Greetings, and welcome to the Fall 2014 AANS/CNS Section on Tumors Newsletter! With this issue, the Tumor Section celebrates 30 years since its founding. In December 1984, the section gained approval by the executive committees of both the American Association of Neurological Surgeons (AANS) and Congress of Neurological Surgeons (CNS), and it held its first session at a national meeting of the AANS in 1985. The first officers were Mark Rosenblum, MD, FAANS (chair); and Michael Apuzzo, MD, FAANS(L) (secretary-treasurer). Celebrations of the 20th and 25th anniversaries of the section’s founding have included both a special issue of the Journal of Neuro-Oncology and a special banquet. Our 30th anniversary will be no exception. Section historian Tony D’Ambrosio has edited a special Journal of Neuro-Oncology issue that will be published in time for the upcoming CNS meeting. The issue incorporates state-of-the-art reviews on brain tumor pathology, imaging, chemotherapy and radiosurgery treatment, immunotherapy, stem cell biology, and neurosurgical involvement in clinical trials, as well as a look at brain tumor treatment from the patient’s perspective. Additional articles review the Tumor Section’s activities in clinical practice guideline generation, its development efforts, and the history of the section’s prizes and awards and of its satellite meetings. As with previous Tumor Section special issues, most articles were authored by members of the section’s executive committee, as well as some special invited guests. Section members enjoy Journal of Neuro-Oncology subscriptions as a benefit of membership, so check it out!

Tumor Section program chair John Kuo, MD, PhD, FAANS, has assembled an exciting special seminar for the upcoming CNS meeting in Boston, focusing on “Emerging technologies in tumor visualization and therapy.” Mike Vogelbaum, MD, PhD, FAANS, will discuss the definition of a tumor margin in gliomas; Aaron Cohen-Gadol, MD, FAANS, will discuss fluorescence-guided resection (FGR) in gliomas; David Roberts, MD, FAANS, will discuss FGR in meningiomas, and Ed Laws, MD, FAANS(L), FGR in pituitary tumors. Steve Kalkanis, MD, FAANS, will review new work in Raman spectroscopy at the tumor margin, and Dr. Kuo will describe a novel class of alkylphosphocholine analogs for FGR. In a change from previous CNS meetings, the section’s special seminar will meet from 7-8:30 a.m. on Monday morning, Oct. 20, 2014. Section Original Science abstracts will be presented on Tuesday morning from 7-8:30 a.m., and the Neurosurgical Forum is from 4:15-5:30 p.m. Tuesday. Also plan to attend the section’s Young Neurosurgeons reception from 5:30-7 p.m. Tuesday, with Ennio Chiocca, MD, PhD, FAANS, as featured speaker. Section members will also be interested in consensus sessions on glioma management and management of metastatic tumors of the spine, as well as controversy debates on extent of resection in skull base tumors and on the role of radiosurgery before resection of metastatic brain tumors (neo-adjuvant radiosurgery).
Boston is a special city for historically minded section members because Harvey Cushing spent his prime surgical years there, as surgeon-in-chief at the Peter Bent Brigham Hospital. The dawn of his career was also in Boston, as a Harvard medical student and intern at Massachusetts General Hospital. A special exhibit focusing on the beginning of Cushing’s career, hosted by the Paul S. Russell Museum of Medical History at the Massachusetts General Hospital, is timed to coincide with the October CNS meeting and will be of interest to many section members. On display will be the original hospital records of the first tumor craniotomy witnessed by Cushing as a medical student (with his handwritten autopsy notes) and of the patient in whom he, as an intern, first noted slowing of the pulse from increased intracerebral pressure (later to be developed into the triad now known as the Cushing reflex). Also on display will be the original “ether charts” kept by Cushing (the first anesthesia records), including the operation that interested him in brain surgery; and his earliest sketches of the pituitary gland and brainstem as a first-year medical student. These records and images have not been publicly displayed since their creation 120 years ago, and most are unpublished, so consider taking a quick taxi ride from the convention center to view some of the founding documents of modern neurosurgery while in Boston. It should be a great meeting!

Harvey Cushing, age 28, and the ether chart he kept during the first tumor craniotomy he saw as a medical student. Across the top he has written “Best case [I] ever had.”

Frederick G. Barker II, MD, FAANS
This year marks the 30th anniversary of the founding of the American Association of Neurological Surgeons (AANS)/Congress of Neurological Surgeons (CNS) Section on Tumors. In 1984, Edward R. Laws Jr., MD, FAANS(L), suggested forming this organization, and Mark Rosenblum, MD, one of our distinguished contributing authors to this publication, was the section’s first chair. Since its inception 30 years ago, the AANS/CNS Section on Tumors has been committed to providing a forum through which neurosurgeons and allied specialists who focus on brain tumor research, diagnosis and treatment can communicate, educate and inspire each other toward the common goal of improving outcomes for our patients and their loved ones.

As research and technology continue to advance at an exponential rate, so does our understanding of the mechanisms behind, and the treatment opportunities for, tumors of the nervous system. The first 10 special contributions to this 30th Anniversary Supplement are designed to summarize the multiple advances in brain tumor research, diagnosis and management that have evolved over the past decade. Section chair, Fred Barker, MD, FAANS, discusses the critical role neurosurgeons play in brain tumor treatment, as well as the future challenges in the field. Dr. Rosenblum has made two contributions discussing the world of neuro-oncology as seen through the patient’s eyes. Advances in genetic and epigenetic analyses of gliomas are discussed in great detail by Drs. Tsankova and Canoll. The evolving role of imaging in neuro-oncology is thoroughly reviewed by Sarah Jost Fouke, MD, FAANS, and her group. Recent achievements and failures in medical neuro-oncology, including the most recent findings on bevacizumab are eloquently discussed by Drs. Ahluwala and Chang. Advances in fractionated radiation and stereotactic radiosurgery for both malignant and benign nervous system tumors are summarized by Jason Sheehan, MD, PhD, FAANS, and his group. Current Tumor Section secretary-treasurer Andrew Parsa, MD, PhD, FAANS, addresses recent discoveries and ongoing challenges in the field of vaccine therapies for patients with glioblastoma. Finally, Isabelle Germano, MD, FAANS, provides an extensive review and discussion on our past, present and future understanding of stem cells and gliomas.

As our neuro-oncology knowledge base has expanded over the last 10 years, so has the Section on Tumors as an organization. The latter half of this special issue includes five articles describing the section’s academic and organizational accomplishments, as well as the challenges to be faced in the future. In an ongoing effort to educate physicians through evidence-based medicine methodology, Dr. Mitchell and coauthors provide a current update on clinical practice guidelines in the Tumor Section. Ian Parney, MD, PhD, FAANS, provides an update on the importance of ongoing clinical trials in neuro-oncology with an emphasis on the vital role neurosurgeons must play in this process. Drs. Waziri and Curry provide a description of the evolution, current status and future challenges in the ongoing development of the Section. Awards, lectures and fellowships are eloquently described by Manish Aghi, MD, PhD, FAANS; and coauthors. The supplement concludes with a look back at the History of the AANS/CNS Tumor Section Biennial Symposia as authored by Drs. Lang and Barker.

