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## Chairman's Message



Joseph M.  
Piepmeier, MD

I want to thank the membership of the AANS/CNS Section on Tumors for the opportunity to serve as your Chairman for the past two years. During my tenure as Chairman, I have had the pleasure of working with outstanding members of the Executive Committee who have

dedicated their time and considerable talents to supporting the activities of the Section.

Following the 2001 AANS Annual Meeting in Toronto, Jim Rutka, MD, will become Chairman and Raymond Sawaya, MD, will become the Secretary/Treasurer. These are internationally recognized leaders in neuro-oncology and the Section will be in very good hands.

During the past two years the Section has offered several venues for education in neuro-oncology through the AANS and CNS annual meetings as well as a Satellite Symposium, which was a great success. In addition, the Section has financially supported the Washington Committee and the *USA Today* insert, launched the online service *Select*

*Review*, established an outreach process for young neurosurgeons to learn about the Section, increased membership and worked on guidelines for management of low-grade gliomas, metastatic tumors and glioblastoma. These efforts are designed to enhance your practice and improve the quality of care for patients.

The treatment of primary brain tumors continues to be a challenge. However, those of you who have attended our scientific sessions and symposia already know that we are entering a new era in the treatment of gliomas. Novel strategies including immunotherapy, targeted toxins and gene therapy are emerging.

The Section will continue to provide the educational experience for neurosurgeons to learn about the future of our discipline.

I want to thank the Pediatric Brain Tumor Foundation, the Brain Tumor Society, National Brain Tumor Foundation, the Preuss Foundation, the American Brain Tumor Association and the Farber Foundation for their generous support in helping us recognize the clinical and laboratory work that is vital for finding a cure. This is an exciting time for neuro-oncology and I encourage all of you to get involved in this effort.

*Joseph M. Piepmeier, MD, Chairman, AANS/CNS Section on Tumors.*

## Section on Tumors Officers

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Joseph M. Piepmeier, MD

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Mark Bernstein, MD

### Secretary-Treasurer

James T. Rutka, MD, PhD

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Raymond Sawaya, MD

### Bylaws

Jack P. Rock, MD

### Education

William T. Couldwell, MD, PhD

### International

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Andrew H. Kaye, MD  
David G.T. Thomas, MD  
Manfred Westphal, MD  
Jun Yoshida, MD

### Membership

Michael W. McDermott, MD

### Membership Services

Anthony L. Asher, MD

### Newsletter

Ronald E. Warnick, MD

### Nominating

Mark Bernstein, MD

### Program

Gene H. Barnett, MD  
Ennio A. Chiocca, MD, PhD

### Research

Roberta P. Glick, MD

### Task Forces

Ian F. Pollack, MD  
Jack P. Rock, MD

### Young Neurosurgeons Liaison

Frederick F. Lang, Jr., MD

# Children's Oncology Group

By Ian Pollack, MD

The Children's Oncology Group (COG) is a multi-institutional cooperative group funded by the National Cancer Institute that is dedicated to improving the treatment and quality of life of children and adolescents with cancer. Two years in the making, this group represents a fusion of the former Children's Cancer Group, Pediatric Oncology Group, and two other smaller cancer study groups. Because brain tumors are the most common solid tumor of childhood and the leading cause of death among childhood cancers, particular attention within the group is focused on improving the outcome for these tumors.

The specific goals of the COG Brain Tumor Committee (BTC) are: 1) to develop comprehensive treatment approaches to improve the survival of children with brain tumors, 2) to develop strategies for reducing treatment-related long-term sequelae, 3) to perform neurobiological investigations of childhood brain tumors and incorporate significant results into aspects of care and 4) to evaluate novel therapeutic strategies for central nervous system (CNS) tumors that are resistant to present treatments.

The BTC is comprised of members from a variety of disciplines, including pediatric oncology, radiation oncology, neurology, neurosurgery, neuropathology, neuroradiology, biostatistics, endocrinology, psychology, neurobiology and nursing. The BTC has liaisons within the COG New Agents Committee, Epidemiology Committee, Biology Committee and Supportive Care Committee. It also has a multi-site Brain Tumor Resource Laboratory that addresses relevant biological questions with existing tumor specimens and endeavors to incorporate fundamental biological questions into future clinical studies of the group.

Structurally, the BTC includes an executive Steering Committee, chaired by Ian Pollack, MD, and comprised of representatives from the aforementioned disciplines and the co-chairs of the following standing disease-specific subcommittees: 1) high-grade glioma, 2) low-grade glioma, 3) medulloblastoma/PNET, 4) ependymoma, 5) brainstem glioma, 6) infant tumors and 7) germ cell tumors. The subcommittees include investigators currently chairing studies within that disease group, a number of established and young investigators working on new protocol concepts and a cadre of other interested investigators.

The steering committee is responsible for maintaining a smooth flow of new study concepts and evaluating the progress of ongoing studies. A new agents subcommittee facilitates the translation of promising agents to the treatment of brain tumors and is a liaison to the Pediatric Brain Tumor Consortium, a NCI-supported phase I consortium.

## Underlying Hypotheses

The Brain Tumor Committee has developed biological and therapeutic studies for each of the major types of childhood brain tumors that are based on a number of common underlying hypotheses. The first hypothesis is that the identification of biological markers of tumor behavior will allow risk-adapted treatment of childhood brain tumors. Ongoing studies within the group are evaluating the following: 1)

molecular prognostic factors for high-grade gliomas, 2) the relationship between proliferation index and outcome for low-grade gliomas and 3) the association between molecular markers and outcome among medulloblastomas. Additional studies are in various stages of concept development.

The second hypothesis being pursued is that optimization of chemotherapy will improve survival for children with high-risk brain tumors. A series of recently completed studies for these tumor types, such as poor-risk medulloblastoma (CCG-9931), high-grade glioma (CCG-9933 and POG 9431) and brainstem glioma (CCG-9941), evaluated the efficacy of various combinations of active agents in a submyeloablative pre-irradiation window in order to identify promising combinations for incorporation in subsequent adjuvant studies. These studies all reached their accrual goals, but have failed to demonstrate an obvious improvement in survival versus that observed historically with conventional approaches; however, longer term outcome analysis for the 9931 and 9933 studies are warranted and are in progress.

