineers and electrical engineers would probably know the efficacy of more than doctors. The point being, are we asking the wrong people to make some of these decisions?

Jessica Eisner
Actually, on the thermometer working group, the lead was a physicist who works for the FDA and he did have guidance for how each type of thermometers should perform. The point of that was because they were classified as Class 2 devices and because they had historically not been looked at very closely, there was no need to submit them to the FDA for review. There have been a lot of advances in the ear and across the forehead thermometers that haven't really been looked at very closely.

Mike Swetnam
I think that speaks to my point.

Jessica Eisner
There are physicists there, and in July of last year they indicated now you do have to submit all of this to us.

Mike Swetnam
But why does the FDA do it? The FDA doesn't know anything about thermometers. NIST over the last 100 years has been very actively doing things like precisely calibrating and qualifying instruments for industry, and to a good degree of prediction. Why do we ask the FDA to approach something that the NIST already does to a high degree of precision?

James Giordano
The FDA tracks these things, and says what you can disseminate. But to some extent, there is a notable disconnect between the scientific standards that allow a judgment about effectiveness in practice, and what you can say with regard to marketing. The two agencies don't necessarily talk to each other. Can you speak to that?

Jessica Eisner
I can't speak to it from a thermometer standpoint. But we do have a standards committee, which does work with external agencies, and they set the standards for something that doesn't necessarily have any more medical input, like a thermometer. But we hold the database of all of the manufacturers and how they can advertise. Are we speaking enough? Apparently not.

Mike Swetnam
I would say it's an inappropriate role for the FDA to measure and approve thermometers. We created NIST for that very reason and NIST has established very rigid standards of measurement accuracy for thermometers. The standards of NIST are set by physicists who study and understand thermal dynamics, and we should be asking physicists whether it is an effective measurement tool, not doctors who really don't know anything about the physics of thermodynamics. You should be asking the FDA whether 105 or 101 degrees is significant. You shouldn't be asking the FDA whether the instrument is accurate enough, because instrument accuracy is the purview of NIST, not the FDA.

Jessica Eisner
Well, there are about two doctors for every 50 engineers, software engineers, mechanical engineers, physicists, in the center for devices, so it is truly an area that is not doctor-driven.

Mike Swetnam
Then we should disband NIST and just go to FDA for standards?

Jessica Eisner
No, standards are developed by NIST and the physicists look at them when they are reviewing applications. So the FDA doesn't do any of this testing, unless there is a problem and then they

usually get NIST or whoever they need involved. It usually is the bonus of the person wanting to market the thermometer to provide all the data, and they should also say what guidelines they use. It is not that the FDA that is doing this testing. People who understand the physics are running it.

Mike Swetnam
So what's the FDA doing? Is it saying this is a good thermometer or a bad thermometer?

Jessica Eisner
Jessica Eisner. No, FDA wasn't doing anything on thermometers except for having them all registered and having all the manufacturers registered. Now they are saying they need to submit the data showing the accuracy of their technology.

Mike Swetnam
To the FDA?

Jessica Eisner
Yes.

Mike Swetnam
Why? What's the FDA going to do with that?

Jessica Eisner
They will take the standards of the organizations, standards and physicists and engineers, and line them up to ensure sure they are meeting them.

Mike Swetnam
Well, then the FDA is going to say these ones meet it and these ones don't. The FDA is making a quality judgment on whether somebody's manufactured product meets the NIST standard. NIST sets the standard. Then the FDA says, all you people who are making thermometers, submit your data to the FDA so we can see if they meet the NIST standard.

Jessica Eisner
That's part of it, but there's also the commerce part of it.

Mike Swetnam
Now that's good government.

Jessica Eisner
I can't explain it. I think it's a really inefficient system.

Mike Swetnam
One of the roles of the Potomac Institute is if we can't explain government so it makes sense, we probably ought to be talking about changing it.

Mahesh Shenai
What you're describing is an inherent weakness of a very siloed process. There are different organizations that are looking at it from very different perspectives. A lot of these problems could be solved by just getting a representative from each of the different institutes, buying them beer and pizza, and talking about it for a couple hours, and maybe they'd come up with a solution.