We are exceptionally grateful to Linda Liau, MD, PhD, FAANS, editor-in-chief of the Journal of Neuro-Oncology, for her willingness, dedication and patience with this project. A special “thank you” is in order to all of the staff of the journal for their hard work, responsiveness and unsurpassed quality. We would like to thank all of the contributing authors for their time, effort and resources to make this special issue possible, and the many reviewers who volunteered their time and expertise to ensure a publication of the highest quality.

**Stereotactic Radiosurgery Report: Fall 2014**

**Jason Sheehan, MD, PhD, FAANS**

The American Association of Neurological Surgeons (AANS) has formed a partnership with the American Society for Radiation Oncology (ASTRO) to create a national stereotactic radiosurgery registry. The registry is being supported by corporate peers, including Brainlab and Elekta. It builds on previous successes by the Neuropoint Alliance (NPA), including NPAs highly successful lumbar spine registry. The goals of the registry are to meet the quality care and research needs of those practicing radiosurgery. Quintiles hosted the data repository and provides the analytical support for the registry. The AANS and ASTRO stereotactic radiosurgery (SRS) board has defined the data elements for the registry, and is in the process of identifying the 30 pilot centers for year one of the initiative. Patient accrual to the registry will begin in the next six months. Research support is available for participating centers. Those interested in participating in the national SRS registry should contact me at jsheehan@virginia.edu for further information.

In other matters, Noridian Healthcare Solutions proposed a new coverage policy, restricting SRS to patients with one to three brain metastases. The policy would cover 16 states. A response was prepared and sent to Noridian indicating that level 1 evidence exists for the upfront use of SRS for patients with one to four brain metastases. Also, recent guidelines by ASTRO, as well as numerous other studies, including JLGK0901, support the invalidity of number as a selection criterion for SRS in patients with up to 10 brain metastases. In that same proposed policy, Noridian indicated that it would cover SRS for “[p]atients with more than three primary or metastatic brain lesions who are enrolled in a clinical registry compliant with the principles established in AHRQ’s Registries for Evaluating Patients Outcomes: A User’s Guide.” The national AANS and ASTRO registry is compliant with AHRQ’s registry principles. This policy language by a major payer underscores the increasing importance of outcomes registries for SRS and likely other neurosurgical procedures.
The Tumor Section Awards Committee continues to actively develop the most robust awards program for outstanding research of any of the AANS/CNS joint sections. We are thrilled to have launched two new awards within the last few months:

Columbia Softball Charity Award — given to the best pediatric tumor abstract submitted by a resident or faculty member who is a member of the section on tumors will be given at each AANS/CNS with the recipient receiving an honorarium in the amount of $1,000. The first award will be given at the 2014 CNS meeting (see winner listed below). The section would like to thank Fred Barker, Jeff Bruce, and Rich Anderson for putting together the plan to use a portion of the proceeds from the annual charity softball tournament to sponsor this award.

Brian D. Silber Award — given to the best abstract related to vertebral column or spinal cord tumors in the amount of $500 at the annual AANS and CNS meetings. The first award will be given at the 2015 AANS Annual Scientific Meeting.

After recognizing 10 award winners and one awarded lectureship at the 2014 AANS Annual Scientific Meeting in April, we will be recognizing nine award winners at the 2014 CNS annual meeting. Most of the awards are limited to Tumor Section members, providing an additional incentive for membership. The award winners for this CNS meeting were recognized at the Tumor Section session Monday, April 7, 2014, from 2 to 5:30 p.m. Support for the awards program encourages submission of the highest quality works in neuro-oncology.

Synthes Skull Base Award
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, chair of the Skull Base Committee, was largely responsible for obtaining this award through a generous contribution from the Synthes Corp. The winner for the 2014 AANS Annual Scientific Meeting was Arman Jahangiri of the University of California San Francisco for the presentation, “Incidence of headache as a presenting complaint in over 1000 patients with sellar lesions and factors predicting postoperative improvement.” The winner for the 2014 CNS meeting will be Lukas Andereggen, MD, of Bern University Hospital in Switzerland, for his presentation, “Long-term follow-up of male patients with prolactinomas: Is bone densitometry necessary?” The award includes a $1,000 honorarium.

Preuss Award
The Preuss Award, sponsored by the Preuss Foundation, 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. The winner at the 2014 AANS Annual Scientific Meeting was Loyola Veronique Gressot, MD, of Baylor College of Medicine, for her presentation, “Signal Transducer and Activator of Transcription 5b Promotes Malignant Progression In Glioma.” The winner at the 2014 CNS meeting will be Ricky Raj Singh Kalra, MD, of the University of Utah, for his presentation, “Leptomeningeal Dissemination Cascade in Medulloblastoma.” This award has a $1,000 honorarium.

National Brain Tumor Society
Mahaley Award
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. At the 2014 AANS Annual Scientific Meeting, the award was presented to Kristen Batich, MD, of Duke University, for her presentation, “Tetanus toxoid conditioning enhances migration and efficacy of dendritic cell vaccines in patients with glioblastoma.” The winner at the 2014 CNS meeting will be Cleopatra Charalampaki, MD, PhD, of Hospital Merheim, Cologne, Germany, for her presentation, "Confocal laser endomicroscopy for real time histomorphological diagnosis: Our clinical experience with 150 brain and spinal tumor cases.” The award carries a $1,000 honorarium.

Integra Foundation Award
The Integra Foundation Award, sponsored by the Integra Foundation, is given at each of the AANS and CNS meetings for the best research or clinical paper submitted investigating benign brain, spinal or peripheral nerve tumors. At the 2014 AANS Annual Scientific Meeting, the winner was Jason P. Sheehan, MD, PhD, FAANS, of University of Virginia, for his presentation, “Gamma Knife...”
Radiosurgery for Sellar and Parasellar Meningiomas: A Multicenter Study of 763 Patients.” At the 2014 CNS meeting, the winner will be Derek G. Southwell, MD, PhD, of the University of California San Francisco (UCSF) for his presentation, titled “Intraoperative Mapping During Repeat Awake Craniotomy Reveals the Functional Plasticity of Adult Cortex.” The award carries a monetary honorarium of $1,000.