A comparison of conventional versus dose-intensified chemotherapy over prolonged periods in malignant infant tumors (POG 9233) demonstrated equivalent disease control in the embryonal tumors in this age group but improved outcome in infant ependymomas with intensified chemotherapy. Ongoing studies (CCG-99702, 99703, ADVL0011) are evaluating the feasibility of administering myeloablative consolidation regimens to two particularly high-risk groups—high-stage medulloblastoma/PNET and infant brain tumors—and submyeloablative regimens to children with newly diagnosed high-grade gliomas and bulky residual disease. A study of intensive chemotherapy for malignant germ cell tumors is also under development (ACNS0122).

The third hypothesis is that new radiation technology may improve the therapeutic ratio in pediatric brain tumors. A trial of limited volume, 3-D conformal irradiation after relatively brief induction chemotherapy has just opened in infant medulloblastoma (P9934). Similar methodology will be used in the new ependymoma study (ACNS0121) and is being considered for the next standard-risk medulloblastoma trial and for recurrent, unresectable central low grade gliomas.

The fourth hypothesis is that radiosensitization or combined chemoradiation will improve outcome of high-risk tumors that are resistant to current treatment modalities. This hypothesis is being pursued in high-risk medulloblastoma (CCG-99701 and POG 9631) and brainstem glioma (CCG-09712, CCG-09802, POG 9836, POG 9879, and ACNS0123) and being considered for study concept development in high-grade non-brainstem glioma (ACNS0131).

The final hypothesis is that the rational combination of chemotherapy approaches for selected favorable risk tumors will allow reduction of treatment-related sequelae. Current studies in favorable outcome tumors, such as low-grade glioma (CCG-9952) and standard-risk medulloblastoma (A9961), are comparing two active regimens for each tumor type in a phase III setting, either without radiotherapy (9952) or with doses of irradiation that are reduced in

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# Minutes of the Executive Council Meeting

James T. Rutka, MD

Monday September 25, 2000

San Antonio, Texas

In attendance were Drs. Piepmeier (Chairman), Rutka (Secretary-Treasurer), Bernstein, Couldwell, Black, Barnett, Warnick, Van Loveren, Bruce, Liau, Lang, Asher, Rosenblum, Rock, Sawaya, McDermott, Glick and, by invitation, Mr. Tom Marshall, AANS.

## Committee Reports

### Secretary/Treasurer

The minutes of the Executive Council, which met April 10, 2000, at the AANS Annual Meeting in San Francisco, were reviewed and accepted.

Dr. Rutka reported on the financial statements of the AANS/CNS Section on Tumors. Total assets were \$286,971, up approximately \$21,000 from the year before. The improvement in the Section's finances was attributed to the success of the Satellite Symposium in San Francisco, which brought in a profit of approximately \$30,000. Cash contributions for the awards from the National Brain Tumor Foundation, The Preuss Foundation, the Farber Award and American Brain Tumor Association were received and deposited.

Examples of expenses for the Section include: the newsletter at approximately \$4,000 a year, awards and honoraria at approximately \$16,000 a year, the *USA Today* insert (a \$5,000 one-time charge), and the reception for prospective new members as well as biannual food and beverage charges for the Executive Council at approximately \$5,000 a year. The next Washington Committee donation of \$25,000 from the AANS/CNS Section on Tumors will be made after October 2000.

### Awards

The award winners at the CNS meeting were: Preuss Award, Michael Taylor, MD; Mahaley Clinical Investigator Award (sponsored by the National Brain Tumor Foundation), Ron Warnick, MD; and Young Investigator Award (sponsored by the American Brain Tumor Association), John Yu, MD.

Dr. Sawaya was congratulated for maintaining excellent lines of communication with the ABTA, NTBF and the Preuss Foundation. Plans are being made to meet with executive members of each of these award-sponsoring agencies at the AANS Annual Meeting in April in Toronto.

Follow-up letters of appreciation and thanks after last year's AANS meeting were sent to Naomi Berkowitz of the ABTA, Peter Preuss of the Preuss Foundation and Janice Brewer of the NBTF. Announcements were also made regarding the award winners of the CNS prizes in San Antonio. In addition, photos taken of the award presentations in San Francisco at the AANS meeting were forwarded with a letter from Dr. Sawaya to the ABTA, Preuss Foundation and NBTF.

### Bylaws

Dr. Rock reported there were no new issues concerning the bylaws of the Section.

### Guidelines

Dr. Rock provided an update for the guidelines project for patients with high-grade glioma.

### Membership

Dr. McDermott announced the addition of approximately 70 new members to the Section. Dr. McDermott has been working closely with Sandy Meyer, the new point person in the AANS head office regarding membership for the Joint Sections. Membership, which now stands at 710, can be broken down as follows: 468 active, 49 international, 104 resident, 37 associate, three honorary and 49 adjunct.

Dr. McDermott wrote to the following individuals to act as regional liaisons to the Section in an unofficial capacity to recruit members to the Section: Pacific, Andrew Mamelak; Mountain, Randy Jensen; Central-North, Walter Hall; Central-South, James Markert; Eastern-North, Fred Barker; Eastern-South, Jeff Olson.

Dr. Piepmeier asked for continued monitoring of the role that these regional representatives will play with the Section. McDermott was thanked for his outstanding job with the membership subcommittee.

### Membership Services

Dr. Asher reported on the progress of *Select Review*, which will be launching its second issue very shortly. Issues regarding the AANS and CNS with respect to duplication of membership services were discussed briefly.

Prior to the CNS meeting in San Antonio, an unfortunate error in the establishment of the listserv for the Section led to a barrage of unexpected e-mails. The error was acknowledged as arising from the AANS head office and had largely been dealt with by the time of the CNS meeting in San Antonio.

An apology e-mail will be sent to all members of the Section, and then the listserv will be re-established in a correct fashion. It was hoped that this initial problem would not discourage participation in the Section's listserv. A discussion followed regarding the best mechanism by which the most accurate e-mail addresses for members of the Section could be updated.

### Newsletter

The fall 2000 newsletter appeared prior to the CNS meeting in San Antonio. It contained an update from the Washington Committee, a detailed review of the proceedings of the *Fourth Biannual Satellite Symposium*, and an *Ask the Expert* section featuring Drs. Hassenbusch, Levin and Pietronigro.

Dr. Warnick announced that he will be focusing on the topic of the future treatment of patients with brain tumors in the year 2020 in the next issue of the newsletter. Dr. Warnick was once again thanked for an outstanding job with the newsletter.