Mike Swetnam
Oh, I did all that. I was actually pushing this for a bigger purpose that led to this comment. The FDA is a regulatory body for the efficacy of medical things, to protect us from ourselves, protect us from industries, do our best to at least prevent great harm. So there's a valid, very defensible reason for an FDA. When we talk about neurotech – building brain simulations and you name it – I'm concerned that we don't have the knowledge and expertise to even understand what some of these devices are doing, not necessarily from a medical aspect but from a physical aspect, within 100 miles of the FDA.

Charles Mueller
I was going to ask a question of all of you, and I think you introduced my question very well. We've been talking about the ineffectiveness of our current models – the inability to plug in data that we're getting to obtain an understanding of the mind and the body, and a predictive outcome of how it is going to work, whether that is regulatory-wise or medicinal-wise. Our ultimate goal is that when we have data and when we have a new treatment – say, a new electrode we're going to put in – we can know it's going to work before we do it, because we have such a good model. That's where we should be heading. The question is, how do we get there? Is it that we need more data or better quality data? Or is it stepping back a little bit, looking at the existing data, and trying to patch together a better model, a better theory to help explain all the different nuances of TBI or Parkinson's? As we're moving forward, we really need to think about that, and develop a strategy for how we want to get to that end state that I think we all agree on. Could you all speak to how we get there, or what we really need to wind up there?

Stacy Suskauer
I think it's a combination. There are plenty of data that currently exist but are not being harnessed right now in a way that helps us, plus there's additional data we're not collecting now, and we need do need gadgets, as well. I think ideally there is a grand structure, which allows new pieces to be layered in continually, and ideally the big data machine is set up to account for that.

Mahesh Shenai
I think that models come from somewhere – all models at a basic level come from data. A model is only going to be as good as the data that leads to it. By having models, I think that's necessarily included in initial due diligence, but I think at the end of the day, models may not

predict the unexpected because if it was expected, then by virtue of this expectation it would be included in the model. Models can miss "black swan" types of phenomena that they are just not created to identify. They may get to the obvious of what's known, but there are things that you just aren't going to predict until you put them through practice a number of times. I think the real issue is having some sort of structure that identifies early things that are happening that are off the trend and being able to nimbly react to that.

Jennifer Buss
I want to extend that a little bit further, because really what we are looking at is getting into personalized care. So we need those models. How does the society in general with the demographic test every individual? It's really not a matter of the thermometer being off by one or two degrees. For this person it's the same thermometer the entire time, so it doesn't matter that it's off by one or two degrees. It's really nice to have it exact, but it's always comparative. So yes, I want to know if it's a 100 degree or 105 degree temperature, but for that person. In theory, we should have significantly more data surrounding that person, so we're not relying just on temperature to know, say, if they're going to go into shock. We certainly don't have the information today to do that personalized care. We're never going to have enough information. We always want more to make the best decision, but we need to be looking toward an individual and their normal, rather than the general society. I think this is really more of a statement than a question. We really are getting there technologically, but the analysis that we are going to do hasn't been understood.

Participant
People have observed that Parkinson's patients, when they are sleeping, are not tremoring anymore. Do we understand this phenomenon?

Mahesh Shenai
You know, I'm sure there is a lot of research into that – it's a well-known phenomenon. If you tell patients to concentrate in the clinic, they can suppress their tremor. The way we get the tremors out so we can examine them is to have the patient start counting backwards from 100 by seven – we start to distract them, and the tremors come out. A lot of it has to do with the overall connectivities of our brain – it's a very complex layered organ that has multiple pathways. I'm sure there is research on that, but I can't speak specifically to it. It is a generally well-known phenomenon.

Participant
There was a recent finding about a person who had Parkinson's, but he could ride a bicycle and they had him do that for several weeks, and they found him shaking less afterwards. How do you compare a bicycle to a recent treatment?

Mahesh Shenai
Yes, if you look historically – I remember an anecdote from the late 1800s, when horseback riding was actually thought to be a cure for Parkinson's. The feeling was that somehow being

on top of this horse was contributing to correcting the tremor. I think every generation has had something like this – for example, a device that actually shakes the Parkinson's patient to make the tremors go away. I think right now there's actually a device out there – I don't know if it's FDA approved or not – that is being marketed to that effect.