**Springer Journal of Neuro-Oncology Award**

The Journal of Neuro-Oncology Award is sponsored by Springer Publishers and is presented at both the annual AANS and CNS meetings to a highly ranked abstract in either clinical or basic science as related to neuro-oncology. The winner for the 2014 AANS Annual Scientific Meeting was Manish K. Aghi, MD, PhD, FAANS, of University of California San Francisco (UCSF), for the presentation, “Replicating retrovirus Toca-511 delivered using convection-enhanced real-time MRI guidance for recurrent glioblastoma.” The winner at the 2014 CNS meeting will be Scunggi J. Han, MD, of UCSF for his presentation, “The effect of timing of radiotherapy (RT) in patients with newly-diagnosed glioblastoma multiforme (GBM) receiving Temozolomide (TMZ): an analysis based on the UCSF experience.” A $500 award and a framed certificate are given to the winner.

**Stryker Neuro-Oncology Award**

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 AANS and CNS annual meetings, and the senior author of the paper must be a member of the AANS/CNS Section on Tumors. The winner for the 2014 AANS Annual Scientific Meeting was Javier Figueroa, BS, of MD Anderson Cancer Center, for the paper, “Mesenchymal stem cell exosomes enhance glioma stem cell viability and stemness via delivery of microRNA.” At the 2014 CNS meeting, the winner will be Sabih Tariq Effendi, MD, of MD Anderson Cancer Center for his presentation, “Insular Glioma Resection: The MD Anderson Experience.” A monetary component of $1,000 is included with an award certificate.

**Columbia Softball Charity Award**

The “Columbia Softball Charity Award” will be 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. Current Section on Tumors chair Fred Barker, MD, FAANS; previous Section on Tumors chair Jeff Bruce, MD, FAANS; and pediatric neurosurgeon Richard Anderson, MD, from Columbia University were instrumental in putting together a plan to use a portion of the proceeds from the annual charity softball tournament to sponsor this award. The first award will be given at the 2014 CNS meeting to Xuezhe Han, MD, PhD, of Children’s Hospital in Boston for his presentation, titled “Urinary Biomarkers Identify Pediatric Brain Tumors Non-invasively and Correlate with Prognostic Risk Factors.” The award carries an honorarium of $1,000.

**BrainLAB Community Neurosurgery Award**

The BrainLAB Community Neurosurgery Award is awarded at each AANS and CNS meeting 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. At the 2014 AANS Annual Scientific Meeting, the award was given to Jan Coburger, MD, from the University of Ulm in Germany, for his presentation, “5-Aminolevulinic acid fluorescence exceeds Gd-DTPA enhanced intraoperative MRI in tumor detection at the border of glioblastoma multiforme: A prospective study based on a histopathological assessment.” At the 2014 CNS meeting, the award will be given to Stephen J. Price, BSc, MBBS, FRCS, PhD, of The University of Cambridge for his presentation, “IDH-1 mutated glioblastomas have a less invasive phenotype than IDH-1 wild type glioblastomas: a diffusion tensor imaging study.” The award carries a $1,000 honorarium.

**American Brain Tumor Association Young Investigator Award**

Sponsored by the American Brain Tumor Association, the Young Investigator Award is given at each AANS and CNS meeting 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. At the 2014 AANS Annual Scientific Meeting, the award was given to Eric M. Thompson, MD, of The Hospital for Sick Children and University of Toronto, for his presentation, “The Clinical Importance ofExtent of Resection in Medulloblastoma is Dependent on Molecular Subgroup.” At the 2014 CNS meeting, the award will be given to Brian V. Nahed, MD, of Massachusetts General Hospital, for his presentation entitled “Circulating Tumor Cells in Patients with Glioblastoma.” A $2,000 honorarium accompanied this award.

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Leksell Radiosurgery Award
Begun in 2009, this award, presented at each AANS Annual Scientific Meeting, is given to the best paper on stereotactic radiosurgery related to brain tumors. The award comes with a monetary component of $2,000. At the 2014 AANS Annual Scientific Meeting, the award was given to Isabelle M. Germano, MD, FAANS, of the Mount Sinai Hospital, for her presentation, “Clinical Outcome and Risk of spine deformity and vertebral compression fracture after Spine radiosurgery.”

Ronald L. Bittner Award
The Ronald Bittner 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 Annual Scientific Meeting on Brain Tumor Research by a resident or junior faculty member. This award includes a $1,000 honorarium. At the 2014 AANS Annual Scientific Meeting, the award was given to Shawn Hervey-Jumper, MD, of UCSF, for his presentation, “Awake craniotomy to maximize glioma resection: methods and technical nuances with 561 patients.”

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. Congratulations to the 2014 CNS Annual Meeting award winners.

The two lectureships supported by the section are not being given at the 2014 CNS meeting but are listed below, along with the names of the most recent winners:

Bittner Lecture
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, to be presented during the main scientific program component of the AANS Annual Scientific Meeting. At the 2014 AANS Annual Scientific Meeting, the Bittner Lecture was delivered by Fred Lang of MD Anderson. Nominees for the Bittner lecturer for the 2015 AANS Annual Scientific Meeting will be taken after the EC meeting occurring at the 2014 CNS meeting.

The Abhijit Guha Award
The Abhijit Guha Award and Lecture are jointly sponsored by the Section on Tumors and the Society for Neuro-Oncology (SNO) and is given annually alternating between the SNO and Tumor Section meetings. The first annual award was given to James Rutka, MD PhD at the SNO meeting in 2012 and the second award was given to Henry Brem, MD, at the 2013 CNS meeting. The 2014 award will be given at the SNO meeting in November 2014 to Ken Aldape, MD, with the next award given at the 2015 CNS meeting, for which nomination should begin to be collected by the EC in late 2014 and early 2015 in order to give the SNO and Tumor Section committees sufficient time to choose a winner.

2014 AANS Annual Scientific Meeting Recap
Jennifer Moliterno Gunel, MD
The Tumor Section enjoyed a successful and educational program at the 2014 AANS Annual Scientific Meeting in San Francisco. The two special seminars, “State of the Art Endoscopic Surgery” and “Interpreting the “New” Pathology Report: What the Tumor Surgeon Needs to Know for Clinical Applications,” featured some of the most prominent neurosurgeons and experts in the field and fostered great questions and conversations. We greatly appreciate our speakers and look forward to the CNS meeting in Boston!
The Tumor Section Guidelines Committee celebrated the endorsement and publication of the Progressive Glioblastoma Guidelines in the July 2014 issue of the Journal of Neuro-Oncology (JNO). Under the leadership of Jeff Olson, MD, FAANS; and Tim Ryken, MD, FAANS, and with major support from Laura Mitchell and the CNS national guidelines committee, these guidelines received unanimous final approval from the AANS/CNS Joint Guidelines Committee in May and were published in an expedited fashion, thanks to the support of Linda Liau, MD, PhD, FAANS, JNO Editor-in-Chief. We would like to especially thank the senior authors of each of the major chapters, including Drs. Ryken and Olson, Steven Kalkanis, MD, FAANS; Daniel Brat, MD, PhD; Samuel Ryu, MD; Patrick Wen, MD; Lakshmi Nayak, MD; John Buatti, MD; and Johnathan Morris, and many others in our writing groups from the Tumor Section and also from our multidisciplinary collaborations in radiation oncology, medical oncology, neuro- oncology, neuroradiology and neuropathology. This guideline initiative focuses on the difficult questions asked in tumor boards across the country: How best to treat GBM at recurrence? Specific chapters address the following questions in the clinical management and treatment of progressive GBM: Outcome assessment and Neurocognition; Role of Neuro-imaging (progression vs. radiation change); Role of Biopsy; Role of repeat Cytoreductive Surgery; Role of Radiotherapy Techniques (re-irradiation, stereotactic radiosurgery, brachytherapy); Role of Chemotherapy; and Future Innovations.