### Nominating Committee

Mark Bernstein, MD, circulated a letter that reviewed the protocol by which the next Section Executive Committee will be selected. A subcommittee has been organized, and they will put forth the name of Dr. Rutka for Chairman. Two individuals whose names have been forwarded to the subcommittee will be put forward for a vote for the position of Secretary-Treasurer. Dr. Bernstein will endeavor to have these names available to the Section membership in the next two months.

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### Education Committee

Dr. Couldwell reported on the Medical School Curriculum Committee, which had received contributions that have become encyclopedic. In addition, Dr. Couldwell mentioned an interest in developing an educational Web site for the Senior Society, AANS and the CNS. After discussion it was suggested that the *Select Review* process and organization as coordinated by Dr. Asher within the Section would be the best vehicle for these groups. Dr. Couldwell was asked to transmit this information back to the Education committees of the AANS and CNS.

### Program Committee

Dr. Barnett described the program in place for San Antonio. Unfortunately, Greg Cairncross, MD, could not travel to San Antonio due to an unforeseen illness. It was suggested that Drs. Eric Holland and John Couldwell increase the time of their lectures to cover the time slot previously provided for Dr. Cairncross.

Dr. Chiocca had provided a written update of the program in Toronto, and this was reviewed. Dr. Rutka will help organize the CNS meeting in San Diego in 2001. Planning for this meeting is now under way.

### International Committee

A report was received from Andrew Kaye, MD, who was soliciting volunteers among the Section for participation in the World Federation of Neurosurgeons meeting in Sydney, Australia, in September 2001. Interested members were encouraged to write directly to Dr. Kaye.

### Young Neurosurgeons Report

Fred Lang, MD, organized a reception for the Section in San Antonio. The date was September 26 in the Marriott River Center Hotel. The purpose of the reception was to continue to recruit new members and to provide a forum for active members to come together in a social venue.

### Research Report

Dr. Glick reported on major issues with respect to gene therapy trials. There are now perceived structural difficulties between the FDA and local institutional IRBs. The NIH and FDA are providing stringent guidelines that protect patients from being approached for gene therapy trials.

### Washington Committee

Dr. Chin had provided information regarding the latest reports from the Washington Committee. Members were encouraged to read this information to understand the ways in which the \$25,000 donation provided last year by the Section was being used to support the Washington Committee.

### Satellite Symposium

The Satellite Symposium in San Francisco was a resounding success thanks to the efforts of Dr. Warnick. Through Dr. Warnick's active fund-raising efforts and superb organizational skills, the Satellite Symposium made approximately \$30,000 in profit.

The reviews of the Symposium were analyzed. Attendees requested more discussion time, more opportunity to visit posters and more time for an interactive social venue. The concept of

having a separate, stand-alone meeting was again discussed. The next Tumor Satellite Symposium is scheduled for 2002 in Chicago at the AANS Annual Meeting.

### Select Review

Dr. Asher has written formally to the Section requesting one quarter salary support for a secretary to look after the issues of *Select Review*. A vote was held, and it was passed that \$7,000 per year would be forthcoming to Dr. Asher. Dr. Rutka will ensure that Dr. Asher receives this on an annual basis. Support for a three-year time period was approved. This support will be reviewed annually. Dr. Asher will provide biannual updates as to how this support is being used to further *Select Review* initiatives.

### Cell Phone Issue

In response to a request from Stan Pelofsky, MD, President-Elect of the AANS, Dr. Rutka will write a position statement regarding the association of human brain tumors and the use of cellular telephones. This position statement then will be reviewed by the AANS Executive Committee for final recommendations.

### Drug and Development

Corey Raffel, MD, had sent a letter stating that there was no new business to relate at this time.

### USA Today

A letter was received from Dr. Dunsker, AANS President, thanking the Section for its \$5,000 contribution to the *USA Today* insert, which featured the field of neurological surgery.

### Membership Services

E-mail correspondence regarding the role of the Section's pursuit of active members from the resident pool was placed in the program booklet. It was suggested that the AANS and CNS headquarters offices notify all resident members of their potential to join the Section as active, full members following the completion of their residency training.

### AANS/CNS Relations

E-mail correspondence from the AANS regarding a possible merger with the CNS were attached in the program booklet. It was conceded that this was a major issue facing all of organized neurosurgery. The officers of the AANS and CNS met in July but their stances were still far apart. The role of the Council of State Neurological Societies was discussed. The CSNS may play a role in determining how the relations between the AANS and CNS will be settled.

### Neurosurgical Focus

Information was provided from Dr. Weiss regarding *Neurosurgical Focus* and contributions from the Section. Drs. Liau and Glick have agreed to be representatives for the Section for *Neurosurgical Focus*.

### AANS Board of Directors Information

The information that was made available to Dr. Rutka regarding the AANS Board of Directors' meetings was presented in the program book. The AANS has eliminated 12 staff positions. The CNS pulled its annual meeting coordination from the AANS. The finances of the AANS this past year were discussed briefly. It was stated that membership dues for the AANS would not be increased at this time.

*James T. Rutka, MD, is Secretary-Treasurer, AANS/CNS Section on Tumors.*

# Tumor Highlights at the AANS Annual Meeting

## Saturday, April 21

### Practical Clinics

1-5 PM

#### 010 Intracranial Endoscopic Techniques

Director: *Alan R. Cohen*

Faculty: *Jacques Caemaert, Enrique Ferrer, Andre Grotenhuis, Nakamasa Hayashi, Carl Barnes Heilman, Tenoch Herrada-Pineda, Wesley A. King, Kim Herbert Manwaring, Axel Perneczky, Gerard S. Rodziewicz*

#### 011 Radiosurgery: The Art and Science of Dose Planning

Director: *Antonio A. F. DeSalles*

Faculty: *David W. Andrews, Kenneth H. Ott, Farzard Massoudi, William A. Friedman, Frank J. Bova, T. Solberg, Steven Goetch, Stafford Chenery*

#### 013 Practical and Technical Aspects of Transsphenoidal Surgery

Director: *William F. Chandler*

Faculty: *Hae-Dong Jho, Edward H. Oldfield*

## Sunday, April 22

### Practical Clinics

8 AM-NOON

#### 017 Skull Base Tumors

Directors: *Jeffrey T. Keller, Harry R. Van Loveren*

Faculty: *Khaled Abdel Aziz, Norberto Andaluz, Michael J. Link, Walter Jean, Troy D. Payner, Michael R. Chicoine, Szymon S. Rosenblatt, Adam Lewis, Ali Nader-Sepahi, Mario Zuccarello, Sebastien Froehlich*