Beth Russell
So this is a question about a scenario I've been thinking about for a long time that I want to pose to you. Dr. Eisner, and you all, have landed on it a little bit – this concept of what are the driving factors between some of our limitations. The biggest factor that keeps playing out at different stages of this personalized medicine or medical revolution issue is liability. Whether FDA gives their approval or disapproval of something is liability, whether a doctor will be liable if he's not covered by an insurance plan, whether a hospital makes decisions based upon their liability. Do we need to rethink liability in a medical and research context?

Jessica Eisner
As far as I know in medicine that's been the mantra for over twenty years. We need to rethink liability. Not just in terms of medical care but in terms of medical research.

Beth Russell
What would that look like to you? What kind of environment or system do you think would work?

Jessica Eisner
Well, one can only fantasize. A lot of doctors practice defensive medicine, although not necessarily defensive research – for example, not using biomarkers or not using treatments, even though you might want to, because it's not covered by insurance and your organization or you are going to take the hit financially or legally. As for a vision, I'm going to need a couple of minutes.

Mahesh Shenai
There's an overall fear that drives how multiple domains and stakeholders react when it comes time for innovation. I'll bring up health IT for example. There's a lot of liability involved there. I think what drives it is that there is a huge potential for IT to really drive healthcare, but each one of us practitioners has different ways we want to use emerging technologies to help patients. On the IT side and the administrative side there will be people saying, "we are overwhelmed by all the very customized requests that we're getting to use information in that way," so the easy answer to that is no, we're not going to allow it. There's this culture of "no" that is really preventing us from moving ahead. I think if we look at it on a case by case basis – if I was just able to sit down with an administrator for five minutes and say this is what I want to do, it's very easy, there's really no sinister thing happening here. On that level I think they would say that's not a problem. But it's a problem of scale, of handling each and every little individual variation. Does it come down to liability? Yes, it does come down to different types of liability that we may think of as physicians, such as insurance – but system and institutional negligence and liability are also certainly in play.

Stacy Suskauer
I think the conceptualization of cost as well as liability is really important. I think with a lot of individual cases, we are not sure how something is going to work for a particular patient or child. There are certain research processes for taking on high-risk scenarios. I think the idea of cost comes from so many levels and I like the idea of considering how we reward individuals and how we reward larger systems. Everything shouldn't be about how we streamline cost but how we balance that with high financial-risk projects that could be a huge leap in innovation.

Beth Russell
I am sure at some point in all of your lives, you experience some type of malpractice. We have all sorts of insurances from driving insurance to life insurance, but we don't have research insurance. We don't say that you can ensure a research project and if someone gets hurt in the context of this research then they would get money back.

Stacy Suskauer
When I hear research insurance, the first thing I think of as a researcher is about the funding. I think there are avenues to encourage participation in high risk studies, particularly for patients whose have limited other options for successful treatment.

Beth Russell
In some sense, it could be like venture capitalism. The insurance is a gamble but the people will get some of the profits if it turns out to be successful. These things are interesting for me to think about.

Mahesh Shenai
I'm not an expert on insurance but I would assume that in coming up with their policies, insurance companies do cost calculations of research to some extent. For example, I think a policy for Johns Hopkins would be different and higher risk than that of a lower level project of some sort. An interesting point is not so much insurance as we know of insurance, but how do you get to the point where innovators are able to grasp or reveal with you the downside of innovation. The big concept when talking about physicians who have a day job are that they got into medicine because it is a very stable field.

Mike Swetnam
I think the key point is that we need to find a stable way that doesn't stifle innovation while compensating for the downside of novel problems with the insurance side of it. Insurance industries incentivize those who buy insurance to not pay credit. The riskier you are, the more your insurance costs – so if you're not careful, then what you are doing is stifling innovation. I, for one, don't think that we have read enough into innovation and risk taking in our system to incentivize that and that insurance might have exactly the opposite of that. The traditional government policies for these types of risk problems have been done in government and in

application with industry. This is what we did with places in California when we employed them to a nuclear laboratory for instances like this. I suspect if we really want innovation on the research end of this then we are going to have to identify those who are doing it and say that you can't be sued under certain parameters or you cant be punished for failing experiments. There is a culture of risk aversion whether it is insured or not and we need to give people within bounds a pass.

