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From the Chair



*Steven N. Kalkanis,
MD, FAANS
Chair, Section on Tumors*

Dear Tumor Section
Colleagues:

I'm very much
looking forward to
seeing all of you
in Boston at the
upcoming Congress
of Neurological
Surgeons' (CNS)
meeting. The Tumor
Section has assembled
a spectacular line-up
of practical courses,

seminars and special scientific program offerings, thanks to the incredible efforts of our program co-chairs, Drs. **Pamela Jones** and **Adam Robin**. Pamela and Adam, working closely with our section scientific program chair, **Jason Sheehan**, developed two special sessions for our Boston meeting: nonfunctioning pituitary adenoma (Monday afternoon) and a WHO Classification update based on new predictive and prognostic molecular markers in neuro-oncology (Tuesday afternoon). Please also check the meeting schedule for a myriad of other important CME offerings involving new technology and scientific advances for brain tumors, important guidelines updates led by **Jeff Olson** and **Manish Aghi**, as well as mentoring opportunities for young neurosurgeons.

I am delighted to announce that **Russ Lonser** has agreed to be the featured honored guest at the Tumor Section's Young Neurosurgeons Reception in Boston. Also, in what is a time-honored tradition for the Section, we look forward to celebrating the achievement of the winner of one of our most prestigious awards being given in 2017. A joint committee from the Tumor Section and the Society of Neuro-oncology (SNO) considered multiple candidates worthy of lifetime

achievement recognition in our specialty to honor the triple aims of clinical excellence, world class academic research and mentorship, as embodied by the late Ab Guha; the 2017 **Guha Award** will be given to former Tumor Section Chair **Fred Lang** for his many contributions to our field, and he will deliver his address at the upcoming CNS meeting in Boston.

This has also been a momentous summer for the Section. In May, **Costas Hadjipanayis** and I had the honor of testifying before the Food and Drug Administration Medical Imaging Drugs Advisory Committee in support of the use of 5-ALA as an imaging agent, to facilitate the real time detection and visualization of malignant tissue during glioma surgery. Costas served as the lead study investigator and has been working tirelessly for many years, along with **Walter Stummer** from Germany, to provide evidenced-based support for the use of 5-ALA in the U.S. In fact, many in the tumor section participated in training sessions and the national multi-institutional clinical trial now being led by **Isabelle Germano**, to study the efficacy and positive predictive value of 5-ALA. The FDA panel has great respect for neurosurgeons and brain tumor specialists in particular, and they clearly put forth a considerable effort in grappling with a complex subject in order to expand our surgical armamentarium in the ongoing fight against malignant brain tumors. In a rather unusual step, the advisory committee voted unanimously 11-0 in favor of this proposal to recommend 5-ALA approval with a broad indication for "glioma surgery" to the FDA. Official FDA endorsement occurred last month, and the Gliolan 5-ALA product is expected to be available for widespread commercial use

beginning in October 2017. Congratulations Costas, Isabelle and to all of you who participated in the 5-ALA journey over the last several years.

Thanks to the herculean efforts of Awards Chair **Isabelle Germano** and our Tumor Section EC awards team, we have distributed a record number of grants, fellowship and honors to young neurosurgeons ready to start their careers in neurosurgical oncology, including Brainlab, Journal of Neuro-oncology, ABTA, Preuss, Stryker Neuro, Integra, Synthes Skullbase and Columbia Softball Pediatric Brain Tumor awards – all of which will be given to the recipients in Boston at the CNS meeting. Please check out our webpage and the awards section of the newsletter for a listing of all the individual winners. I'm also pleased to announce that our three section-based NREF Honor Your Mentor funds offer additional great opportunities for the Section to impact the careers of young neurosurgeons. The Parsa Fund has already started to disperse fellowship awards and has a balance of \$694K; the newer Wilson (\$75K) and Rutka (\$15K) funds are also open for contributions. Finally, the Section has also partnered with Mr. Phil Yagoda and Ian's Friends Foundation, which is hosting a shark-tank like "whatIFF Symposium" to disperse grant awards for pediatric

brain tumor research in Atlanta this Fall.

Finally, please be on the lookout for important membership surveys which will help guide the course of our field through guidelines and best practice paradigm development; you will soon be receiving an important survey on your current practices in tumor radiosurgery, developed by **Ron Warnick, Orin Bloch, Isaac Yang, Jason Sheehan and Randy Jensen**.

For the latest details on Tumor Section activities and for information on becoming a member, please visit our website, www.tumorsection.org.

Sincerely,



Steven N. Kalkanis, MD, FAANS
Chair, Section on Tumors

AANS 2017 Meeting Highlights

Peter Fecci, MD, PhD, and Shawn Hervey-Jumper, MD

The 2017 AANS Annual Scientific Meeting was held in Los Angeles on April 22-26. The scientific program of the Tumor Section featured the following themes: (1) the impact of perioperative management on quality of life - Session II and (2) the changing landscape surrounding brain tumor immunotherapy - Session III. Monday's Scientific Session featured the annual Ronald L. Bittner lecture, delivered by Russell R. Lonser, MD, FAANS, followed by open abstract presentations and four award-winning abstracts.

Given recent evidence highlighting the importance of quality of life concerns as a driving force behind how patients make decisions about their care, Tuesday's Scientific Session II featured a team of internationally recognized speakers addressing this emerging topic. The session featured an overview of language, motor and neurocognitive functional assessment measures, discussion of the interaction between performance outcomes and health-related quality of life, an overview of novel imaging modalities to assess functional networks, a summary of quality of life endpoints in clinical trial design and examination of its potential socioeconomic value. Our list of speakers included Terri S. Armstrong, PhD, ANP-BC, FANN, FAANP, from NCI; Richard W. Byrne, MD, FAANS,

from Rush University; Edward F. Chang, MD, FAANS, from University of California, San Francisco; and Cameron Piron, MD, from Synaptive Medical.

Wednesday's Scientific Session III focused on the changing landscape surrounding immunotherapy for brain tumors. This session drew attention to evolving areas of interest with an eye toward the future of therapies and interfaces with neurosurgery and industry. These topics included "The Developing Field of Immunogenomics," "Emerging Advances in Immunotherapy," "Technological Interfaces: Neurosurgery and Immunotherapy," "The Industry Perspective: Opportunities in Brain Tumor Immunotherapy" and "Immunotherapeutic Challenges: Where are We Now and Where Do We Need to Be?" Wednesday's speakers included Gavin P. Dunn, MD, PhD, FAANS, from Washington University; Amy B. Heimberger, MD, FAANS, from MD Anderson Cancer Center; Eric C. Leuthardt, MD, FAANS, from Washington University; Peter Fecci, MD, PhD, from Duke University (delivering a talk for Tom Davis of Celldex Therapeutics); and John H. Sampson, MD, PhD, FAANS, from Duke University.

Congress of Neurological Surgeons 2017 Meeting Highlights

Pamela Jones, MD MPH and Adam Robin, MD

The 2017 CNS Annual Meeting will be held in Boston on October 7-11 and is slated to be a truly transformative event. Themed “Transformation & Celebration,” the meeting will feature concepts that challenge traditional neurosurgical paradigms, presented and reviewed by luminaries in our field.

As for the tumor programming, the AANS/CNS Section on Tumors has established the first comprehensive guidelines for the management of non-functioning pituitary adenomas, which evaluated literature spanning over five decades and was published last year in *NEUROSURGERY*. Brooke Swearingen, MD; Jason Sheehan, MD, PhD; and Edward Laws, MD, moderate our first Tumor Session on Monday, October 9 at 2:45 p.m., which focuses on these guidelines. Manish Aghi, MD, PhD; Ian Dunn, MD; and Gabriel Zada, MD, will help us break down the guidelines, the genetics of adenomas and modern techniques used in surgery for pituitary tumors, respectively. Oral abstract presentations will follow beginning at 3:30 p.m.