8 AM-5 PM

#### 026 Interactive Image Guided Spinal and Cranial Surgery

Director: *Robert J. Maciunas*

Faculty: *Richard D. Bucholz, Kevin T. Foley, Haring J. W. Nauta, Gene H. Barnett, Iain H. Kalfas, Charles Joseph Hodge Jr., Christopher R. Mascott, Ronald E. Warnick, William D. Tobler*

#### 027 Update on Tumors for the General Neurosurgeon

Director: *Jeffrey N. Bruce*

Faculty: *Ossama Al-Mefty, Michael W. McDermott, Mitchel S. Berger, Thomas C. Origitano, Joseph M. Piepmeier, Corey Raffel, James T. Rutka, Raymond Sawaya, Jack P. Rock, James Perry*

## Monday, April 23

### Breakfast Seminars

7:30-9:30 AM

#### 102 Surgical Approaches to the Anterior Skull Base

Moderator: *Donald C. Wright*

Panelists: *Axel Perneczky, Jon H. Robertson, Hae-Dong Jho, William T. Couldwell, Gail L. Rosseau*

#### 104 How I Do It: Brain Tumors

Speaker: *M. Gazi Yasargil*

#### 111 Advanced Techniques for Stereotactic Resection of Intracranial Lesions

Moderator: *David W. Roberts*

Panelists: *M. Peter Heilbrun, Richard D. Bucholz, Thomas M. Moriarty*

#### 112 Intraoperative MRI

Moderator: *Rudolph Fahlbusch*

Panelists: *Moshe Hadani, Eben Alexander III, Antonio A. F. DeSalles, Gene H. Barnett*

#### 114 Malignant Brain Tumors: State-of-the-Art Treatment

Moderator: *Mitchel S. Berger*

Panelists: *Peter McL. Black, Linda M. Liau, John Buatti, Raymond Sawaya*

#### 117 How I Do It: Skull Base Tumors

Speaker: *Vinko Dolenc*

#### 121 Third Ventricle Tumors

Moderator: *Michael L. J. Apuzzo*

Panelists: *Albert L. Rhoton Jr., Kim Herbert Manwaring, William Shucart, James T. Rutka*

### Plenary Session I

9:45-11:40 AM

#### 701 Surgical Outcome of 918 Brachial Plexus Injuries and Tumors

*Daniel H. Kim, Andrew C. Kam, Padmavathi Chandika, Robert L. Tiel, David G. Kline*

Discussant: *Alan R. Hudson*

#### 704 Chordoma and Chondrosarcoma of the Cranial Base: Results of Surgical Treatment in 124 Patients

*Amitabha Chanda, Laligam N. Sekhar, Chandrasekar Kalavakonda, Donald C. Wright, Chandranath Sen*

Discussant: *H. Alan Crookard*

### Scientific Session I

2:45-5:15 PM

#### 709 Comparison of Microneurosurgery to Stereotactic Radiosurgery in the Treatment of Solitary Brain Metastases

*Shekhar A. Dagam, Michael Link, Brian O'Neill, Bruce Pollock*

Discussant: *Mark Bernstein*

#### 710 The Role of Radiosurgery for Patients with Multiple Brain Metastases

*Walter A. Hall, Kwan Cho, Bruce Gerbi, Patrick Higgins*

Discussant: *Raymond Sawaya*

#### 711 Radiation-Induced Complications Following Single-Dose Gamma-Knife Stereotactic Radiosurgery for Intracranial Metastases

*Mark A. Liker, Zbigniew Petrovich, Cheng Yu, Steven Giannotta, Steven J. O'Day, Timothy S. Kristedja, Michael L. J. Apuzzo*

Discussant: *Philip H. Gutin*

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**712 Surgery After Failed Radiotherapy for Acoustic Neuroma**

Charles H. Tator, John A. Rutka, Mandeep S. Tamber, Patrick J. McDonald

Discussant: L. Dade Lunsford

**714 Endoscopic Transnasal-Transsphenoidal Resection of Pituitary Tumors: Long Term Results**

Prem Pillay, Drahambir Sethi

Discussant: William T. Couldwell

**715 Reversal of Cranial Nerve Deficits after Focused-Beam Radiotherapy for Cavernous Sinus Meningioma**

Khaled M. Abdel Aziz, Sebastien C. Froelich, Abhay Sanan, Harry R. Van Loveren, John C. Breneman, John M. Tew Jr.

Discussant: Laligam N. Sekhar

**717 Correlation of Molecular Genetics With Tumor Physiology and Metabolism in Patients with Low-Grade Oligodendrogliomas**

Peter C. Warnke, Carol Walker, Trevor Smith, Y. Machell, K.A. Joyce, Surajit Basu, Paul Eldridge, Sobhan Vinjamuri, Klaus Kopitzki, Daniel DuPlessis, John Broome

Discussant: Michael L. J. Apuzzo

**Scientific Session II**

**2:45-5:15 PM**

**719 Glioblastomas Induce Apoptosis of Invading T-Lymphocytes**

David S. Baskin, Bruce Frankel, Hop Ngo, Vladimir Didenko

Discussant: Nicolas de Tribolet

**720 Glioblastoma after Conventional Brain Radiation: Radiological, Histological and Genetic Analysis**

Tung T. Nguyen, Stuart Walbridge, Svetlana Pack, Alex Vortmeyer, Nitin Gogate, Aytac Akbasak, Thomas Goffman, Hunt Bobo, Jeff Olson, Zheng Ping Zhuang, Edward H. Oldfield

Discussant: Zvi Ram

**722 Meningioma Radiosurgery: Results from 190 Consecutive Patients Managed over a Nine-Year Period**

Scott L. Stafford, Bruce Pollock, Robert Foote, Deborah Gorman, Michael Link, Paula Schomberg

Discussant: Ossama Al-Mefty

**723 Expression of Fas Ligand on Brain Tumor Endothelium: Implications for Immune Escape**

John S. Yu, Moneeb Ehtesham, Ken Samoto, Keith L. Black

Discussant: Robert L. Martuza

**724 Non-Vestibular Schwannomas of the Brain**

Laligam N. Sekhar, Sajjan Sarma, Chandrasekhar Kalavakonda

Discussant: Bruce E. Pollock

**725 Gamma Knife Radiosurgery Boost in High Grade Gliomas**

Rufus J. Mark, Ronald Young, Deane Jacques, Brian Copcutt, Sandra Vermeulen, Steve Lee