We are also pleased to report that a compendium of the history of all guidelines ever produced by the Tumor Section in the last 20 years was recently published in the August 2014 issue of Journal of Neuro-Oncology in honor of the 30th Anniversary of the Tumor Section. This historical summary, spearheaded by Mark Linskey, MD, FAANS; and Dr. Olson, also offered a paradigm for future guidelines and a path toward a more rigorous outcomes analysis of the impact of guidelines in actual clinical practice.

Future guidelines projects nearing completion include the Low Grade Glioma Guidelines, led by Drs. Olson, Ryken, Linskey and Kalkanis; these guidelines have been submitted to the Joint Guidelines Committee for final approval and endorsement, and we anticipate publication within a few months. Low-grade glioma guidelines chapters include Role of Imaging (Sarah Jost Fouke, MD, FAANS), Role of Biopsy (Brian Ragel, MD, FAANS), Role of Surgical Resection (Manish Aghi, MD, PhD, FAANS), Neuropathology and Molecular Markers (Daniel Cahill, MD, PhD, FAANS), Role of Radiation (Ian Parney, MD, PhD, FAANS), Role of Chemotherapy (Mateo Ziu, MD), Options for Recurrent Low Grade Glioma (Brian Nahed, MD) and Emerging Therapies for LGG (Andrew Sloan, MD, FAANS).

The multidisciplinary Pituitary Adenoma guideline, with full participation by neuro-endocrine and neuro-ophthalmology specialists, is now being led by Dr. Aghi, along with Chirag Patil, MD, FAANS; and Zack Litvack, MD. Final drafts will be submitted to the Joint Guidelines Committee this winter.

We welcome all participants, and anyone interested in working on guidelines projects is strongly encouraged to contact me at skalkan1@hfhs.org.

2014 CNS Meeting Preview

John S. Kuo, MD, PhD, FAANS

There are many exciting educational Tumor Section activities at the annual CNS meeting, Oct. 18-22, 2014, in Boston. The preliminary meeting program is available at www.cns.org.

Many tumor-related practical courses are scheduled on the weekend of Oct. 18-19. Multiple tumor-related luncheon and dinner seminars are also scheduled.

A new meeting format features Tumor Section sessions for the mornings of Monday, Oct. 20, and Tuesday, Oct. 21, followed by general scientific and other sessions.

Monday, from 7-8:30 a.m., the Tumor Section session is Emerging Technologies in Tumor Visualization and Therapy from Drs. Michael A. Vogelbaum, Aaron A. Cohen-Gadol, Nader Sanai, David W. Roberts, Edward R. Laws, Steven N. Kalkanis and John S. Kuo, MD, PhD, FAANS.

Monday afternoon, the Controversy session showcases debates by Drs. Andrew T. Parsa and Ossama Al-Mefty on the Extent of Skull Base Tumor Resections, and Drs. Anthony L. Asher and Douglas S. Kondziolka on Neoadjuvant Radiosurgery Followed by Resection of Brain Metastases: Yes vs. No. The following Consensus session features Management of Gliomas presented by Drs. Michel S. Berger, E. Antonio Chiocca, Andrew E. Sloan and Susan Chang. On Tuesday, from 7-8:30 a.m., award-winning and top-scoring tumor abstracts will be presented. Tuesday's Consensus session includes Management of Metastatic Tumors of the Spine by Drs. Ziya L. Gokaslan, Jason P. Sheehan, Timothy C. Ryken and John E. O’Toole. Selected oral posters from the Tumor Section will be presented at the afternoon Neurosurgical Forum.

At the Wednesday morning general scientific session, Dr. Fred Barker will present Tumor Trials – Are We Better Off Today Than Five Years Ago?

We look forward to seeing many Tumor Section colleagues and welcoming new members in Boston!
INTERNATIONAL COMMITTEE REPORT EC MEETING SPRING 2014

Isabelle M. Germano, MD, FAANS, Chair

The International Committee was involved in numerous projects over the past six months as highlighted below by some of our International members. In addition, it is worth mentioning two upcoming meetings of high interest to our membership. The European Association of Neuro-Oncology (EANO) will hold its biannual meeting in Turin, Italy, on Oct. 9-12, 2014. The European Association of Neurological Societies (EANS) Annual Meeting will be held in Prague, Czech, on Oct. 12-17, 2014, with numerous sessions on Neurosurgical Oncology.

ASIA

China

Yonggang Wang, MD, PhD

Highlights:
Professor Jizong Zhao was elected to be academician of China Academy of Science on Dec. 19, 2013. He is the leader of Chinese neurosurgery. He is also the director of neurosurgery center of Beijing Tiantan hospital and Chinese Association of Neurosurgery. He made outstanding contributions to the development of neurosurgery in China.

Two major neuro-oncology meetings were held in the past six months: the Annual Meeting of neuro-oncology, April 11-13, 2014 in Hefei, China, and the 3rd CSNO-SNO Joint Meeting, which was organized by Chinese Society of Neuro-oncology and American Society of Neuro-oncology, held on March 21-23, 2014 in Guangzhou. Many international neuro-oncologists were invited to give lectures at both meetings.

Future meetings:
• 9th Chinese Congress of Neurological Surgeons and 2nd international congress on minimally invasive technique in neurosurgery, Sept. 12-14, 2014, Xi’an, China; http://www.ccc2014.org
• 8th Chinese Conference on Oncology and 13th Cross-Strait Academic Conference on Oncology, Sept. 11-14, 2014, Jinan, China; http://www.csn.org.cn/2012/reg.asp
• 13th annual meeting of the Chinese neurosurgical society Nov. 6-8, 2014, Xiamen, China; http://www.cnsmeeeting.com/2014/cn/page.asp?hid=&pageid=1.html

Japan

Fumio Yamaguchi, MD, PhD

Highlights:
Japan Ministry of Health, Labour and Welfare approved the insurance claim for awake surgery for brain tumors from this April. The additional amount on the brain tumor resection (1,321,300 yen; $13,213) is 45,000 yen ($450). The minimum requirements for insurance claim are #1. Two neurosurgeons and one anesthesiologist in the hospital who have more than five years of experience and have attended a lecture by Japan Society for Awake Surgery, #2. One of the neurosurgeons has experienced more than five cases of awake surgery procedure. Also photodynamic therapy for malignant brain tumors using talaporfin sodium (NPe6) has been approved for its insurance claim for 100,000 yen ($1,000). These movements will promote the use and development of this kind of advanced technologies in brain tumor surgery.