Jessica Eisner
The other aspect of not punishing people for research that doesn't work out is how it impacts the culture.

Jennifer Buss
We need to change the culture.

Jessica Eisner
The good studies and positive results need to get published and I have long thought that there should be a journal of the negative results because that is a system that you change. If you have done a very well-designed and controlled study but it turned out negative, that still contributes just as much as the positive studies in reference to knowledge.

Jennifer Buss
If we don't start agitating for risk-taking then are we ever going to revolutionize? Are we ever going to make that leap or are we just going to continue to slowly progress?

Mahesh Shenai
I would like to back that question up because the risk taking that we are talking about is after the point that we are talking clinically. We are talking about using it on patients and that is kind of more than halfway down the stream. As a physician, if I have a great idea, there is an activation energy that needs to get over to start implementing to get funding or do I do it in my garage? There is no kind of organized pipeline for innovation. Nobody wants to pay for that initial risk and take his or her Saturdays and Sundays and build this amazing device in the basement. I am already involved with clinical care and I am not going to get over that activation energy to do that.

Mike Swetnam
You are making a good point that has been a topic of discussion here within the Potomac Institute group called CReST. If you look across the spectrum of funding for real hard science research, you start to run out of gas when it comes to innovation for real hard science. When you get to the point where it seems like a pretty good idea but it's far enough from the mainstream that a sizeable percentage of the funders that exist today would score it so that it is a little far outside. The real hard innovation doesn't have easy funding sources and it almost gets to the point where you could say that we need a federal fund or agency administered by someone. This agency could come out and say that a group of people thinks you are not proposing something like a professional motion machine or something really impossible, you will only be reconsidered for funding if you have been turned down by DARPA and NIH.

Participant
I think part of the challenge there is that the mechanisms and business processes that we have to fund innovation don't work for anything that is higher risk.

Mike Swetnam
Current processes might just be failing.

Stacy Suskauer
I think there is also something to be said that these processes are in place, and there is funding, and really there are great ideas proposed by non-researchers, but most people can't just call their local researcher and say, "I think you should do this..." It would be important to have a mechanism in place for moving some projects through the pipeline in an expedited fashion. The pediatric oncology model is that for some cancers, most children receiving care are involved in a study. This allows information to be gained at a more rapid pace, which translates to ongoing refinement in care.

Paul Syers
This may be a shift in the topic slightly but you mentioned in your statement that we need better imaging of what a healthy brain looks like and different methods when you having a longer case. How are things going towards efforts in gathering more baseline data and what a healthy brain looks like? Is there any shift in the medical community that does research or a program that gathers data? What I really like about the 23andme company is that they gather a bunch of genetic data that they use for healthy functional models, then you don't need to randomize the clinical trials because you already have the baseline data.

Jessica Eisner
The Allen Institute for Brain Science is doing a lot of fundamental work investigating normal brains and partnering with the NIH and other research institutes, as well. From there, they are exploring how other people are studying the anatomical function down to genetic expression in the brain to try and get to there.

Paul Syers
Is that helping?

Jessica Eisner
I think it's a long way away because they ultimately want to understand not only how gene expressions and syntax function, but also how we perceive and make decisions based on this kind of data. There is that kind of magic area in there that no one understands right now, but that is their goal, so I think it is happening.

Mike Swetnam
I really like your thoughts on this related to your talk, as well as at kind of a superficial level. I'm far more interested in very Big Data, a precise model on me. Not a general human in the population,

but me because that will tell me more. The simple analogy is that Ford builds Mustangs and they build all these Mustangs to be mechanically about the same thing. Fifty thousand miles into the Mustang, they all have their own personality, different makings and tastes even though they were all built to be exactly the same. The analogy of the mustang is outrageously simple compared to the human genome. I would think that my particular model and treatment would be very unique to me and now I have a problem that I propose to you. What do I do about the fact that the more I understand my model and genome that treatment becomes unique to me is outside the realm of both what is considered to be accepted protocol? My doctor or health care provider is almost always treating me outside the norm of what they are treating the majority of people. It almost caused my doctor to be a professional in their profession in dealing with me because my genome requires the use of drugs, etc. How do we deal with that?