Moving beyond a diagnostic system based largely on tissue histology, the 2016 World Health Organization Classification on Tumors of the Central Nervous System now includes hybridized

classifications that incorporate molecular data. These changes are summarized and the clinical implications are explained in our second tumor session on Tuesday, October 10 at 2:45 p.m. This session is moderated by Fred Barker, MD, and Steven Kalkanis, MD. Keith Ligon, Bob Carter, MD, PhD, and Fred Lang, MD, will help explain this new classification system, its prognostic and predictive value, and update us on current clinical trials and targeted therapies for glioma. Oral abstract presentations will again follow beginning at 3:30p.m.

The CNS 2017 program also features a variety of dinner seminars on the contemporary management of skull base tumors as well as interactive breakout sessions, including one on keyhole cranial access and another on brain metastasis. More than a dozen tumor-focused practical courses and luncheon seminars will also be offered, including the traditional full-day brain tumor update and a program spotlighting new clinical trials directed by Michael A. Vogelbaum, MD, PhD.

We hope you will join us to celebrate the many accomplishments of neurosurgeons from around the world and look forward to seeing you in Boston!

AANS 2018 Update

By Wajd Al-Holou MD, and Rohan Ramakrishna, MD

AANS 2018 is shaping up to be an exciting event! Our members have had many invaluable suggestions related to improving the educational content of both our scientific sessions and seminars. One of the suggestions was to incorporate spinal neuro-oncology into the program as this had not been a focus in recent years.

To that end, we devoted one of our scientific sessions to the spine and expect this to be educational and stimulating for both the general and subspecialty neurosurgeon. We will hear presentations given by experts in the field including Ziya Gokaslan, MD, FAANS; Mark Bilsky, MD, FAANS; Claudio Tatsui, MD, IFAANS; and Lawrence Rhines, MD. These discussions will cover up-to-date material for management of primary and metastatic spinal tumors. Additionally, the presentations will be followed by an interactive panel discussion simulating a Spinal Tumor Board with audience polling.

Our second scientific session relates to viral oncolytic therapy in glioma. The last decade has seen tremendous scientific progress made in designing viruses for oncolytic purposes with many phase 2/3 trials underway. To put this all in perspective, showcase its promise, describe its limitations and point the way forward we have assembled a stellar group. These luminaries include Robert Martuza, MD, FAANS; Nino Chiocca, MD, PhD; Frederick Lange, Jr, MD, FAANS; James Markert Jr., MD, FAANS; and our special guest, Juan Fueyo, MD. We expect this to be a tremendous scientific exchange.

See you in New Orleans!

Medical Neuro-Oncology Report

Susan M. Chang, MD

Updates from the American Society of Clinical Oncology Annual Meeting 2017

The theme of the 2017 annual American Society of Clinical Oncology (ASCO) meeting was “Making a difference in cancer care with you.” For central nervous system tumors, the highlights focused on advances in the genomic makeup of tumors and the impact on clinical care. In addition to providing more robust prognostic information, the molecular and genomic makeup can inform on avenues for developing new treatments. More importantly, the hope of identifying groups of patients who may benefit from a targeted approach to care brings us closer to the ideal of precision medicine: the right treatment for the right patient.

Several brain tumor types were highlighted ranging from the classification of medulloblastoma and ependymoma in children that have influenced clinical trial approaches with studies specifically targeting subgroups of patients. In addition, because specific mutations (H3 K27M) can be present in midline gliomas, not only can this be a diagnostic tool, but therapeutic strategies are now being developed against this mutation.

In the adult setting, innovative targeted therapeutic approaches in brain metastases using agents specific to an aberrant signaling pathway in lung cancer, melanoma and breast cancer were discussed. For primary brain tumors, strategies beyond standard chemotherapy for glioma and the challenges of specifically targeting abnormal pathways that are dysregulated in the tumor but not in normal tissue were reviewed. An example was the presentation by Hyman et al. reporting the results of the open labeled, histology independent VE-BASKET study of vemurafenib in patients with BRAF mutation positive glioma patients, demonstrating antitumor activity. In addition, the results of a clinical trial for meningioma using everolimus and octreotide (Graillon et al.) were reviewed.

The need for improved therapies beyond precision based approaches were also highlighted. Recognizing the role that the blood brain barrier plays in preventing high concentrations of agents to reach the tumor, there were several presentations that discussed early results of novel strategies. A phase I study of a radio-labelled monoclonal antibody ¹²⁴I-8H9 administered into brain stem glioma using convection enhanced delivery demonstrated that this was tolerated without worsening of neurological function and had the added advantage of being able to track the distribution of the antibody using PET imaging (Souweidane et al.). In addition, Lang et al. presented the results of a Phase I study of the oncolytic adenovirus DNX-2401 administered with and without interferon gamma.

Immunotherapy continues to be actively pursued in glioblastoma and this was the topic of several educational sessions, as well as original abstracts at the meeting. An example was the phase III trial of a personalized peptide vaccination (PPV) in human leukocyte antigen (HLA)-A24 positive recurrent glioblastoma presented by Mizukiko Terasaki, MD, on behalf of 20 Japanese hospitals. 88 HLA-A24-positive recurrent GBM patients were

randomly assigned 2:1 to receive PPV treatment (58 patients) or best supportive care (BSC; 30 patients). Four peptides chosen from 12 peptide candidates based on pre-vaccination IgG levels specific to each peptide or four corresponding placebos were injected subcutaneously once weekly for 12 times at the first course, followed by biweekly vaccinations until disease progression. The primary endpoint of OS was not met in this clinical trial with median overall survival of 8.4 months with PPV and 8 months with BSC. The investigators proposed several factors that may have accounted for this and performed a subgroup analysis showing possible benefit in younger patients with good performance status who had received PPV without specific SART2-derived peptides and further prospective studies in selected patients would need to be performed.

The ASCO annual meeting in San Francisco from November 16-29, 2017, will be another forum for investigators to present the results of both basic science and clinical research efforts in neuro-oncology. In addition, the joint conference with the Society for CNS Interstitial Delivery of Therapeutics (SCIDOT) led by Mike Vogelbaum, MD, PhD, FAANS, will be held November 15-16 and will address the multiple advances in interstitial delivery of therapeutics.

Tumor Education and Meetings

Committee members have already been busy developing the scientific program for the 2018 AANS Annual Meeting in New Orleans. Drs. Sheehan, Ramakrishna and Al-Wallou have been working with section leadership to develop scientific content. Please contact them with any suggestions or questions.

Regarding the 2017 CNS meeting, working with Drs. Pamela Jones, Adam Robin, and Tumor Section leadership, including Drs. Steven Kalkanis and Manish Aghi, a comprehensive and vibrant scientific program has been developed. The Tumor Section guidelines initiative will be featured in the general scientific session on Monday, October 9 from 7-8:30 a.m. Also, this year's program features a new clinical trials course directed by Dr. Michael Vogelbaum. The brain tumor update is divided into two parts and this practical course is offered on Sunday, October 8. Dr. Bruce also directs a half-day course on the management of challenging brain tumors on October 8.

A dinner seminar on contemporary management of skull base tumors will be offered and moderated by Dr. Morcos. General tumor section sessions will focus on the new WHO Classification for Gliomas and another on Guidelines and Contemporary Management of Nonfunctioning Pituitary Adenomas. More than a dozen tumor-focused practical courses and luncheon seminars will also be offered, including the full-day brain tumor update course. Further information will be available through the CNS Annual Meeting website.

Tumor Section Awards Update - Fall 2017

Isabelle M. Germano, MD, MBA, FAANS

The Tumor Section Awards Committee continues to actively develop the most robust award program for outstanding research of any of the AANS/CNS sections. At the AANS each year, the AANS/CNS Section on Tumors sponsors 12 awards and one named lectureship, the Ronald L. Bittner Lecture. At the CNS each year, we offer nine awards and one lectureship every other year, the Abhijit Guha Lecture. Additionally, we offer three awards at our Biennial Tumor Satellite Symposia. The 12 AANS 2017 award winners are shown below. Congratulations to each awardee!