Future meetings:
• The 33rd Annual Meeting of the Japan Society of Brain Tumor Pathology. May 29-30, 2015, in Takamatsu, Japan. http://btp33.umin.ne.jp

EUROPE

Switzerland

Dominik Cordier, MD

Highlights:
Swiss Glioma Network. Establishment of a central national database for data collection of glioma patients to study: The impact of complete resection of enhancing tumor on survival of patients with CRET-eligible glioblastomas: a retrospective

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multicenter study (CRET: complete resectability of enhancing tumor).

Stress, exercise behavior and survival in patients with newly
diagnosed glioblastoma and in a close partner (TOGETHER-
study): a prospective multicenter cohort study.

Also established fellowships in Montpellier, France, at the
Neurosurgical Department of Prof. Hugues Duffau (D. Cordier/
Basel and W. Surbeck/ St. Gallen) to increase theoretical
background and practical knowledge in the technique of awake
craniotomy under cortical/subcortical electrostimulation with
concomitant neuropsychological monitoring.

Additional research projects for 2015

Targeted radionuclide treatment of meningiomas not amenable
to surgical or conventional radiotherapeutical treatment
(Neurosurgery/Nuclear Medicine, University Hospital Basel).
Predictors of outcome in grade II/III glioma (Multicenter/ Swiss
Glioma Network)

Future meetings:
• National Meetings of the Swiss Society of Neurosurgery and
  Joint Meeting with the National Societies of Neurology and

CENTRAL AMERICA
Jose Edgardo Valerio-Pascua, MD, FAANS

Highlights
New neurosurgery oncology groups were developed to increase the
knowledge of new technology in the field in the following Central
American countries: Mexico, Honduras, El Salvador, Costa Rica,
Panama, Jamaica and Dominican Republic.

Between October 2010 and March 2014 in Latin America,
we structured and developed a new group of neurosurgeons
who specialize in neuro-oncology who participated at the Clan
2014 (Congress of Latino Americans Surgeons) in Isla Margarita
Venezuela, at the 2014 AANS meeting and now at the CNS
meeting.

Dr. Valerio-Pascua was elected Vice President of the Tumor
section for the FLANC (Federation of Latino America
Neurosurgeons) and will be the President for the Tumor section at
the CLAN, Cancun 2016.

In March we started multiple lectures in Honduras and
established a Neurosurgical office for management of brain tumors
and education for patients and physician. Since that time we have
been able to help around ten different patients with brain tumors,
metastasis, spine tumors, pituitary adenomas and skull base tumors
and we will establish a second office in Mexico City. This ability
to network allowed us to develop academic and business models
all around Central America, creating a new way to practice global
medicine, help underdeveloped countries and support medical
tourism.

In April, the government of Honduras charged Dr. Valerio-
Pascua to develop a Charter City with a hospital featuring the latest
technology, to focus on Medical tourism.

In El Salvador, Dr Eduardo Lovo developed the first Gamma Knife
Center in El Salvador, creating a Center of treatment and education
for all Central America. This has an important impact in the group
of Neurosurgeon with whom I work, in our mission to improve the
quality of care in the treatment in brain tumors and the ability to
bring the latest technology to Central American countries.

Recent Past meetings:
January 2014, we participated in Montego Bay in the National
Neurosurgery Congress, presenting lectures to discuss the
innovations and new techniques related to brain tumors.

February 2012, I had the opportunity to start an academic
relationship with the Department of Neurosurgery Oncology of the
Centro Medico Nacional Sieglo XXI, in Mexico City. I was invited
by the Mexican Neurosurgery Society to present a two-hour lecture
on the advances in neurosurgical oncology and radio surgery; we
also participated in the training for stereotactic frameless biopsy in
eloquent areas.

March 20-24, 2014 we participated in the 3rd International
Brain Tumor and Spine Surgery Symposium with cadaver lab
and in conjunction with the SLANC Society of Latino American
Neurosurgeons in USA and University of Miami, Cleveland
Clinic., Pittsburgh, New Mexico

July 2014, we participated in the International Brain Tumor
Symposium in San Salvador, El Salvador, with participation of
Neurosurgeon of the MD Anderson and Cleveland Clinic

July 2014, we participated in the Neurosurgery Oncology
symposium in Villa Hermosa, Tabasco, Mexico in the chapter of
the South East of Mexican Neurosurgery Society.

August 2014, we participated in the Annual Neurosurgery
meeting in Rosarito, Mexico, in the chapter of the northwest of
Mexico.
The current role of chemotherapy in the management of patients with glioma was the subject of one of the invited articles in the AANS/CNS Tumor Section’s 30th Anniversary Supplemental publication to the Journal of Neuro-Oncology (1). Medical therapies are an important adjunctive therapy for gliomas, and in the last 10 years, several randomized phase III trials were updated and reported clear success for the use of nitrosourea-based chemotherapy with radiation therapy in newly diagnosed high-risk, low-grade glioma (2) and anaplastic oligodendrogial tumors with loss of heterozygosity of 1p19q (3-4). Although some progress has been made in glioblastoma, (5) considerable work needs to be done to improve the outcome of patients with anaplastic astrocytoma and glioblastoma. Despite promising results in the recurrent setting, randomized trials of anti-angiogenic strategies have not conferred a survival benefit in newly diagnosed glioblastoma.

The recent molecular characterization of gliomas has clarified a framework of different subtypes of these tumors and has revealed pathways that will help the development of more effective targeted therapies. The diagnosis of gliomas is currently based primarily on a clinicopathological assessment. Although this is a valuable approach that permits the distinction of different grades within the same tumor type that may be of prognostic value, there are drawbacks to this classification system. Inter and intra observer reporting variability, especially for the lower grade and mixed histologies, are major limiting factors. Genomic analyses can provide insight into the underlying tumor biology that can further classify different subtypes of tumors that may inform treatment plans, impact patient outcome and improve response to treatment. For example, recent discoveries of pathogenic mutations in IDH1, IDH2, ATRX, CIC and FUBP1 have helped genomic characterization of gliomas and appear to provide more robust prognostic information, regardless of whether classified as grade II or III glioma. These mutations form the framework of molecular pathogenesis of these tumors and offer robust markers that not only enhance classification but can also guide treatment.

Integration of pathogenic mutations is planned in the revision of the World Health Organization grading system for central nervous system tumors.