Discussant: Gene H. Barnett

**Breakfast Seminars**

**7-9 AM**

**206 Frameless Cranial Stereotaxis**

Moderator: Richard D. Bucholz

Panelists: Keith M. Rich, Isabelle M. Germano, David W. Roberts, M. Peter Heilbrun

**209 Low Grade Gliomas: State-of-the-Art Treatment**

Moderator: Joseph M. Piepmeier

Panelists: Mitchel S. Berger, Mark Bernstein, John Buatti, Edward H. Mkrdichian

**218 Treatment of Spinal Cord Tumors**

Moderator: Russ P. Nockels

Panelists: Fred J. Epstein, Jacques Brotchi, Hiroshi Abe, Isao Yamamoto

**222 Evaluation and Management of Primary and Metastatic Vertebral Column Neoplasms**

Moderator: Paul R. Cooper

Panelists: Ziya L. Gokaslan, Narayan Sundaresan, Donald D. Dietze Jr., Richard G. Perrin

**Versalius Award Presentation**

**4-4:15 PM**

**Harvey Cushing's Meningioma Text and the Historical Origin of the Resectability of the Anterior One-Third of the Superior Sagittal Sinus**

Raj K. Shrivastava, presented by T. Glenn Pait

**AANS/CNS Section on Tumors**

**3-5:45 PM**

**Symposium**

**3-3:45 PM**

**Novel Biologic Therapies for Gliomas**

Moderator: Peter McL. Black

Speakers: Michael O'Reilly, Xandra Breakfield, Antonio Chiocca

**Special Lecture**

**3:45-4:15 PM**

**Farber Award Presentation and Lecture**

Robert L. Martuza, to be presented by Charles Wilson

**Award Presentation**

**4:15-4:20 PM**

National Brain Tumor Foundation Award

**Scientific Session**

**4:15-5:45 PM**

**819 Preuss Award Winner**

**Relationship between ENU-Induced Neural Precursor Cell Apoptosis and Brain Tumor Formation**

Jeffrey R. Leonard, Cleta D'Sa-Eipper, Kevin A Roth, to be presented by Joseph M. Piepmeier

**820 Mahaley Award Winner**

**Long-Term Follow-Up Results of Induction Chemotherapy Followed by Reduced-Volume Irradiation for Newly Diagnosed CNS Germinoma**

Yutaka Sawamura, Hiroki Shirato, Jun Ikeda, Hidefumi Aoyama, Nobuaki Ishii

**821 Young Investigators Award**  
**Intracranial Inhibition of PDGF-Mediated Glioblastoma Cell Growth by an Orally Active Kinase Inhibitor**  
*Turker Kilic, John A. Alberta, Pawel R. Zdunek, Melih Acar, Palma Iannarelli, Terence O'Reilly, Elisabeth Buchdunger, Peter McL. Black*

**822 Radiosurgery for Cystic Hemangioblastoma: Effect on Adjoining Cyst**  
*Randa Zakhary, Penny K. Sneed, Michael McDermott*

**823 Magnetic Resonance Spectroscopy Prediction of Survival in Patients with Supratentorial Gliomas**  
*Richard Leblanc, Yevgeniy Kuznetsov, Douglas Arnold*

**824 Intraoperative Detection of Brain Tumors by a Multispectral Fluorescence Guidance System**  
*Victor Yang, Paul Muller, Peter Herman, Brian Wilson*

## Scientific Session VI

9:45-11:15 a.m

**760 Cancer Therapy Using a Self-Replicating Nucleic Acid Vaccine**  
*Han Ying, Wolfgang W. Leitner, Rong-fu Wang, Kari K. Irvine, Christopher J. Wheeler, Keith L. Black, Nicholas P. Restifo*  
Discussant: *Jeffrey J. Olson*

**761 Phase I Clinical Trial of Adenovirus-mediated p53 Gene Therapy for Recurrent Glioma: Biological and Clinical Results**  
*Frederick F. Lang, Gregory N. Fuller, Michael D. Prados, Raymond Sawaya, W. K. Alfred Yung*  
Discussant: *Henry Brem*

**762 Photodynamic Therapy of Malignant Gliomas - Clinical Trials**  
*Paul J. Muller, Brian Wilson, Lothar Lilje, Victor Yang, Tim Fullagar, Fred Hetzel, Qua Chen, Robert Fenstermaker, Robert Selker, Judith Abrams*  
Discussant: *Andrew H. Kaye*

**763 Intraarterial Chemotherapy Followed by Radiation Therapy Prolongs Survival in High-Grade Astrocytoma**  
*Arthur P. Rosiello, Stefan Madajewicz, James Manzione, Patricia Hentschel, Raphael Davis*  
Discussant: *John Buatti*

**764 Can Systemic Administration of Anti-Angiogenic Gene Therapy Slow the Growth of Intracranial Human Glioblastoma?**  
*Oscar Szentirmai, Calvin Kuo, Martin Ollennu, Filip Farnebo, Jeng-Shin Lee, Richard Mulligan, Bob S. Carter*  
Discussant: *Mark L. Rosenblum*

**765 Results of Re-Operations for Low-Grade Gliomas Without Adjuvant Therapy**  
*Meic H. Schmidt, Mitchel S. Berger, Michael McDermott, Kenneth Aldape, Susan Chang*  
Discussant: *Keith L. Black*

## Scientific Session VII

9:45-11:15 AM

**769 Less Invasive Endoscope-Assisted Endonasal Transsphenoidal Microsurgery for Pituitary Tumors with an Augmented Reality Navigation System**  
*Takakazu Kawamata, Hiroshi Iseki, Ritsuko Ishizaki, Shuji Kamikawa, Tomokatsu Hori*  
Discussant: *Albert L. Rhoton Jr.*

**770 Vaccination with GM-CSF Secreting Cells and Dendritic Cells Induce Intracranial Cytotoxic T Cell Responses**  
*John S. Yu, Paul M. Zeltzer, Christopher J. Wheeler, Richard Trauger, Richard Bartholemew, Georgia Thefan, Han Ying, Paul Lee, William Yong, Keith L. Black*  
Discussant: *Walter A. Hall*

## Section Session

AANS/CNS Section on Stereotactic and Functional Surgery

## Resident Award

3:30-3:45 PM

**Acute Effects of Stereotactic Proton Beam Irradiation on the Rat Hippocampus**  
*Jonathan L. Brisman, to be presented by Philip L. Gildenberg*