The AANS/CNS Section on Tumors would like to thank the award sponsors for helping to encourage submission of the highest quality work in neuro-oncology. Most of the awards are limited to Tumor Section members, providing an additional incentive for membership. The section is looking forward to recognizing the 9 awardees at the 2017 CNS Annual Meeting, as summarized in the table below.

Isabelle M. Germano, MD, FAANS
Chair, AANS/CNS Tumor Section Awards



Congratulations to the AANS/CNS Joint Tumor Section AANS 2017 Awardees!

2017 American Association of Neurological Surgeons Awardees

Ronald L. Bittner Lecture

Russel R. Lonser, MD, FAANS, delivered the Ronald L. Bittner lecture at the 2017 AANS Annual Scientific Meeting on Monday, April 24, 2017, opening the Scientific Session on Tumors. He was introduced by Steven Kalkanis, MD, FAANS, AANS/CNS Section on Tumors Chair.



Dr. Russel R. Lonser receives the Bittner Lecture Award from Dr. Steven Kalkanis, AANS/CNS Tumor Section Chair, and Dr. Isabelle M. Germano, AANS/CNS Tumor Section Awards Chair.

In addition to the Ronald Bittner Award, the Bittner Family Foundation sponsors an annual Bittner Lectureship, awarded by the AANS at its annual meeting. The lectureship is awarded to an established investigator and is presented during the scientific program component of the meeting.

Selection of the Bittner Lecturer is made by the Senior Scientific Program Committee of each AANS Annual Scientific Meeting.

American Brain Tumor Association Young Investigator Award

Anthony Wang, MD, was the recipient of the American Brain Tumor Association Award at the 2017 AANS Annual Scientific Meeting for the work entitled: “Desmoplastic infantile ganglioglioma/astrocytoma” presented during Scientific Session I: Tumor on April 24, 2017.



Dr. Wang receives the ABTA Young Investigator Award from Dr. Germano

Sponsored by the American Brain Tumor Association (ABTA), the Young Investigator Award is given at the AANS and the CNS meetings to a young faculty member involved in neuro-oncology research who has demonstrated outstanding potential for future basic science research. The applicant must have been out of training for less than six years. A \$2,000 honorarium accompanies this award.

Ronald L. Bittner Award

Anath Vellimana, MD, was the recipient of the Ronald L. Bittner Award at the 2017 AANS Annual Scientific Meeting for the work entitled: “Multisector Whole-exome Sequencing of Glioblastoma Reveals Profound Intratumoral Diversity: Implications for Precision Medicine” presented during Scientific Session I: Tumor on April 24, 2017.



Dr. Vellimana receives the Ronald L. Bittner Award from Dr. Germano

This award is endowed by Mrs. E. Laurie Bittner in memory of her husband, Ronald L. Bittner. It is awarded to the best abstract paper submitted to the AANS meeting on brain tumor research by a resident or a junior faculty member. This award includes a \$1000 honorarium.

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BrainLab Neurosurgery Award

Sandro Krieg, MD, was the recipient of the BrainLab Neurosurgery Award at the 2017 AANS Annual Scientific Meeting for the work entitled: “Plasticity of motor representations in patients with brain lesions” presented during the Section on Tumors I on April 25, 2017.



Dr. Sandro Krieg receives the BrainLab Neurosurgery Award from Dr. Germano.

The Brainlab Neurosurgery Award is presented at the annual meetings of the AANS and CNS. This award is given to a neurosurgeon practicing in a nonacademic or international setting with the best abstract related to central nervous system tumors. Previous AANS/CNS Section on Tumors chairs Michael McDermott, MD, FAANS, and Ronald Warnick, MD, FAANS, were instrumental in securing this award, given through the generosity of Brainlab. The award carries an honorarium of \$1000.

Columbia Softball Charity Award

Eric Thompson, MD, FAANS, was the recipient of the Columbia Softball Charity Award at the 2017 AANS Annual Scientific Meeting for the work entitled: “Angiogenesis plays a critical role in Group 3 medulloblastoma pathogenesis” presented during the Section on Tumors I on April 25, 2017.



Dr. Eric Thompson receives the Columbia Softball Charity Award from Dr. Germano.

The Columbia Softball Charity Award is given to the best pediatric tumor abstract submitted by a resident or faculty member who is a member of the section on tumors at each AANS/CNS meeting. The section would like to acknowledge previous Section Chairs Jeff Bruce, MD, FAANS, Fred Barker, MD, FAANS, and Rich Anderson, MD, FAANS, for putting together the plan to use a portion of the proceeds from the annual tournament to support this award. The award carries an honorarium of \$1000.

Integra Foundation Award

Mark Youngblood, MD, was the recipient of the Integra Foundation Award at the 2017 AANS Annual Scientific Meeting for the presentation entitled: “Clinical and Molecular Features of Genomic Subgroups in Meningioma” presented during the Plenary Session III on April 26, 2017.



Dr. Mark Youngblood receives the Integra Foundation Award from Dr. Germano.

The Integra Foundation Award, sponsored by the Integra Foundation, is given at both the AANS and CNS meetings for the best research or clinical paper submitted investigating benign brain, spinal or peripheral nerve tumors. The award carries an honorarium of \$1000.

Leksell Radiosurgery Award

Jason Sheehan, MD, FAANS, was the recipient of the Leksell Radiosurgery Award at the 2017 AANS Annual Scientific Meeting for the presentation entitled: “Early versus Late Gamma Knife radiosurgery following transsphenoidal surgery for nonfunctioning pituitary macroadenomas: a matched multi-center cohort study” presented during the Section on Tumors I on April 25, 2017.



Dr. Jason Sheehan receives the Leksell Radiosurgery Award from Dr. Germano.

This award, presented at each AANS meeting since 2009, is for the best paper on stereotactic radiosurgery related to brain tumors and is given through the generosity of Elekta. The award includes a honorarium of \$2000.

National Brain Tumor Society Mahaley Clinical Research Award

Matthew Garrett, MD, was the recipient of the National Brain Tumor Society (NBTS) Mahaley Clinical Research Award at the 2017 AANS Annual Scientific Meeting for the presentation entitled: “Olig2 as a novel target for IDH1 mutant tumors” presented during the Plenary Session I on April 24, 2017.



Dr. Matthew Garrett was awarded the NBTS Mahaley Clinical Research Award from Dr. Germano.

The NBTS Mahaley Award is given at each of the AANS and CNS meetings to a neurosurgery resident, fellow or attending physician who submits the best clinical study in neuro-oncology. The award carries a \$1,000 honorarium.

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Preuss Award

Javier Figeroa, MD, was the recipient of the Preuss Award at the 2017 AANS Annual Scientific Meeting for the work entitled: “Detection of wtEGFR Amplification and EGFRvIII Mutation in CSF-Derived Extracellular Vesicles of High-Grade Glioma Patients” presented during the Scientific Session I: Tumor on April 24, 2017.

Sponsored by the Preuss Foundation, the Preuss Award is given at each of the AANS and CNS meetings to a young scientist investigating brain tumors, within 10 years of training, who has submitted the best basic science research paper. This award has a \$1,000 honorarium.



Dr. Javier Figeroa receives the Preuss Award from Dr. Germano.

The Brian D. Silber Award

R. Everson, MD, was the recipient of the Brian D. Silber Award at the 2017 AANS Annual Scientific Meeting for the work entitled: “Laser Thermoablation for Spinal Metastatic Disease provides Comparable Local Control, Reduced Morbidity and Shorter Delay to Systemic Therapy Compared to Open Surgery” presented during the Scientific Session II: Spine on April 24, 2017.