Precision therapy or tailor-made treatment based on the molecular evolution of glioma will require implementation of an efficient workflow for tissue acquisition and processing, and standardization of biomaterial extraction. Sequencing of tissue employing high-throughput genomic technology, and bio-informatic support for data analysis to generate therapeutic recommendations for each individual, will need to be coordinated. The genomic profiling may not only inform diagnosis but could alter treatment approach as more targeted agents are available in the future. In addition, clinical trials are being conducted that focus on repositioning FDA-approved agents using a precision medicine approach.

References

The use of minimally invasive procedures in surgical neurooncology is a young and rapidly growing field. Laser-induced thermal therapy (LITT) has shown promise over other minimally invasive techniques, due to its superiority in delivering an ablative dose of thermal energy in a highly controlled manner with minimal collateral damage\(^1\). The use of magnetic resonance imaging (MRI) has enhanced the functionality of LITT by its ability accurately visualize lesions intra-operatively and control the delivery of thermal energy in real time\(^6\).

**LITT Background**

LITT delivers laser energy through a fiberoptic catheter to a target area of interest, where thermal diffusion of the absorbed laser energy leads to damage of target tissue\(^2\). The technique involves placing a water- or saline-cooled catheter into tissue and transferring light energy to the tissue in the form of heat. The thermal energy induces damage to intracellular DNA and DNA binding structures, ultimately leading to cell death\(^4\). The traditional laser utilizes a neodymium-doped yttrium aluminum garnet (Nd:YAG) transmitting a wavelength of light of 1064nm to the optical diffusing tip, creating a spherical volume of thermal radiation exhibiting a 2-3cm diameter of coagulative necrosis and a surrounding spherical annulus extending to a total of 3-4cm in diameter where sub-coagulative heating occurs\(^4,5\). The goal of LITT is to create a well-circumscribed focal lesion of predictable dimension, while avoiding extreme heating, which can lead to tissue vaporization, cavity formation, damage to normal tissue or initiation of char, which reduces the penetration of the light within tissue\(^6\). The extent of the lesion is therefore limited by the rate of heating and thermal diffusion, and one of the key components of the LITT procedure is manipulating the amount and rate of thermal energy delivered to the target tissue\(^6\).

LITT provides the controller with a means of controlling the temperature at the applicator tip\(^7\); however, this demands a very accurate method of identifying tissue temperatures at a very fine spatial resolution. MRI, which is well suited to image the soft tissue of the brain, also provides the sensitivity needed to view the temperature changes induced by LITT\(^3\), and when used thus intraoperatively to guide LITT is referred to as magnetic resonance-guided LITT (MR-LITT, or sometimes seen as MRgLITT).

**Patient selection**

Patients should be functionally independent and without contraindications to MRI. Ideally, the area of recurrence should be typically less than 3cm diameter, well circumscribed, enhancing and noninfiltrating. Sizes larger than 3cm pose a significant risk of post-ablation edema that cannot be controlled medically.

Careful precautions must be made while choosing a trajectory. Special planning considerations must be made for highly eloquent areas (thalamus, basal ganglia, brainstem) in order to avoid unnecessary post-ablation edema. In some cases, passing through virgin white matter should take priority over creating the shorter trajectory if the shortest trajectory involves eloquent tissue.

**Advantages of MR-LITT**

There are several advantages of MR-LITT when compared to resection of recurrent HGG. There is decreased risk of injury to structures superficial to the tumor as compared to open surgery. In addition, the ability to reach tumors in locations too difficult to attempt reaching by open resection is also afforded. The hospital stay is shorter as the median length of stay is one day, and the recovery period is shorter in duration as well. Patients are at much less risk of wound breakdown as the stab incision required for placement of the catheter is significantly smaller than reopening a previously irradiated craniotomy incision. Furthermore, the minimally invasive approach allows patients to receive further adjuvant radiation or resume previous chemotherapy, such as bevacizumab, more quickly than standard re-resection. The procedure can also be repeated if needed for new areas of recurrence.

**Current Literature**

Early published results using MR-LITT for recurrent HGG suggest that MR-LITT may provide a survival benefit in patients with recurrent glioblastoma\(^8\). Standard surgical treatment of recurrent glioblastoma has been cited to only increase prognosis by eight weeks within the range of three to five months survival from the diagnosis of recurrence\(^1\). Early literature on MR-LITT has demonstrated a median survival from diagnosis of recurrence between 9.4-18 months, seemingly increasing prognosis when compared to invasive surgery. In the largest neurosurgical MR-LITT study to date, Mohammadi et al., in 34 patients with 35 cases of HGG\(^9\), finding that patients whose tumors were ablated >95 percent of their volume exhibited a median PFS of 9.7 months, compared to 4.6 months in patients whose tumors were ablated <95 percent of their volume. This suggests that survival may be correlated to volume of recurrent tumor ablated. Permanent complications from MR-LITT occurred in 16.7 percent of cases and were: hemorrhages/hematomas (7.6%), 3 wound infections (4.5%), permanent worsening of focal neurologic deficit (3%), and white matter tract injury leading to hemiparesis (1.5%). This is comparable to the complication rates seen in literature for open surgery for recurrence.

**Conclusion**

To date, use of MR-LITT has been explored as a minimally invasive option for the treatment of recurrent HGG. Early published literature suggests that MR-LITT can be used safely and effectively to improve survival outcomes and quality of life of patients with recurrent HGG. Further data, in the form of a

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*continued on page 12*
prospective trial, will be needed to further assess its adjunctive role in neuro-oncology.

References
This year continues to be very busy, with lots of opportunity for academic interaction regarding skull base tumors. In April, the 82nd AANS Annual Scientific Meeting in San Francisco offered numerous abstracts, proffered papers and practical courses dealing with all aspects of the management of skull base tumors.

The European Skull Base Society meeting was held in Paris, June 26-28, 2014. There was extensive representation of members of the AANS/CNS Section on Tumor on the program. Additionally, international skull base experts, such as Bernard George, MD; Mario Sanna, MD; and Madjid Samii, MD, PhD, discussed their decades-long experience managing some of the most difficult problems in skull base surgery. There were 31 panels covering a broad spectrum of pathologies, 10 keynote lectures, seven instructional seminars and 248 abstracts accepted for oral presentation in 28 sessions. The pre-meeting practical course, organized by Sebastian Froehlich, included cadaveric dissections of endoscopic and microscopic approaches to the skull base at the state-of-the-art IRCAD facility in Strasbourg, France.

Similarly, the North American Skull Base Society (NASBS) summer resident course was held July 11-13, 2014, at the Louisiana State University (LSU) dissection facility in New Orleans and featured hands-on cadaver dissections of endoscopic trans-nasal and microscopic approaches to the anterior, lateral and posterior skull base. Twenty-nine senior residents from programs across the U.S. attended and participated.