## Wednesday, April 25

### Breakfast Seminars

7:30-9:30 AM

#### 302 Acoustic Schwannoma: State-of-the-Art

Moderator: *Michael J. Ebersold*  
Panelists: *David W. Rowed, Jack P. Rock, Madjid Samii*

#### 309 Management of the Difficult Meningioma

Moderator: *Harry R. Van Loveren*  
Panelists: *Michael W. McDermott, John Buatti, William T. Couldwell, Jacques Brotchi*

### Scientific Session V

9:45-11:15 AM

**754 Surgical Treatment of Brain Stem Gliomas: Approaches and Technique**  
*Albino Bricolo*  
Discussant: *Fred J. Epstein*

**756 Pediatric Dorsally Exophytic Brainstem Gliomas: Value of Aggressive Surgical Resection**  
*Renatta J. Osterdock, Dwight E. Heron, Richard L. Heideman, Robert A. Sanford, Larry E. Kun*  
Discussant: *Rick Abbott III*

**757 Survival of Surgically Treated Malignant Glioma Patients – Data from the Glioma Outcomes Project**  
*Edward R. Laws Jr., Cynthia Sullivan, Anthony Asher, Mitchell Berger, Mark Bernstein, Raymond Sawaya, Andrew Sloan, Glioma Outcomes Project Investigators*  
Discussant: *Jack P. Rock*

**758 Gamma Knife Radiosurgery for Meningiomas**  
*Ronald F. Young, Rufus Mark, Sandra Vermeulen, Robert Meier, Deane Jacques, Brian Copcutt, Francisco Li*  
Discussant: *Harry R. Van Loveren*

**759 Surgical Resectability of Sphenocavernous and Clinoidocavernous Meningiomas**  
*Khaled M. Abdel Aziz, Harry R. Van Loveren, Sebastien C. Froelich, Jeffrey T. Keller, John M. Tew Jr.*  
Discussant: *Chandranath Sen*

# Washington Committee Update

By Lawrence S. Chin, MD, and Katie Orrico, JD

## Practice Expenses

*HCFA 2001 Fee Schedule Rule:* The AANS/CNS submitted comments to HCFA on December 29, 2000, registering our continued objections to practice expense methodology, data and the refinement process. We made several specific recommendations with regard to the methodology and the refinement process. In the final rule, HCFA did make some changes to its methodology that shifted some money from primary care back to specialists. Neurosurgery will still expect an overall reduction of 12 to 13 percent when the new PE RVUs are fully implemented in 2002. Continued increases in the conversion factor have mitigated these losses to a certain extent. HCFA also made changes to the malpractice component in response to our comments from last year. These changes slightly increased the RVUs for neurosurgical services.

## Medicare Coverage

*Coverage of Clinical Trials:* On June 7, 2000, President Clinton issued an Executive Memorandum directing HHS to authorize Medicare payment for routine patient care costs for beneficiaries participating in clinical trials. The AANS and CNS submitted comments to HCFA regarding the development of a National Coverage Decision outlining the specifics of this new policy. HCFA issued a final clinical trials coverage decision on September 19, but is still in the process of finalizing some of the details, such as what are "routine" costs. This process is ongoing.

*Pet Scans:* Coverage for PET imaging was recently expanded to include six additional types of cancer scanning. They are lung, colorectal, head and neck, lymphoma, melanoma and esophagus—but not brain or thyroid cancer. Coverage for some patients with refractory epilepsy or patients who are candidates for coronary revascularization was also added. This coverage decision was highly politicized, with Sen. Ted Stevens (R-AK) putting a great deal of pressure on Secretary Shalala, resulting in a coverage decision that did not comport to the normal decision-making process.

## Biomedical Research

*NIH Funding:* The Appropriations bill for Health and Human Services was passed in December during the lame duck session of the 106th Congress. The National Institutes of Health received an increase of 14.4 percent (to \$2.7 billion) that is in keeping with the goal of doubling the NIH budget over 5 years.

AGENCY	FY 2000 Comparable	FY2001 Appropriation	Percent Increase
NIH	\$17.8 billion	\$20.3 billion	14.2%
NINDS	\$1,029,528,000	\$1,176,482,000	14.3%
NIAMS	\$349,407,000	\$396,687,000	13.5%
NCI	\$3,310,992,000	\$3,757,242,000	13.5%

*Stem Cell Research:* The Senate failed to vote on Sen. Arlen Specter's (R-PA) legislation that would permit federal funding of

stem cell research, but that also would make permanent the ban on fetal tissue research. Conservative senators who opposed the measure stalled the bill. The Stem Cell Coalition continues to develop strategy for ensuring that the NIH guidelines (supported by the AANS and CNS) go forward and result in appropriate stem cell research. The coalition recently sent a letter to President Bush urging him to support federal funding for stem cell research. The President has indicated that he may reverse the current NIH policy and ban federal funding of this research. We are monitoring the activities of the Coalition but have not signed on to any of their official statements. There continues to be division within the AANS and CNS leadership about whether we should join this coalition effort. The Society of Neurological Surgeons will likely request the AANS and CNS to support this coalition (or SNS itself may join).

*Lawrence S. Chin, MD, is the Tumor Section's representative to the Washington Committee. Katie Orrico, JD, is Director of the AANS/CNS Washington, D.C. office.*

## Tumor Section Highlights at the 2001 CNS Annual Meeting in San Diego

**Monday October 1 2:00-2:50 PM**

### Section on Tumors I Acoustic Neuroma

#### 1. Natural History of Acoustic Neuromas

*Charles Tator, University of Toronto*

#### 2. When to Operate, and Surgical Approaches

*Dr. Hitzelberger, House Ear Institute, Los Angeles*

#### 3. Role of Radiosurgery

*Bruce Pollock, MD, Mayo Clinic, Rochester*

**Tuesday October 2 2:00-2:50 PM**

### Section on Tumors II Pituitary Tumors

#### 1. Prolactinoma: Recent Advances in Biology and Treatment

*Shlomo Melmed, Cedars Sinai, Los Angeles*

#### 2. Pituitary Tumor Surgery: Lessons Learned

*Edward Laws Jr., MD, University of Virginia, Charlottesville*

#### 3. Endoscopic Pituitary Surgery

*Hae Dong Jho, MD, University of Pittsburgh, Pittsburgh*



## The Brain Tumor Society

The Brain Tumor Society has compiled a 22-page list of books about brain tumors and related conditions. The Brain Tumor Book List offers a brief summary of 86 books.