Established in 2015, this award is given to the best abstract related to vertebral column or spinal cord tumors at the AANS Annual Scientific Meeting. The section would like to thank the family of Brian D. Silber, who passed away in 1996 at the age of 28 from a malignant spinal cord tumor, for their generous support of this award. The award has a \$1,000 honorarium.

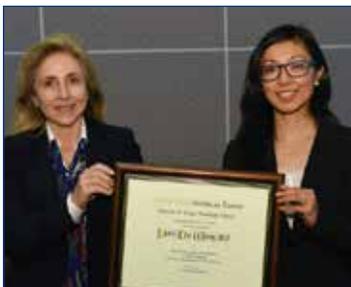


Dr. R. Everson is the recipient of the Brian D. Silber Award

The Springer Journal of Neuro-Oncology Award

Doris Wang, MD, was the recipient of the Springer Journal of Neuro-Oncology Award at the 2017 AANS Annual Scientific Meeting for the work entitled: “Seizure outcome after surgical resection of insular glioma” presented during the Scientific Session I: Tumor on April 24, 2017.

The Springer Journal of Neuro-Oncology Award is presented at both the annual AANS and CNS meetings to a highly-ranked abstract in either clinical or basic



Dr. Doris Wang receives the Springer JNO Award from Dr. Germano.

science as related to neuro-oncology. This award is sponsored by the generosity of Springer. This award carries a \$1,000 honorarium.

Stryker Neuro-Oncology Award

Arman Jahangiri, MD, was the recipient of the Stryker Neuro-Oncology Award at the 2017 AANS Annual Scientific Meeting for the presentation entitled: “Discovery of A Novel Integrin/Tyrosine Kinase Complex That Drives Brain Metastases” presented during the Scientific Session I: Tumor on April 24, 2017.

The Stryker Neuro-Oncology Award is given to a high-ranking brain tumor clinical or basic science abstract submitted by a resident or medical student. The award is presented at the CNS and AANS annual meetings and the senior author of the paper must be a member of the AANS/CNS Section on Tumors. The award is sponsored through the generosity of Stryker and has a \$1000 honorarium.



Dr. Arman Jahangiri receives the Stryker Neuro-Oncology Award from Dr. Germano.

Synthes Skull Base Award

John Lee, MD, was the recipient of the Synthes Skull Base Award at the 2017 AANS Annual Scientific Meeting for the presentation entitled: “Folate Receptor Overexpression Can Be Visualized in Real Time During Pituitary Adenoma Endoscopic Transsphenoidal Surgery” presented during the Section on Tumor II on April 26, 2017.

The Synthes Skull Base Award is given to an attending neurosurgeon, resident or fellow in the Tumor Section who submits the best abstract related to skull base surgery. This award is given at the annual meetings of the AANS and CNS. Franco DeMonte, MD, FAANS, chair of the Skull Base Committee, was largely responsible for obtaining this award through a generous contribution from the Synthes Corporation. The award includes a \$1,000 honorarium.



Dr. John Lee receives the Synthes Skull Base Award from Dr. Germano.

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Congratulations to the 2017 CNS Tumor Section Award Winners. Please join us for their presentations.

Award	Awardee	Talk Title	Date	Time	Session
American Brain Tumor Young Investigator Award	A.Mallela	Topical Vancomycin Reduces Surgical-site Infections After Craniotomy: A Prospective, Controlled Study	Monday, October 9	3:54-4:00	Section on Tumors
Brainlab Neurosurgery Award	A. Bunevicius	Prognostic Role of the Low Tri-Iodothyronine Syndrome in Brain Tumor Patients	Monday, October 9	3:42-3:48	Section on Tumors
Columbia Softball Charity Award	H. Zhang	Interaction Between MELK and EZH2 Regulates Medulloblastoma Cancer Stem-like Cells Proliferation	Tuesday, October 10	4:06-4:12	Section on Tumors
Integra Foundation Award	M. Agam	Complications Associated with Transsphenoidal Pituitary Surgery: Experience of 1,171 Consecutive Cases Treated at a Single Tertiary Care Pituitary Center	Monday, October 9	3:36-3:42	Section on Tumors
NBT Mahaley Clinical Award	T. Juratli	TERT Promoter Mutations in Progressive Treatment-resistant Meningiomas	Monday, October 9	3:30-3:36	Section on Tumors
Preuss Award	M. Garrett	Metabolic Characterization of IDH1 mutant and IDH Wildtype Gliomaspheres Uncovers Cell-type Specific Vulnerabilities	Tuesday, October 10	8:56-9:00	General Scientific Session III
The Springer J Neurooncol Award	R. Jenkins	Small Terminal Deletions/Duplications and Alternative Lengthening of Telomeres are Co-Occur in IDH Mutation Only Gliomas	Monday, October 9	4:00-4:05	Section on Tumors
Stryker Neuro-Oncology Award	S. Suppiah	Genomic Landscape of Radiation-Induced Meningiomas	Monday, October 9	3:48-3:54	Section on Tumors
Synthes Skull Base Award	F. Alkherayf	Reinventing the Wheel: Intraoperative Continuous Flash Visual Evoked Potentials, a Novel Technique to Lessen Intraoperative Optic Nerves and Chiasmatal Injury in Endoscopic Skull Base Surgery	Monday, October 9	4:06-4:12	Section on Tumors

Tumor Section Membership Committee Fall 2017

Jennifer Moliterno-Gunel, MD, FAANS

Membership in the American Association of Neurological Surgeons (AANS)/Congress of Neurological Surgeons (CNS) Section on Tumors currently includes over 2,000 members. Our section continues to have a very large resident and fellow contingency that continues to grow significantly. This is in large part due to the Section waiving membership dues for resident and fellow members.

We have begun significant outreach to attempt to capture more members. More recently, we have reached out to young attendings who have recently completed the Oral Boards and specifically reported their sub-specialty practice in tumors. Moreover, we have also reached out to those AANS/CNS members who have attended our Scientific Program and offered membership into our section. We are hoping these efforts allow us to better incorporate those surgeons who share a passion for the subspecialty of tumor surgery.

New members are shown here as well as current membership statistics.

Tumor Section Membership Statistics

Class Code	Subclass Code	2017 Dues	# of Members
ASSOCIATE	15D	\$0	71
ADJUNCT	60D	\$37.50	22
ACTIVE	01S	\$150.00	530
INTERNATIONAL	40S	\$150.00	63
INTERNATIONAL/ Developing Country	40SD	\$75.00	7
HONORARY	45S	\$0.0	20
Medical Student	15M	\$0.0	12
Resident/Fellow	50R	\$0.0	1,799

Update from the Clinical Trials Committee

Michael A. Vogelbaum, MD, PhD

The AANS/CNS Tumor Section, in collaboration with the CNS, will be offering a clinical trials course at the 2017 CNS Annual Meeting in Boston. Faculty includes recognized leaders in clinical research from neurosurgery, medical oncology, neuro-oncology and the FDA. The half-day course (PC-30), which runs from 12:30-4 p.m., is intended for neurosurgeons who are interested in developing clinical trials, and it will include talks about various aspects of clinical trial design, statistics and regulation, as well as pearls from neurosurgeons who have experienced the ups and downs of clinical research. Full details about the course are listed on the 2017 CNS Annual Meeting and the Tumor Section websites. Feel free to contact me for more information at vogelbm@ccf.org.

Also, I would like to call attention to the recently opened prospective phase III trial that randomizes patients with newly diagnosed WHO grade II (atypical) meningiomas that have been

subjected to a Simpson grade 1 – 3 resection to observation vs. adjuvant fractionated radiotherapy (NRG BN-003). This study follows on the heels of RTOG 0539, which was one of the first cooperative group trials to be completed in meningiomas, and showed that use of radiotherapy in this group of patients was associated with a clear improvement in PFS, compared to historical control, and that this benefit may have translated into an OS benefit as well. Neurosurgical participation in BN-003 will be essential for it to succeed, and the trial design will definitively answer the controversial question of whether radiotherapy is warranted after gross total resection of a grade II meningioma. This trial also provides the Tumor Section and organized neurosurgery as a whole the chance to participate meaningfully in NCI funded clinical research.