Mahesh Shenai
It is a very interesting theoretical discussion because we are here talking about two important things that are high priority from our healthcare system. On one end we are talking about personalization and the other part is standardization. On the personalization side, we want to come up with a very specific cure or therapy for that one patient. If you switch gears to Big Data, which has billions of units of information, how do we come up with insights and knowledge from all these types of Big Data? I think that we all have struggled with patients and we investigate if this problem has occurred before. We look at different studies and try to see how our patient fits into each study. Are they in the same age group? Does that research apply to that one person? I think it's two extremes of thought, and both are valid. We have to have standardization and personalization of certain things. I think that's where you can have a very highly scalable system that can at some point detect which part of that spectrum we need. If there is an incident where someone has a brain leak from a motor accident injury, then there isn't too much personalization in that. The solution would be to take the patient to the operating room and take the blood clot out. When you talk about Parkinson's or other conditions similar to that, there may be various genotypes in which you would have to address. I think that is where human intelligence comes in and decides which side of the spectrum we need to use.

Jennifer Buss
I want to interrupt for just a second because I'd like to comment on the standardization of the blood clot, but to me there are a ton of personalized methods from the anesthesia to the way I recover from the operation. There are thousands of factors that are personalized to me and sometimes only the patient knows about them.

Mahesh Shenai
That's why the spectrum works in this case. When we are doing a brain surgery, everyone's brain is different. There are different veins and the ways that the brain looks differs, because everyone is truly different. It's very theoretical in a sense that everyone is different and the same as well.

Stacy Suskauer
I think a part of it is that we need to get to the point where between the two pathways of genotypes, it would be ideal that as we have that knowledge, training will change.

Charles Mueller
Let's say we look at the next 50 years – here is the standardization of my particular makeup so I can start using personalized treatment as well as developing personalization standardization for our neurons and maybe that's the world we should be striving for.

Stacy Suskauer
To some extent those exist, I think when we talk about a disease like breast cancer, you get put on a different pathway based on that type of information.

Jennifer Buss
I think when you consider the Big Data world, there is just a small little image that can change a lot from day to day. An example would be if a group of people drive past a nuclear plant and have a reaction to it. The next day, everybody who drove past that one spot is now sectioned into another group. We don't even have the capability to see any differences right now, but it could really make a difference when five days later all these people have the same reaction. Currently, there is no way of knowing that all of these people traveled the same path based on the information that a doctor would obtain.

Jessica Eisner
On the spectrum of standardization to personalization, I'd like to make a couple of comments on leaning towards the standardization. If you look at medicine in the last 100 years, we have been more diseased focused – that is sort of western medicine. We haven't gone back to fundamental physiology for things that we think we understand. An example would be the brain because we know we don't understand the brain. Even things like the liver – out of 1,000 biochemical functions, we can only measure a handful, and then, we are not measuring the function, but measuring the damage. We are not understanding everything that this critical organ does and having no standardized tests for its function, I think there is a good argument for bringing all the new technology to the forefront of creating a better standardization of a healthy human liver.

Mike Swetnam
We use the word standardization, but while fighting disease and looking for different applications, it would really be nice to use all this data to have a deeper understanding of the fundamental principles of the organism. If we have some fundamental theories of biology, I think we'd be a lot further than we are today. Personally, if we miss that big opportunity of data to understand our universe better then we are missing a great opportunity. The explosion of data should give us a deeper understanding of fundamental organisms and complex biochemistry.

CLOSING REMARKS

JENNIFER BUSS

We have reached our time limit but I want to thank all of you for coming. One of the things that didn't come up today was what the Potomac Institute really does to help matters like this. We bring together industry to hear the perspectives of former government employees so as to, at very least, tell them what is going on, and attempt to impact policy with recommendations. Today, we started with very basic research, clinicals, technology development, and how technology is reintegrated into industry, as well. To conclude, I just want to mention the importance of data that relates to myself and then from person to person. We need complete information on everybody to see the collective, but you also want to examine specific individual data instead of removing it from the equation. I understand the privacy concerns associated with specific data, but at a certain point you need to collect it. It is a collection problem – moreover, it is a data analytics problem, so we need to start building models. I think we had a good conversation today, the Center for Neurotechnologies is focused on recent neuro related topics and through our seminars and discussions, we recognize that it is a big issue. We want to thank you all for your time.