For physicians and healthcare professionals who want to help their patients, the legwork has already been done for you. "This is one-stop shopping," says Donna Dello Iacono, RN, MS, a neurosurgical nurse. "Everything is in one place. I love the breadth of resources!"

Topics include:

- brain and spinal cord tumors
- seizure disorders
- cancer, chronic illness and caregiving
- pediatrics
- children's fiction
- brain and spinal cord injury
- related conditions (hearing and vision loss, etc.)
- grief and bereavement support
- general reference
- "Coming Soon!" (books in press)

The Brain Tumor Book List includes every item profiled in the society's newsletter, *Heads Up*. You can also find information about how to order many of the books.

To order a free copy, call (800) 770-8287, ext. 13. It can also be accessed on the Web at [www.tbts.org/bibres.htm](http://www.tbts.org/bibres.htm). Be sure to ask for an extra copy for your local library!

The Brain Tumor Society is a national nonprofit group that provides resources and services to patients, survivors, friends and professionals. It also funds basic science brain tumor research.

## Pediatric Brain Tumor Foundation of the United States

In 2001, the Pediatric Brain Tumor Foundation of the United States (PBTfUS) will support research projects, awards and programs in search of the cause and cure of childhood brain tumors. The funding committed to these research and program efforts by the PBTfUS totals more than \$3 million. Funding has been committed to the following:

### Basic Research Grants

- Michael E. Berens, PhD, Barrow Neurological Institute
- Jaclyn A. Biegel, PhD, Children's Hospital of PA
- Mario R. Capecchi, PhD, Howard Hughes Medical Institute
- Daniel W. Fults, MD, University of Utah
- Russell O. Pieper, PhD, UCSF Cancer Center
- Jeremy N. Rich, MD, Duke University Medical Center
- Murray A. Stackhouse, PhD, Univ. of Alabama at Birmingham
- Erwin G. Van Meir, PhD, Emory University
- Cynthia Wetmore, MD, PhD, St. Jude Children's Research Hospital
- Carol Wikstrand, PhD, Duke University Medical Center

## Clinical Research Project Grants

- Elana Farace, PhD, University of Virginia
- Kalkunte S. Srivenugopal, PhD, MD Anderson Cancer Center
- Mryam Foladi, MD, St. Jude Children's Research Hospital

## Translational Research Project Grant

- Darell Bigner, MD, PhD, Duke University Medical Center

## Pediatric Brain Tumor Consortium

- Neuroimaging Center Grant

## Central Brain Tumor Registry

- Epidemiology Grant – continuance of Founding Grant awarded by PBTfUS in 1991

## Atypical Teratoid/Rhabdoid Tumor Workshop

Jointly funded with NCI

- Grant to fund workshop

## 2001 Annual Peter Steck Memorial Research Award

- Researcher Award of Excellence & Memorial Lecture, MD Anderson Cancer Center

## 2001 Society for Neuro-Oncology Awards of Excellence

- Award of Excellence in Basic Pediatric Brain Tumor Research to be awarded in November 2001
- Award of Excellence in Clinical Pediatric Brain Tumor Research to be awarded in November 2001

## 2001 Award of Excellence in Social Work

- Association of Pediatric Oncology Social Workers Award of Excellence to be awarded at 2001 APSOW Annual meeting

## Basic and Clinical Research Grants Available

- **Basic Pediatric Brain Tumor Research Projects:** Request for applications deadline is May 1, 2001. Two-year \$70,000 grants. For grant guidelines applications see [www.pbtfus.org](http://www.pbtfus.org).
- **Clinical Pediatric Brain Tumor Research Projects:** Request for applications deadline is August 1, 2001. Two-year \$100,000 grants. For grant guidelines and applications see [www.pbtus.org](http://www.pbtus.org).
- **Clinical Research Fellowships in Pediatric Neuro-Oncology:** Request for applications deadline August 1, 2001. Two-year \$100,000 grants. For guidelines and applications see [www.pbtus.org](http://www.pbtus.org).

## 2001 Advocacy, Patient and Family Programs

Family Support Program

- Staff social worker to provide assistance to patient families
- Patient education and resource materials
- Help line: 800-253-6530
- Patient Web site: [www.pbtfus.org](http://www.pbtfus.org)
- Live Internet interactive patient conferences
- *Helping Hand* quarterly newsletter

*continued on page 10*

### **Ride for Kids® Program**

An organized advocacy effort on behalf of the needs of the patient population and their families to:

- Raise awareness about the disease
- Encourage advocacy on behalf of patients
- Provide emotional support for patients and families
- Raise funds for research

### **North American Brain Tumor Coalition**

May 6-12 has been designated as Brain Tumor Awareness Week (BTAW) in the United States and Canada. The week is sponsored by the North American Brain Tumor Coalition, a network of 12 charitable organizations representing the interests of its combined constituency.

During the week the coalition will host activities in Washington, D.C., and will use the Brain Tumor Progress Review Group Report to emphasize the importance of increasing the budget for biomedical research funding.

Hospitals are encouraged to host a Brain Tumor Awareness Day during the week. The activity can be as simple as having a table in the hospital lobby with brain tumor information to something more elaborate, such as a brain tumor education meeting for patient/families or medical professionals.

The coalition can supply posters, brochures and brain tumor information. Let them know if your institution intends to sponsor an activity or what they can do to help. For information, call Naomi Berkowitz, Chair of the BTAW Outreach Committee, at (847) 827-9910 or e-mail her at [naomi@abta.org](mailto:naomi@abta.org).

### **National Brain Tumor Foundation**

#### **Newsletter Available**

The latest issue of the National Brain Tumor Foundation (NBTF) newsletter has an interview with David Louis, MD, of Massachusetts General Hospital on genetic research. For a copy of the newsletter, visit the NBTF Web site at [www.braintumor.org](http://www.braintumor.org) or call (800) 934-2873.

#### **Teleconference on the Web**

An audio version of a teleconference co-sponsored by the NBTF and the Brain Tumor Society is available on the NBTF Web site at [www.braintumor.org](http://www.braintumor.org). The teleconference, "Choosing and Managing Brain Tumor Treatments," featured Roberta Calhoun, ACSW, of the Brain Tumor Society, and Mary Lovely, RN, PhD, of NBTF.