Report from the Liaison to the Alliance for Clinical Trials in Oncology

J. Bradley Elder, MD, FAANS

The Alliance for Clinical Trials in Oncology is a National Cancer Institute-funded cooperative created in 2011 with the merger of the North Central Cancer Treatment Group (NCCTG), American College of Surgeons Oncology Group (ACOSOG) and the Cancer and Leukemia Group B (CALGB). The Alliance is comprised of multiple multidisciplinary disease committees such as neuro-oncology, leukemia, breast and respiratory, which coordinate clinical trials within their field. Modality Committees (e.g. radiation oncology, oncology nursing) provide multidisciplinary support for each of the disease committees. Scientific and operational support are provided by programs, including Statistics and Data Management and Central Protocol Operations, that interface with each disease committee as needed, based on requirements of the clinical trials.

The Alliance meets regularly in Chicago, and the next meeting of the Neuro-Oncology Committee is Friday, November 3, 2017. Currently open and actively recruiting clinical trials supported by the Alliance that are relevant to neuro-oncology are listed in the table below. Updates regarding new and existing clinical trials supported by the Alliance are published regularly in the AANS/ CNS Section on Tumors Newsletter. The most recent Newsletter highlighted a study of ABT-414 in subjects with newly diagnosed Glioblastoma (GBM) with Epidermal Growth Factor Receptor (EGFR) amplification. A number of other studies not listed on the table are potentially available for investigators to bring to their institution, but are not currently actively accruing patients.

Neurosurgeons interested in further information regarding the Alliance are encouraged to contact Dr. Brad Elder (brad.elder@osumc.edu) to discuss possible opportunities for involvement.

ClinicalTrials.gov Search Results 08/23/2017

Title	Recruitment	Study Results	Conditions	Interventions
1 Corticosteroids + Bevacizumab vs. Corticosteroids + Placebo (BEST) for Radionecrosis After Radiosurgery for Brain Metastases	Recruiting	No Results Available	• Radionecrosis • Brain Metastases	• Drug: bevacizumab • Drug: corticosteroids • Other: placebo
2 Radiation Therapy With Concomitant and Adjuvant Temozolomide Versus Radiation Therapy With Adjuvant PCV Chemotherapy in Patients With Anaplastic Glioma or Low Grade Glioma	Recruiting	No Results Available	• Brain and Central Nervous System Tumors	• Drug: concomitant temozolomide (TMZ) • Radiation: radiotherapy • Drug: procarbazine • Drug: adjuvant temozolomide (TMZ) • Drug: CCNU • Drug: vincristine
3 Armodafinil in Reducing Cancer-Related Fatigue in Patients With High Grade Glioma	Recruiting	No Results Available	• Fatigue	• Drug: armodafinil 150 mg • Other: Placebo • Drug: armodafinil 250 mg
4 Vismodegib and FAK Inhibitor GSK2256098 in Treating Patients With Progressive Meningiomas	Recruiting	No Results Available	• Intracranial Meningioma • Recurrent Meningioma • NF2 Gene Mutation	• Drug: vismodegib • Drug: GSK2256098

U.S. National Library of Medicine | U.S. National Institutes of Health | U.S. Department of Health & Human Services

Stereotactic Radiosurgery Update

By Jason Sheehan, MD, PhD, FAANS

Contact JSheehan@virginia.edu

Radiosurgical Registry Update

The AANS and ASTRO SRS registry has expanded to include 28 initiated sites from across the U.S. Thus far, 2181 patients had been accrued to the SRS registry as of early July 2017. One of the first interim scientific analyses will be conducted in early fall. For further information, please contact Dr. Sheehan at jsheehan@virginia.edu.

Radiosurgical Education and Meetings:

In June, the AANS and ASTRO, along with NREF, hosted a senior resident course on intracranial and spinal SRS at the University of Pittsburgh. Local host for the course was L. Dade Lunsford, MD, FAANS, and course directors included Dr. Sheehan from UVA and John Suh, MD, from Cleveland Clinic. The two and a half day course hosted over 50 senior neurosurgery and radiation oncology residents from throughout the country. Special gratitude is given to the faculty who taught at the course, many of whom are tumor section members. Also, educational grants from many corporate partners to NREF helped to fund this course and this support was most appreciated. The next senior resident course in SRS will be held in 2019.

The International Gamma Knife Research Foundation held its meeting in June at the University of Pennsylvania. The meeting was the largest for the group to date and brought participants from across the globe. Topics included big data and multicenter retrospective and prospective trials, many of which were on brain tumors.

The Novalis Circle International Meeting was held in May in

Chicago. This too had broad attendance and focused on many topics, including SRS for brain metastasis. The SRS registry was also a topic of discussion at this meeting.

Upcoming radiosurgical scientific meetings include the following:

1. Radiosurgical Society Annual Meeting, November 2-4, 2017 in Las Vegas, Nevada. Additional details are available at <https://www.regonline.com/builder/site/Default.aspx?EventID=1851725>
2. Leksell Gamma Knife Society Meeting, March 4-8, 2018 in Dubai. Further information is available at <http://www.lgks2018.com/app/attendee/default.asp?PageId=53201&MenuItemId=46319&ProjectId=8523>
3. The 14th International Stereotactic Radiosurgery Society meeting will take place in Rio de Janeiro, Brazil. It is hosted by Tony De Salles, MD, PhD. For further information, please see <http://www.isrsy.org/>

Also, for those interested in SRS webinars, the ISRS has a series of SRS-focused webinars, which are available for free. Further information and registration for webinars can be found at <http://www.isrsy.org/en/courses/webinars/>

Finally, an SRS survey on education and training requirements is being devised. The effort, led by Dr. Ron Warnick, MD, FAANS and assisted by Drs. Jensen, Yang, Bloch, and Sheehan with support from Steven Kalkanis, MD, FAANS, will evaluate the current training in SRS for residents and help to identify opportunities for improvement.



Figure above: Lecture at the 2017 AANS and ASTRO SRS Resident course held at UPMC in June 2017.

Society of Neuro-Oncology Update

By Gelareh Zadeh, MD, PhD, FAANS

Scientific Program Chairs Manish Aghi, MD, PhD, FAANS; Frank Furnari, MD; and Vinay Puduvalli, MD, are hard at work putting the finishing touches on the Society for Neuro-Oncology's (SNO) 22nd Annual Scientific Meeting and Education Day, which will be held November 15-19, 2017, at the Marriott Marquis Hotel in San Francisco. This year's meeting will highlight a number of the Blue Ribbon Panel Recommendations related to the "Cancer Moonshot" program. W.K. Alfred Yung, MD, a member of the Blue Ribbon Panel, will present an introduction to the Moonshot program and three prominent keynote speakers will offer presentations related to the specific recommendations. In addition, SNO is pleased to report a record number of abstracts submissions this year – over 1,300 – with accepted papers presented as oral talks, e-posters and traditional posters. Full meeting details are available on SNO's website, www.soc-neuro-onc.org.

In keeping with the main meeting theme, the Education Day on November 14 will focus on two of the Cancer Moonshot Blue Ribbon Panel recommendations: "Developing Ways to Overcome Resistance" and "Minimizing Cancer Treatments Debilitating Side Effects." Concurrent tracks in both basic science and applied neuro-oncology will offer a comprehensive look at these two recommendations. Education Day is co-chaired by Khalid Shah, PhD; Albert Kim, MD, PhD, FAANS; Susan Bell, RN, MS, CNRN; and Robert Cavaliere, MD.