GENERAL AL GRAY

Chairman of the Board of Regents, Member of the Board of Directors, and Senior Fellow, Potomac Institute for Policy Studies

In 1991, Al Gray retired after 41 years of service to the United States Marine Corps. From 1987-1991, General Gray served as a member of the Joint Chiefs of Staff, was the 29th Commandant of the Marine Corps, and was advisor to both Presidents Reagan and George H. W. Bush. As Commandant, he instituted and published a Warfighting Philosophy for Marines based on the Maneuver Warfare Thought Process. General Gray developed and implemented a new long-range strategic planning process for the Marine Corps, established the Marine Corps University, and implemented other longstanding changes, such as ensuring that every Marine is a rifleman first and that the Marine Corps was Special Operations Capable. General Gray holds a B.S. from the University of the State of New York. He also attended Lafayette College, the Marine Corps Command and Staff College and the Army War College. General Gray is the recipient of two honorary Doctor of Law degrees, one from Lafayette College and the other from Monmouth University, and was awarded a Doctor of Military Science from Norwich University. He was the first awardee of an Honorary Doctorate of Strategic Intelligence degree from the Defense Intelligence College (now the Joint Military Intelligence College), and also was awarded an Honorary Doctorate for Leadership from the Franklin University, and an Honorary Doctorate from the American Public University System.

JENNIFER BUSS, PhD

Vice President, Science and Technology Policy and Director, Center for Neurotechnology Studies, Potomac Institute for Policy Studies

Dr. Jennifer Buss is the Vice President of Science and Technology Policy and the Director of the Center for Neurotechnology Studies at the Potomac Institute for Policy Studies. We develop meaningful science and technology policy options through discussions and forums and ensure their implementation at the intersection of business and government. She manages a variety of OSD programs including an outreach effort for the Department of Defense to the start-up community across the country to find innovative technologies to meet the challenges faced by the Services and Government agencies. She performs science and technology trends analysis and recommends policy solutions to some of the countries most pervasive problems. The Center for Neurotechnology Studies (CNS) is dedicated to ascribing meaningful policy solutions to one of the most influential science and technologies of our time. Dr. Buss earned a doctorate in biochemistry from the University of Maryland Department of Chemistry and Biochemistry. Dr. Buss received her BS in biochemistry with a minor in mathematics from the University of Delaware.

STACY SUSKAUER, MD

Co-Director, Center for Brain Injury Recovery and Director, Brain Injury Clinical Research Center, Kennedy Krieger Institute

Dr. Stacy J. Suskauer is a research scientist and the codirector of the Center for Brain Injury Recovery at the Kennedy Krieger Institute, as well as an associate professor of physical medicine and rehabilitation at the Johns Hopkins University School of Medicine. She leads several projects at the institute with the primary focus of understanding and optimizing outcomes after childhood brain injury. These efforts include investigating the use of neuroimaging and neurobehavioral assessments to improve understanding of brain-behavior relationships after traumatic brain injury, identifying the relationship between early physiological and functional variables and longterm outcome after brain injury, and optimizing evaluation and treatment of children with disorders of consciousness after brain injury. She is also interested in evaluating functional outcomes in individuals with SturgeWeber Syndrome and caring for children with limb deficiencies. Dr. Suskauer completed her undergraduate and medical education at Duke University. She completed a combined residency program in pediatrics and physical medicine and rehab ilitation at Cincinnati Children's Hospital Medical Center and the University of Cincinnati. She moved to Kennedy Krieger and Johns Hopkins University for a research fellowship in pediatric rehabilitation, and subsequently joined the faculty of these institutions in 2007.