The abstract site is currently open for the 25th annual meeting of the NASBS to be held February 20-22, 2015, at the Tampa Convention Center in Tampa, Fla. There will be a pre-meeting practical course for residents, fellows and practicing surgeons on Feb. 18-19, 2015, at the Center for Advanced Medical Learning and Simulation (CAMLs) lab adjacent to the Tampa Convention Center, encompassing the broad range of technical skills necessary to undertake skull base surgery. Included this year for the first time will be an opportunity to practice microvascular anastomosis on live animals. The theme of this year’s meeting is “The whole is greater than the sum of the parts,” emphasizing the multidisciplinary teamwork involved in caring for patients with skull base tumors. This year’s honored guests include Harry van Loveren, MD, FAANS; Dade Lunsford, MD, FAANS; and Edward Laws Jr., MD, FAANS(L).

Plans are already underway for the Skull Base Techniques for Senior Residents course, sponsored by the Neurosurgery Research and Education Foundation (NREF), at the Medical Education & Research Institute (MERI) facility in Memphis, Tenn., led by former AANS President Jon Robertson, MD, FAANS, on March 12-15, 2015. This course offers senior residents the opportunity to learn from a very experienced faculty and perform dissections, based on the 3D anatomy lectures by Albert Rhoton Jr., MD, FAANS(L).

Finally, of course, the upcoming CNS meeting, Oct. 18-22, 2014, in Boston, promises to once again offer a large number of educational opportunities pertaining to skull base tumors. There is a new exciting controversy session regarding Extent of Resection of Benign Skull Base Tumors, featuring experts in the field debating this pertinent topic. There are practical courses, including Brain Tumor Update, Endoscopic and Keyhole Approaches to the Anterior Skull Base and Cranial Neurosurgery Complication Avoidance and Management. There are luncheon seminars planned, including an interactive lunch on neuro-oncology, a luncheon reviewing pituitary tumor surgery techniques and a luncheon dedicated to new frontiers and innovations in radiosurgery.

Tumor section members interested in skull base tumors should continue to keep in mind that there are several awards offered by the tumor section specifically targeting skull base topics, such as the Integra Foundation Award for the best abstract regarding benign brain, spinal or peripheral nerve tumors and the Synthes skull base award. Additionally, skull base abstracts could be considered for the Stryker Neuro Oncology Award and the Leksell Radiosurgery Award.

I look forward to seeing everyone in Boston and Tampa prior to the next AANS Annual Scientific Meeting, May 2-6, 2015, in Washington, D.C.
The 2014 Society for NeuroOncology (SNO) Annual Meeting will be held in at the Loews Hotel in Miami Beach, Nov. 13-16, 2014. Note that these dates are one week earlier than the usual meeting dates. Details and registration information are currently available on the SNO website.

SOT Executive Committee member Gelareh Zadeh, MD, is co-chair of SNO’s 2014 Annual Meeting, and she and co-chair, Patrick Wen, MD, have made a number of changes to the program designed to provide more diversity to the sessions. In particular, they have increased the number of surgically relevant oral presentations. For this meeting there will be five or six Sunrise Sessions each day (increased from three), and three concurrent afternoon sessions (increased from two). Platform presentations will be reduced from 15 minutes to 10 minutes, and this change will allow for the inclusion of a new class of presentations, called Rapid Reports. These reports will be five minutes in length, with a discussant summarizing the reports at the end of each hour. Finally, this meeting will introduce ePosters to supplement the traditional board posters. Overall, there will be 102 full oral presentations, 71 rapid reports, 574 traditional posters and 122 ePosters.

Other changes include the development of electronic resources during the meeting for online access to abstracts and the program. Special sessions will include two Town Halls: a Response Assessment in Neuro-Oncology Criteria (RANO) update on Saturday, and a World Health Organization Classification update on Sunday. There will be a mini-symposium on Immunotherapy and another symposium on Tumor Metabolism, which will include talks by Craig Thomson, Tak Mak, Matthew Vander Heiden and Sarah Nelson. There will be three lunch sessions, including one on the Six Pillars surgical technique. Finally, there will be evening symposia on Thursday (Brain Metastases) and Friday (Immunotherapy).

SNO and the AANS/CNS Section on Tumors continue to have discussions regarding a possible joint meeting in 2017. As you may recall, we have had several joint meetings in the past, all of which were considered to be successful in terms of both scientific content and financial performance. The first of these meetings occurred in 2009, when SNO did not have its own annual meeting, due to the World Federation of Neuro-Oncology meeting, which was held in Japan. The CNS/Section on Tumors administered that meeting, and SNO served as a partner with a clearly defined financial contribution and return. In 2011, a joint meeting between SNO and Section on Tumors was administered by SNO, and the Tumor Section had equal representation on the scientific program committee. This meeting was an unprecedented financial success for the Section on Tumors, due to the inclusion of a provision that allowed the section to retain all revenue from neurosurgery-dedicated vendors that it secured independently from SNO. In 2013, SNO and the Tumor Section partnered to support a multidisciplinary Symposium on Meningiomas, which was well attended.

Currently, SNO is planning its 2017 Annual Meeting, to be held in San Francisco. There have been preliminary discussions regarding about holding the Section on Tumors Satellite Meeting in conjunction with the SNO meeting, in an arrangement similar to the one used in 2011. From the perspective of SNO, the scientific program committee and chairs for the 2017 meeting will not be named until after the next officer election cycle in late 2015. That said, the SNO board of directors is supportive of continuing to run joint meetings with the Section on Tumors. Ultimately, the decision as to whether or not to partner with SNO in 2017 rests with current Tumor Section leadership.
**Update from the Young Neurosurgeons Committee**

**Ian F. Dunn, MD, FAANS; and Kaisorn Chaichana, MD**

The Tumor Section/Young Neurosurgeons Committee reception was held at the AANS Annual Scientific Meeting in San Francisco in April, where we were fortunate to welcome James Markert Jr., MD, FAANS, chair at the University of Alabama-Birmingham, as the honored guest. Dr. Markert shared a David Letterman-style list of “top 10” lessons for younger neurosurgeons beginning neurosurgical careers, with a focus in neuro-oncology:

10. Develop an individual strategic plan (and don’t be afraid to change it).
9. Don’t be afraid to say no (but say yes at the right time).
8. Establish a database and a means to feed it.
7. Carve out time to reflect.
6. Don’t be afraid of philanthropy.
5. Get involved.
3. Develop and maintain friendships, collaborations and relationships with individuals at other institutions — neurosurgical and outside neurosurgery.
2. Develop collaborative, multi-disciplinary teams.
1. Utilize mentors.

Before all else: Maintain a source of inspiration and be true to your ideals.

All were grateful to Dr. Markert for sharing his experience and insight during a terrific evening.