In a special pre-meeting event, SNO and the Society for CNS Interstitial Delivery of Therapeutics (SCIDOT) will hold a joint Conference on Therapeutic Delivery on November 15-16, also at the Marriott Marquis. This conference is jointly hosted by SNO and SCIDOT. This year's conference will address the multiple laboratory and clinical advances that have been made in the field of interstitial delivery of therapeutics. The joint conference has been championed by Michael Vogelbaum, MD, PhD, FAANS.

Back for a third consecutive year, the Neuro-Oncology Review Course will be held Wednesday, November 15. This fast paced, full-day activity will provide high quality education and CME credits for all participants. Practicing physicians, residents and fellows, medical students, nurse practitioners, nurses and all those interested in reviewing and enhancing their knowledge in the principles of clinical neuro-oncology will benefit from this program. The faculty of the course, selected from top neuro-oncology programs, will offer a comprehensive overview of clinical neuro-oncology. The Neuro-Oncology Review Course is Chaired by Maciej Mrugala, MD, PhD, MPH.

The introduction of new technology to improve the conference

experience and enhance learning opportunities is an on-going strategic priority for the Society. Led by technology committee chair Erik Sulman, MD, PhD, SNO has made significant investments in event technology in recent years. This has included development of a robust meeting app, that this year will have a new feature allowing attendees to claim CME credit directly through a mobile device. Additional technology features this year include an enhanced "text to moderator" electronic Q&A feature, integrated oral eTalks and traditional poster presentations, selected sessions simulcasted on hotel in-room TV channels, expanded e-posters with 45 flat screens placed throughout the meeting space, a new presentation management system for easier upload of oral presentations and the capture of selected content for a new post-meeting education site.

The SNO annual meeting has experienced significant growth in recent years, presenting a challenge to the leadership to find hotels that can accommodate upwards of 2,500 participants. Consequently, SNO plans to transition from hotels into convention centers starting in 2020, when the meeting will be held in Austin, Texas. With more room for plenaries, concurrent sessions, satellites and exhibit space, the new convention center model is expected to greatly improve the on-site experience for all attendees. And, as the 2020 meeting will coincide with the 25th anniversary of the Society, the transition to convention centers provides a tangible indicator of how far SNO has come since its inception.

For the past three years, SNO has held a career lounge to help facilitate on-site interviews and in-person meetings between trainees and faculty, as well as candidates and hiring institutions.

I would like to take this opportunity to recognize the significant contribution and commitment of Chas Haynes to SNO, as executive director he ensures the society is vibrant and dedicated to its mission.

Skull Base Surgery Update

Michael J. Link, MD, FAANS, Mayo Clinic, Rochester, Minn.

Daniel Prevedello, MD, Ohio State University, Columbus, Ohio.

The second half of 2017 is looking to be very busy and exciting for the skull base societies and skull base surgeons. The 27th Annual Scientific Meeting of the North American Skull Base Society (NASBS) was held at the Roosevelt Hotel in New Orleans, March 3–5, 2017. Once again, it was a resounding success with a record number of abstracts (412), record attendance (869) - including record number of international registrants (36 countries represented) - and an exciting program of plenary sessions, expert opinion panels, proffered papers and critical evaluation of submitted surgical videos of complex skull base procedures. Most notably, there was a tribute to Al Rhoton Jr., MD, FAANS(L) who had served as the third president of the NASBS and died last year after an incredible career of service to the field. Many generations of his prior fellows came and spoke about his life's work and legacy. Eric Rhoton, MD, FAANS, and his wife also attended, and represented the Rhoton family. As usual, there was a pre-meeting hands-on dissection course; this year held at the world class lab at LSU, New Orleans. President Jacques Morcos, MD, FAANS, presided over the meeting with Roberto Heros, MD, FAANS(L); Alan Crockard, DSc; and Fred Gentili, MD, FAANS, MSc, as his honored guests.

Ian Witterick, MD, Head and Neck Surgeon from University of Toronto was elected the 28th president of the NASBS. The summer practical course was held July 6–9, 2017, also in New Orleans. Residents and fellows from all over the U.S. learned from experts in open and endoscopic skull base surgery techniques. The 28th Annual Scientific Meeting of NASBS is scheduled February 16–18, 2018, at the Loews Hotel on Coronado Island, California. The pre-meeting practical course will be February 14–15, 2018. The theme of the meeting is *Dynamic mentoring of the skull base surgeon: Training our future*. As usual, all abstracts will be published in the official journal of NASBS, *Journal of Neurological Surgery, Part B, Skull Base*. We hope to see everyone on Coronado Island for what will certainly be a dynamic and cutting edge scientific meeting.

Likewise, the 13th Congress of the European Skull Base Society is scheduled for April 19–21, 2018, in beautiful Warsaw, Poland. Congress Presidents, Prof. Kazimierz Niemczyk, MD, Medical University of Warsaw; and Prof. Arimantas Tamasauskas, MD, Lithuanian University of Health Sciences; invite you to submit an abstract and register at www.esbs.eu/2018. Also, it is notable that the 19th International Leksell Gamma Knife Society Meeting is scheduled in Dubai, UAE, March 4–8, 2018. More information can be found at www.lgks2018.com.

Multiple studies continue to enroll patients with difficult skull base tumors, such as chordomas and atypical and malignant meningiomas. More information can be found at clinicaltrials.gov.

We are looking forward to seeing everyone in Boston, October 7–11, 2017, for the annual CNS meeting. Once again, this year's meeting offers numerous opportunities to expand knowledge of skull base disorders. Practical courses on Saturday and Sunday include Contemporary Management of Meningiomas (PC06), Comprehensive Endoscopic Skull Base Surgery (PC01 & PC14) and Management of Pituitary Adenomas and other Sellar Pathology (PC08), to name a few. Of course there will be numerous abstracts and electronic posters dealing with the breadth and depth of skull base pathology.

International Committee Update

Ricardo J. Komotar, MD, FAANS, FACS

The International Committee has had a successful year thus far in 2017. To briefly summarize, the World Federation of Neurosurgical Societies (WFNS) has two neurooncology courses planned for this coming year. The European tumor section continues to demonstrate significant growth under Colin Watts, achieving membership of over 200 individuals. The WFNS is also actively integrating into the AANS/CNS Tumor Section with collaborative training courses and clinical trials. The Indian Society of Neuro-Oncology has rapidly expanded its annual meetings with high attendance and plans to host a live brain tumor surgery workshop in late 2017. The Chinese Neurosurgery Society is formalizing an exchange program for their neurosurgeons to observe in the U.S., allowing an open forum for integrated educational opportunities. The Chinese Neurosurgery Society is also planning to lead a journal issue entirely dedicated to international neurosurgery. The Argentinean Neurosurgery Society has a Brain Tumor Awareness Symposium planned for this year and has also agreed to support an International Fellowship program for residents to come to the U.S. for three months. This fund will support the resident with the best abstract at their national meeting. The Continental Association of African Neurosurgical Societies is planning their third Congress in Nigeria as a follow-up to the last one in Cape Town, July 2016, with excellent attendance. Finally, the Federation of Latin American Neurosurgeons (FLANC) is very interested in expanding collaborations with the AANS/CNS Tumor Section. Led by Danny Prevedello, MD, this collaboration will be finalized this year.

AANS/CNS Section on Tumors - Young Neurosurgeons Reception

Submitted by Ricardo Komotar, MD, FAANS

AANS Annual Meeting
April 25, 2017
Walavan Sivakumar, MD

Mitchel S. Berger, MD, FAANS, Professor and Chair of Neurosurgery at the University of California, San Francisco Hospital and former president of the AANS, was the honored guest at the AANS/CNS Section on Tumor's Young Neurosurgeons Reception, co-hosted by the Young Neurosurgeons Committee, at the AANS Annual Scientific Meeting on April 25, 2017.