MAHESH B. SHENAI, MD, MSE, MBA

Medical Director, Functional and Restorative Neurosurgery, Inova Neuroscience and Spine Institute

Dr. Mahesh B. Shenai is a neurosurgeon and the Director of Functional and Restorative Neurosurgery at the Inova Neuroscience and Spine Institute. He specializes in the surgical treatment of movement disorders such as Parkinson's disease, with expertise in deep brain stimulation (DBS) therapy. Dr. Shenai has a special interest in bringing new surgical technologies to Inova, and has been on the forefront of intraoperative imaging and computeraided surgical navigation for complex spine instrumentation, allowing for maximum precision and accuracy during spinal surgery. More recently, Dr. Shenai performed an "asleep" DBS implantation directly in an MRI scanner – the first procedure of its kind in the DMV area. Dr. Shenai completed his undergraduate and graduate degrees in biomedical engineering at Johns Hopkins University. After graduating from the University of Michigan Medical School, where he was awarded a Howard Hughes fellowship, he completed his residency and fellowship at the University of Alabama at Birmingham (UAB). Before arriving at Inova in 2013, Dr. Shenai served as a clinical instructor in neurosurgery at UAB, where he also directed the charity care clinic.

JESSICA EISNER, MD

Senior Fellow, Potomac Institute for Policy Studies and Former Senior Medical Officer, FDA

Dr. Jessica Eisner is a Senior Fellow at the Potomac Institute for Policy Studies, and has over twenty years of experience as a physician, global health educator, leader, medical director, and advisor in industry and government. Her primary career focus has been in drug development and global health, but she has scientific facility in a variety of fields, such as water resources, ocean health, education, and chemical and biological defense. As a Senior Medical Officer at the FDA in both CDER and CDRH, she completed medical review of over one hundred INDs, 510(k) s and "de novo" applications, as well as NDAs, protocols, clinical trial design, adverse event and periodic reporting submissions for a variety of drugs, biologics, and medical devices. While in CDRH, Dr. Eisner was appointed Medical Liaison to CDER to the Office of Combination Products for InterCenter Consults for DeviceDrugs and DeviceBiologics. In addition, she represented the CDRH General Hospital Device Branch as policy assistant for various crossCenter projects and issues. Dr. Eisner has served as Senior Science Advisor at the US Department of State, functioning as diplomatic liaison between UNESCO Paris and the U.S. Government for all national and international UNESCO science and science policy activities. She also served as Civilian Deputy Director for the Military Infectious Disease Research Program, a $400 million triservice R&D effort to diagnose, prevent, and treat malaria, dengue, bacterial diarrhea, wound infections, and HIV/AIDS. She was awarded the US Army Achievement Medal for Civilian Service during her tenure. Dr. Eisner has been on the Board of Trustees for a toprated US HMO insurance company and currently sits on the American Association for the Advancement of Science (AAAS) Fellowships Advisory Committee; she is also a member of the U.S. Army Medical Materiel and Research Command Institutional Review Board. After graduating from Cornell College and completing a tour in the Peace Corps, Dr. Eisner received her M.D. from the University of California at San Diego; she completed her medical residency at the University of Washington.

KATHRYN SCHILLER-WURSTER

Director, Center for Revolutionary Scientific Thought (CReST), Potomac Institute for Policy Studies

Kathryn Schiller Wurster is the Director for the Center for Revolutionary Scientific Thought (CReST) at the Potomac Institute for Policy Studies. CReST serves as the Institute's internal research and development and futures group, using innovative techniques to anticipate the policy impacts of emerging technologies. Ms. Schiller Wurster is currently leading a study for IARPA to develop an assessment methodology for forecasting the potential consequences of technology development. She also supports the Defense Microelectronics Activity on strategic planning efforts, supply chain risk management and trust issues for microelectronics parts. Her past research projects have included work for DARPA, DDR&E, Air Force, Congress, and other agencies. Symposia and events she has managed include: "Global Climate Change and National Security: The Science and the Impact," "Developing Ethics Guidelines for Research and Use of Neurotechnologies," "Every Crisis is a Human Crisis: Disaster Preparedness," and "Glaucoma Screening and Treatment: Driving Towards a Unified Federal and Private Sector Policy Approach." Ms. Schiller Wurster helped launch the Center for Neurotechnology Studies (CNS) and participated in drafting the National Neurotechnology Initiative legislation, which contributed to the development of the President's BRAIN Initiative. Ms. Schiller Wurster attended the University of Virginia as an Echols Scholar and graduated in 2002 with a Bachelor of Arts in Political and Social Thought. She joined the Potomac Institute in May 2005.