We are equally excited to announce E. Antonio Chiocca, MD, PhD, FAANS, chair of the department of neurosurgery at the Brigham and Womens’ Hospital, as the speaker for the next installment of the Tumor Section/Young Neurosurgeons Committee reception, to be held at the upcoming CNS meeting in Boston. Details to follow for what will be another great event.

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**Washington Committee Update**

**Andrew Sloan, MD, FAANS**

The Washington Committee continues to request increased transparency and rational changes to Centers for Medicare and Medicaid Services (CMS) policy with respect to physician performance data, Physician Quality Reporting Systems (PQRS) and Value-based Payment Modifier (VM) Programs. The committee has pushed vigorously for the National Neurosurgery Quality and Outcomes Database (N2QOD), which currently is comprised primarily of spine data but will soon incorporate stereotactic radiosurgery and tumor surgery to be accepted as a Qualified Clinical Data Registry (QCDR). The Washington Committee has also suggested that all neurosurgeons collaborating with industry consider reviewing the “Open Payments” website for accuracy prior to Sept. 8, 2014. Finally, recent reviews reveal that neurosurgery has the highest frequency of open claims at 19.1 percent versus 7.4 percent for all physicians on average.
Clinical Trials

Each issue of the Tumor Section Newsletter will feature a more in-depth look into two clinical trials; one sponsored by the Alliance for Clinical Trials in Oncology, and the other by the Radiation Therapy Oncology Group. The focus will be on those trials that may be of particular interest to neurosurgeons.

RTOG Trial Highlight

NRG Oncology: Legacy group study RTOG 1205 – Randomized Phase II Trial of Concurrent Bevacizumab and Re-Irradiation Versus Bevacizumab Alone as Treatment for Recurrent Glioblastoma
Daniel Cahill, MD, PhD, FAANS; and Michael Vogelbaum, MD, PhD, FAANS

In 2014, the National Surgical Adjuvant Breast and Bowel Project (NSABP), the Radiation Therapy Oncology Group (RTOG) and the Gynecologic Oncology Group (GOG) successfully unified as a National Cancer Institute (NCI)-funded cancer clinical cooperative group known as “NRG Oncology.” The three legacy groups have continued to carry out NCI-supported trials as independent but collaborative entities during the transition to integration. As of the second quarter of 2014, the new cooperative group’s federal research activities are now managed through the NRG Oncology Operations Center. The legacy RTOG is currently leading three glioma clinical trials that are open for recruitment (http://www.rtog.org/ClinicalTrials/ProtocolTable.aspx).

Here, we highlight one study for recurrent glioblastoma patients, RTOG 1205, which is a randomized phase II study bevacizumab with and without re-irradiation. The protocol notes, “Based on the long history and clinical experience of re-irradiation of recurrent glioblastoma, we wish to obtain prospective multi-institutional safety and efficacy data regarding the combination of bevacizumab and re-irradiation in improving overall survival in bevacizumab-naive recurrent glioblastoma patients. ... Despite numerous randomized chemotherapy studies as well as novel targeted agents studied to date, no regimens have shown significant improvement in overall survival compared to bevacizumab alone. Single-agent bevacizumab is currently the mainstay of treatment in recurrent glioblastoma, but the overall survival remains limited at approximately 8 to 9 months. ... The goal of this study is to test the hypothesis that re-irradiation combined with an effective targeted agent, bevacizumab, will improve the overall survival of bevacizumab-naive recurrent glioblastoma patients. This trial will also be the first prospective multi-institutional study to evaluate survival, response, and patterns of failure following re-irradiation.”

The key contribution of neurosurgeons for patient enrollment in this trial comes through the identification of glioblastoma patients who, at recurrence, are considering salvage treatment options, whether surgery or bevacizumab or other experimental options.

Alliance Trial Highlight

J. Bradley Elder, MD

Additional information regarding the Alliance is available on the website allianceforclinicaltrialsinoncology.org.

Past report highlights have included a trial for recurrent glioblastoma and another for resected brain metastases:

- A Phase II Randomized Trial Comparing the Efficacy of Heat Shock Protein-Peptide Complex-96 (HSPPC-96) (NSC #725085, ALLIANCE IND # 15380) Vaccine Given With Bevacizumab Versus Bevacizumab Alone in the Treatment of Surgically Resectable Recurrent Glioblastoma Multiforme (GBM).
  - PI: Andrew T. Parsa, MD, PhD; Northwestern University Medical Center

The trial highlighted in this report focuses on another common entity in neurosurgical oncology — anaplastic glioma. Specifically, this trial focuses on the roles of postoperative adjuvant radiation and chemotherapy for patients with 1p/19q co-deleted anaplastic gliomas. The clinical trial is titled:

- Phase III Intergroup Study of Temozolomide Alone Versus Radiotherapy With Adjuvant PCV Chemotherapy in Patients With 1p/19q Co-deleted Anaplastic Glioma

This clinical trial will enroll patients with newly diagnosed or less than three months from surgical diagnosis of an anaplastic glioma (oligodendrogloma, astrocytoma or mixed oligo-astrocytoma) which is co-deleted for 1p and 19q. Patients must be greater than two weeks from surgery (gross total resection, partial resection or biopsy) and be fully recovered from surgery.

After stratification based on cooperative group, age and ECOG performance score, patients will be randomized to one of three treatment arms:

- Arm 1: Radiation therapy followed by PCV chemotherapy
- Arm 2: Radiation therapy with concomitant temozolomide, followed by monotherapy with temozolomide
- Arm 3: Temozolomide

Primary objective:

- Determine if radiation therapy with concomitant temozolomide followed by adjuvant temozolomide improves progression free survival compared to patients who receive radiation therapy followed by PCV chemotherapy
Secondary objectives:
• Determine whether patients who receive temozolomide alone have longer time to neurocognitive, clinical or radiographic progression compared to patients in the other two treatment arms who receive radiation as part of their therapy
• Determine survival differences based on translocation status and MGMT promoter hypermethylation status
• Descriptive comparisons of secondary outcome endpoints, including overall survival, tumor response and quality of life
• Descriptive comparison of toxicities in each treatment arm
• Determine differences in neurocognitive and quality of life effects between treatment arms
• Descriptive comparison regarding timing of radiation therapy by evaluating time to progression and progression free survival

This trial is open at 85 centers in the United States and Canada. The PI is Kurt Jaeckle, MD, at Mayo Clinic. Further information regarding this clinical trial can be obtained from allianceforclinicaltrialsinoncology.org or clinicaltrials.gov. A list of ongoing trials sponsored by the Alliance, current as of August 2014, is attached.

The fall Neuro-Oncology meeting is Friday, Nov. 7, 2014, in Chicago. For details regarding the meeting, please contact myself or Ian Parney, MD, PhD, FAANS.

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