A luminary in the field of neuro-oncology who has authored almost 600 peer-reviewed publications and book chapters and has edited six textbooks, Dr. Berger addressed over 100 young neurosurgeons and leaders of the tumor section with a subdued, yet powerful, empathy that left the audience spellbound. Using the various patient interaction points of the neurosurgeon as his scaffold, he shared lessons that would resonate and cause pause for introspection at frequent points during the surgeon's workday. The principles of his practice culminated in 10 commandments of the next generation that will long be remembered.

In the clinic, he touched on the importance of equal opportunity, transparency and open communication through several anecdotes. From never turning a patient away to always wearing scrubs in front of his patients to illustrate his role on their care team and allowing any and all questions from patients and their families, he highlighted the importance of making the care plan a joint decision between the provider and patient.

Dr. Berger spoke of the importance of the surgeon's charge to maintain the steady vision of the operating room team, with absolute full attention due at all times. In addition to being dogmatic about taking his time in the operating room and never rushing, he insists on keeping the patient's support team involved in the journey with hourly updates. This is followed by a thorough and full explanation of how surgery transpired, including drawings, and what exactly to expect immediately after. Every encounter is closed by the extension of appreciation to the family for the privilege of allowing us to care for their loved one.

In the ICU or ward, that complete dedication is relayed through the ritual of always sitting with the patient while making rounds, always touching the patient and always going thoroughly through postoperative scans, while allowing for any and all questions.

These simple, yet oft forgotten, tenets of the surgeon's commitment to absolute excellence were memorably presented in these 10 commandments to the next generation, reprinted with permission by Dr. Berger.

The 10 Commandments of the Next Generation – Mitchel S. Berger

1. You must believe in yourself and your ability to alter the life of another person and contribute to our profession of neurosurgery.
2. You must strive to achieve a perfect outcome each and every day you care for another individual.
3. You must repeat to yourself every day when you enter the hospital or operating room, "I will give 110% today and stay focused no matter what I encounter."
4. You must leave your personal problems outside of your professional world.
5. You must stay physically and mentally fit.
6. You must periodically evaluate your results and outcomes to determine if you are still making progress, on the plateau or deteriorating.
7. You must always read and learn from others as well as from your failures and successes.
8. You must never compromise in your pursuit of perfection, no matter what forces exist to have you accept less than perfection.
9. You must always make a decision and never be indecisive. If you do this you will always make more right than wrong decisions.
10. You must never be shaken or discouraged by a bad outcome or complication, but you must always feel the pain of the patient and their family and know that you have changed their lives forever. Mourn your errors, mourn your losses, but pick yourself up and fight for the next patient's life.

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The AANS/CNS Section on Tumors and the Young Neurosurgeons Committee are pleased to announce that the honored guest for the Young Neurosurgeons Reception at the 2017 CNS Annual Meeting (Tuesday, October 10 from 6:15-8:15 p.m. in Grand Ballroom C of the Westin Hotel) will be the Chairman of the Department of Neurological Surgery at The Ohio State University and former president of the CNS, Russell R. Lonser, MD, FAANS.

Washington Committee Update for Tumor Section

Katie Orrico, JD, and Brian Nahed, MD

The Washington Committee, chaired by Ann R. Stroink, MD, FAANS, continues to be very active, given the ever-changing health care climate. Below are some highlights of the last few months.

The Washington Committee has been engaging members of Congress and the administration on issues related to Medicare's rules and regulations, including the new Quality Payment Program (QPP), global surgery code reimbursement and quality-related penalties. Progress is being made on these fronts, and the proposed rules governing the Medicare physician fee schedule and payment programs reflect neurosurgery's suggestions. While not final, in 2018, neurosurgeons should see reduced payment penalties and increased flexibility for the QPP. Additionally, the Neurosurgery Quality Council (NQC) continues to coordinate with the NeuroPoint Alliance (NPA) to develop additional Qualified Clinical Data Registries (QCDRs), so neurosurgeons participating in the NPA's Quality Outcomes Database (QOD) program can get credit under Medicare.

A delegation of neurosurgeons from the Washington Committee recently attended the Alliance of Specialty Medicine's Annual 2017 Legislative Conference. Conference attendees heard from key members of Congress, the administration and others, including U.S. Department of Health and Human Secretary, Tom Price, MD, and Reps. Kevin Brady (R-Texas), Gene Green (D-Texas) and Phil Roe, MD, (R-Tenn.). During the two-day conference, the specialty physicians blanketed Capitol Hill to lobby on issues, such

as the repeal of the Independent Payment Advisory Board (IPAB), increased support for graduate medical education (GME) and medical liability reform.

On the medical liability reform front, neurosurgery continues to lead the way, and on June 28, 2017, the U.S. House of Representatives passed H.R. 1215, the Protecting Access to Care Act. This comprehensive medical liability reform bill includes, among other things, a \$250,000 cap on non-economic damages and expert witness reforms.

As to the topic of graduate medical education, organized neurosurgery issued a response to the American College of Surgeons' Policy and Position Paper on GME Reform, highlighting the specialty's concerns with the proposal to create a new government entity to oversee physician workforce and GME funding needs.

The Washington Committee has also been actively engaged in the debate on health care reform. The AANS and CNS have not taken a position one way or another on the various Republican reform proposals; rather they have sent letters commenting on various aspects of the legislation.

Finally, members of the Tumor Section are encouraged to stay informed on health care policy topics by subscribing to Neurosurgery Blog at www.neurosurgeryblog.org, following the Washington Committee on Twitter [@neurosurgery](https://twitter.com/neurosurgery), and keeping an eye out for updates across the AANS and CNS publications.

What Can Gene Expression Tell Us about the Tumor Microenvironment in GBM?

Alexander Ramos, MD, PhD, and Rohan Ramakrishna, MD

Weill Cornell Medicine Department of Neurosurgery

Advances in sequencing technology over the last decade have allowed for the extensive characterization of glioblastoma tumor samples and their gene expression profiles. Moreover, the efforts of multiple consortiums have led to the cataloging of the transcriptome of hundreds of tumors. However, a major challenge when analyzing sequencing data is the RNA is acquired from bulk tumor samples, typically without any purification steps included. Within any biopsy sample, it is estimated that anywhere from 10 to 80% of cells represent tumor microenvironment and not true tumor cells. This tumor microenvironment contains immune cells, including tumor-associated macrophages and circulating T-cells, that both contribute to disease progression as well as serve as putative targets for therapies. Until recently, technology did not exist to extract gene-expression profiles from single cells and to reliably separate tumor from surrounding microenvironment cells. However, within the last two to three years, single-cell RNA sequencing technology has revealed intra-tumor transcriptional heterogeneity, as well as multiple types of tumor-associated immune cells. While promising, single-cell sequencing remains relatively expensive with its own analytical challenges.

A recent paper by Wang et al. attempts to reconcile the expanding database of single-cell data with the already existing rich dataset of whole-genome sequencing.¹ The authors utilized a combination of single-cell data, bulk tumor samples and cultured GBM cells lines to define ‘bona fide glioma genes,’ that is genes associated specifically with glioma cells and not surrounding immune or stromal cells. These bona fide genes were highly correlated with genes found in the traditionally defined proneural (PN), mesenchymal (MES) and classical (CL) subtypes, and the authors could narrow the gene list to a 50-gene set that defines each of these types with high concordance rates.