JOE BECHTEL

Research Assistant, Potomac Institute for Policy Studies

Joe Bechtel is a Research Assistant at the Potomac Institute for Policy Studies in the CEO's Office. Joe Bechtel currently provides research and analytic support to guide discovery of innovative, non-traditional solutions and develop technology assessments for the Rapid Reaction Technology Office (RRTO) in its mission to enable new, affordable capabilities. Joe organizes events, conferences, and discussions for RRTO at the Institute and at other venues, by interfacing and coordinating with government officials, venture capitalists, commercial leaders and academics. He obtained a bachelor's degree in Sociology & Anthropology from Towson University with a focus on Criminal Justice. As an intern at the Potomac Institute in 2014, Joe studied terrorism and counterterrorism subjects as well as attended conferences in the DC and Virginia area. His final project as an intern was on terrorism policy procedures inside a law enforcement agency. In his free time, he volunteers for the Bowie Boys & Girls Club.

KIMBERLY SCHLESINGER

Intern, Potomac Institute for Policy Studies

Kimberly Schlesinger is a doctoral candidate in physics at the University of California, Santa Barbara, where she develops mathematical and computational models to understand the behavior of the human brain and other complex biological systems. As a Science and Technology Policy Intern at the Potomac Institute for Policy Studies, she investigated the impact of big data and rapidly developing technologies on the future of neuroscience and medicine, and identified key policy and research initiatives to overcome challenges and promote a data-driven revolution in our approach to neurological and psychiatric medicine.

FROM DATA TO KNOWLEDGE IN NEUROSCIENCE: BUILDING TOWARD INDIVIDUALIZED MEDICINE

The Potomac Institute for Policy Studies held the seminar "From Data to Knowledge in Neuroscience: Building Toward Individualized Medicine" on September 12th, 2016. The current wealth of data in neuroscience has the potential to lead to groundbreaking neuroscientific discoveries and revolutionize clinical treatments for mental health and neurological disorders. Combining neuroscience data with information in other data-rich fields, such as genomics, will make possible a new paradigm of healthcare, in which medical providers and patients can use multi-faceted information to guide diagnosis and treatment selection, while accounting for the effects of interacting biological, environmental, and lifestyle factors. This seminar highlighted the need to translate neuroscience data into medical knowledge and robust clinical treatments, by improving data sharing and analysis practices and aligning with current precision medicine initiatives. By bringing together a distinguished panel of scientists, medical practitioners, and health policy experts, participants explored the key challenges and opportunities involved in this goal, and discussed strategies and policy solutions for utilizing neuroscience data to improve the mental and neurological health of all Americans.

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The Potomac Institute for Policy Studies is an independent, 501(c)(3), not-for-profit public policy research institute. The Institute identifies and aggressively shepherds discussion on key science, technology, and national security issues facing our society. The Institute hosts academic centers to study related policy issues through research, discussions, and forums. From these discussions and forums, we develop meaningful policy options and ensure their implementation at the intersection of business and government. The Institute remains fiercely objective, owning no special allegiance to any single political party or private concern. With over nearly two decades of work on science and technology policy issues, the Potomac Institute has remained a leader in providing meaningful policy options for science and technology, national security, defense initiatives, and S&T forecasting.

Center for Neurotechnology Studies (CNS) provides neutral, in-depth analysis of matters at the intersection of neuroscience and technology –neurotechnology – and public policy. The Center anticipates ethical, legal, and social issues (ELSI) associated with emerging neurotechnology, and shepherds constructive discourse on these issues. The Center partners with the research community for discourse and consultation on ethically sound neurotechnology research and applications. CNS serves as authoritative counsel to government agencies pursuing neurotechnology by providing expertise in the sciences, law and social policy through discussion on the implications of neurotechnology in academic, administrative, entrepreneurial, regulatory, legislative and judicial enterprises.