Of the 369 tumors analyzed, 8 percent of tumors were found to have gene expression profiles enriched for more than one of these transcriptional subtypes, suggesting a subpopulation of highly heterogeneous tumors. The authors defined a simplicity score from 0 to 1 to give a quantitative measure of the homogeneity of tumor gene expression profiles. Those tumors enriched for more than one subtype all had simplicity scores of <0.05. Survival trends were especially pronounced in the highly homogenous tumors. For example, the higher the tumor simplicity score for proneural tumors, the more favorable the survival outcome, therefore validating the known association of proneural tumors with enhanced survival. In general, MES tumors tended to be less pure (i.e. lower simplicity scores); this increase in transcriptional heterogeneity was found to be due to the increase in microenvironment-derived cells. Gene expression data demonstrated M2 type tumor-promoting macrophages were common; these macrophages can come from activation of local

microglia or from recruitment of peripheral monocytes.² While the source of these M2 cells were not specifically addressed by the authors, the data and processing pipeline could be used to address these questions in future studies, and be expanded to address the observed recruitment of other peripheral immune cells including myeloid precursors to tumors.³ Natural killer (NK) cells were significantly reduced in MES, while dendritic cells significantly increased in CL. These data imply that CL tumors may be the best candidate for dendritic cell-based vaccine therapy, whereas MES subtypes may be least amenable to currently available immune therapy.

Next, the authors compared the gene expression profiles and simplicity scores of matched recurrent and primary tumors. More heterogeneous tumors were more likely to switch subtype, suggesting clonal selection and expansion at recurrence from a heterogeneous tumor. Importantly, homogeneous MES tumors associated with poor outcome, as well as any tumor that recurred as the MES subtype, reinforcing the association of MES with decreased survival regardless of time point. The worst outcome was in dominant MES tumors that recurred as MES, suggesting an additive effect. Most clinically relevant was the analysis of tumor microenvironment after treatment. Temozolomide treatment can generate “hypermutator” tumors at recurrence.⁴ Intriguingly, hypermutators identified in this dataset were more likely to be

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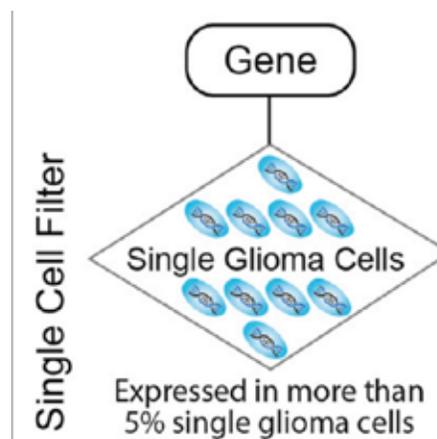


Figure 1: Wang et al. scheme for determining glioma genes. Gene expression data from single cells, glioma stem cells in culture and from histologically defined cellular tumors were filtered as shown to define a set of glioma genes. IDH-WT tumors were then classified based on the expression of these glioma genes to generate mesenchymal (MES), classical (CL), and proneural (PN) subtypes. Figure modified from Wang et al (Cancer Cell 2017)

associated with CD8+ T cells, suggesting hypermutators may be more immunogenic, therefore more susceptible to immunomodulating therapy. The authors also investigated recurrence after radiation, and found that those tumors that had a short-term (6 mo.) relapse after radiation were associated with additional M2 macrophages and CD4 T cells, suggesting macrophage or CD4 targeted therapies may play a role as radio-sensitizing agents. Interestingly, in recurrent tumors there was a decrease in peripheral monocyte infiltration, hinting that the majority of M2 macrophages in recurrent tumors are derived from microglia.

Importantly, the majority of the work is based on *in silico* analysis and reworking of existing datasets. The authors briefly demonstrate the ability of their data to generate testable molecular hypotheses by showing acute loss of the NF1 gene in glioma cell lines serves as a chemoattractant for microglia through an as of yet undetermined mechanism. Many of the associations presented will still require validation through immunohistochemical analysis of tumor samples and further single-cell sequencing of matched primary and recurrent tumors; nevertheless, a major strength of this work is providing an analytical pipeline for analysis of already-

existing sequencing data. In doing so, it has validated known associations and provided data that should provide future directions for both basic tumor biology as well as the design of clinical trials.

1. Wang Q, Hu B, Hu X, et al. Tumor Evolution of Glioma-Intrinsic Gene Expression Subtypes Associates with Immunological Changes in the Microenvironment. *Cancer cell*. 2017;32(1):42-56 e46.
2. Hambardzumyan D, Gutmann DH, Kettenmann H. The role of microglia and macrophages in glioma maintenance and progression. *Nat Neurosci*. 2016;19(1):20-27.
3. Rajappa P, Cobb WS, Vartanian E, et al. Malignant Astrocytic Tumor Progression Potentiated by JAK-mediated Recruitment of Myeloid Cells. *Clinical cancer research : an official journal of the American Association for Cancer Research*. 2017;23(12):3109-3119.
4. Cancer Genome Atlas Research N. Comprehensive genomic characterization defines human glioblastoma genes and core pathways. *Nature*. 2008;455(7216):1061-1068.

Guidelines Committee

Jeffrey J. Olson, MD, FAANS, and Brian V. Nahed, MD, MSc

The AANS/CNS Guidelines Committee remains open to new ideas and projects. Two new proposals are in the pipeline. There is a formal application form that can be obtained from Trish Rehring in the CNS Guidelines Office via the CNS website. Once completed, it can be returned for consideration, first by the AANS/CNS Tumor Section Guidelines Committee and then by the CNS Guidelines Committee where it is prioritized for development, particularly if CNS resources are requested to assist in their construction. The AANS/CNS Tumor Section Guidelines Committee can then serve as consultants for the writers at whatever level is necessary to assist in completion.

The annual CNS meeting will include a training course for new and prospective members of the AANS/CNS Guidelines Committee so as to understand how to review guidelines from throughout the specialty. In view of our sections extensive experience, members of the AANS/CNS Tumor Section will be participating actively in this course. Additionally, a guidelines application is under development by the CNS Guidelines committee for use by the CNS membership to rapidly access guidelines written for maladies across the specialty. Ian Dunn, MD, FAANS, has been instrumental in contributing the content related to brain tumors.

Vestibular Schwannoma Management Guidelines

This nine-part guideline, including 18 authors from multiple specialties, has been approved by the AANS/CNS Guidelines Committee and endorsed by the leadership of the AANS and

CNS. It is being submitted for publication in executive summary form to Neurosurgery in August 2017 and endorsement is being sought from the American Academy of Otolaryngology-Head and Neck Surgery foundation for guideline endorsement to assist in dissemination.

Metastatic Brain Tumor Management Guidelines Update

This nine-part guideline, including 19 authors from multiple specialties, has been submitted to the AANS/CNS Guidelines Committee for review in August 2017. We have been approached for collaboration by ASTRO and Cancer Care Ontario and have sent drafts to them for review. Additionally, we have asked ASCO to consider endorsement of these.

Newly Diagnosed Glioblastoma Management Guidelines Update

Seven manuscripts for this update are in preparation under the leadership of Timothy Ryken, MD, FAANS. Once completed, this will be submitted to the AANS/CNS Guidelines Committee for review with the goal being publication in the *Journal of Neuro-oncology*, as were the original set of guidelines.

Metastatic Spine Tumor Management Guidelines

A streamlined, first portion of these guidelines is in preparation under the direction of Dr. Ryken. Once completed, this will be submitted to the AANS/CNS Guidelines Committee for review with the goal being publication in *Neurosurgery*.

AANS/CNS Section on Tumors Executive Committee Update

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International - EANS

Zvi Ram
Colin Watts

International - Argentina: Alejandra Rabadan

International - Australia: Charlie Teo

International - Central America: Jose Valerio

International - India: Atul Goel

International - Pakistan (South Asia liaison): S. Ather Enam

International - Italy: Francesco Dimeco

International - Germany: Manfred Westphal

International - England: S George amandouras

International - Japan: Fumio Yamaguchi

International - Nigeria (Africa Liaison): Okezie Obasi Kanu

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International - Turkey: Ugur Ture

International - AANS Ambassador for AASNS: Clark Chen

International - AANS Ambassador for CAANS: Brian Nahed

International - AANS Ambassador for EANS: Michael McDermott

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International - AANS Ambassador for FLANC: Danny Prevedello

Journal of Neuro-oncology (Editor): Linda Liao

MATRIX and CAST: Ennio Chiocca

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