#### **Dr. Warnick Wins Award**

Ronald Warnick, MD, of the Mayfield Clinic in Cincinnati, Ohio, was the recipient of the 2000 NBTF Award for Excellence in Clinical Research. This award was presented as part of SNO's annual conference held in November 2000 in Chicago.

#### **Grant Given**

John S. Yu, MD, Co-Director of the Comprehensive Brain Tumor Program at Cedars-Sinai Medical Center in Los Angeles, was awarded a joint research grant from NBTF and American Association of Neurological Surgeons for his work on glioblastoma.

### **New Patient Publications**

NBTF has two new fact sheets for patients. One focuses on the issue of neuropsychology, "How Tumors Affect the Mind, Emotion and Personality," and the other on nutrition, "The Healing Power of your Fork: A Brain Tumor Survivor's Eating Plan." Both of these fact sheets are available by contacting NBTF at (800) 934-2873 or at [www.braintumor.org](http://www.braintumor.org)

### **American Brain Tumor Association**

The American Brain Tumor Association (ABTA) has joined forces with [cancerpage.com](http://cancerpage.com) to launch a new resource for people affected by brain tumors. [Cancerpage.com](http://cancerpage.com) now offers extensive information about brain cancer, its treatment, and support information.

[Cancerpage.com](http://cancerpage.com) turned to the expertise of ABTA to develop its new information section. The goal of ABTA's educational programs is to meet the needs of those affected by brain tumors. The Web site helps them achieve that goal by extending their resources to a broader constituency.

Using the site's easy-to-navigate format, visitors are presented with explanations of symptoms, risk factors, diagnostic tests and brain cancer treatment options.

Based on recent census figures, ABTA estimates that 186,000 people will be diagnosed with brain tumors in 2001. This includes 36,000 primary brain tumors and 150,000 metastatic brain tumors. Founded in 1973 as the first organization to focus on brain tumors, ABTA continues to try to eliminate brain tumors through research and to meet the needs of brain tumor patients and their families.

### **Children's Oncology (continued from page 2)**

comparison to historical standards (9961) to determine which is most effective. A concept under development for germinomas (ACNS0132) will be comparing survival and quality of life for patients who receive conventional doses of radiotherapy with those of patients who receive reduced doses of irradiation in conjunction with chemotherapy.

#### **Neurosurgical Input Needed**

Given the depth and breadth of clinical research activities that are ongoing within COG, there continues to be a strong need for neurosurgical input in terms of study development and completion. Recently, several studies have incorporated important neurosurgical questions, including the role of second-look surgery for infant brain tumors, incompletely resected ependymomas and germ cell tumors. Neurosurgeons within the group play leadership roles in establishing coherent guidelines for surgical decision-making in individual tumor types, in contributing to the design and conduct of clinical studies and in facilitating tissue submission for correlative biological studies. For more information about COG-related activities, contact Ian F. Pollack, MD, Chair of the COG Brain Tumor Committee, or R. Alex Sanford, MD, and Jeffrey Wisoff, MD, Co-Chairs of the COG Neurosurgery Committee.

*Ian F. Pollack, MD, is Chair, COG Brain Tumor Committee.*

# Application for Membership

## AANS/CNS Section on Tumors



American  
Association of  
Neurological  
Surgeons



**Eligibility:** Members of the AANS and/or CNS who have demonstrated a special interest in tumors of the nervous system.

**Note:** *Adjunct Membership is available to non-neurosurgeons. Please contact the AANS office at 847-378-0500 for an Adjunct Membership application.*

### I. Biographical

(A) Name: \_\_\_\_\_

(B) Home Address: \_\_\_\_\_

(C) Office Address: \_\_\_\_\_

Phone: \_\_\_\_\_ Fax: \_\_\_\_\_

(D) E-Mail: \_\_\_\_\_

### II. Category of Membership Requested

Active

International

Resident\*

### III. Membership, Certification and Practice

(A) Are you certified by the American Board of Neurological Surgery?  Yes  No

(B) For Resident Applicants—Expected Residency Completion Date (month/year) \_\_\_\_\_

(C) Are you a member of

1. The American Association of Neurological Surgeons?  Yes  No

2. The Congress of Neurological Surgeons?  Yes  No

(D) Are you currently involved in brain tumor research?

Clinical —  Yes  No Basic —  Yes  No

Suggestions on Section activities that would benefit you:

\_\_\_\_\_

\_\_\_\_\_  
Signature of Applicant

\_\_\_\_\_  
Date

\*Membership dues are waived for applicants currently enrolled in a neurosurgical residency program.

**Please return completed application and curriculum vitae to:**

**Michael W. McDermott, MD, Membership Chairperson**

**University of California, San Francisco**

**505 Parnassus Avenue, M-774**

**San Francisco, CA 94143-0112**

**Phone: (415) 476-1087 • Fax: (415) 753-1772 • E-mail: mcdermottm@neurosurg.ucsf.edu**

# Ask the Expert ...

## The Allos Therapeutics Trial

*Tumor News* interviewed Jean-Francois Liard, MD, PhD, about agent RSR13.

### Q: Can you describe the agent RSR13 that soon will begin Phase III testing?

**Liard:** RSR13 is a small molecule that reduces the hemoglobin oxygen binding affinity by binding to the central water cavity of the hemoglobin tetramer. It enhances the diffusion of oxygen from the blood to hypoxic tissues. Direct measurements of oxygen in human tumors have confirmed significant tumor hypoxia in many types of cancer, including malignant gliomas. Since hypoxia is believed to be a major cause of radiation treatment failure, RSR13 may facilitate the tumor killing effect of radiation therapy through its capacity to increase tumor oxygenation.

### Q: What features make RSR13 a unique radioenhancer for glioblastoma therapy?

**Liard:** RSR13 does not need to cross the blood brain barrier nor does it need to penetrate the tumor tissue to exert its radiation-enhancing effect, since its target is hemoglobin. It has a fast action and a short half-life, making its effect rapid and reversible. It is not a cytotoxic agent and has a favorable toxicity profile.

### Q: What preclinical work formed the basis for this approach?

**Liard:** RSR13, combined with carbogen or oxygen breathing, increased tumor pO<sub>2</sub> in models using breast cancer cell implants, adenocarcinoma 13762 and EMT6. RSR13 combined with radiation produced tumor growth delays in the Lewis lung and MB49 bladder cancer models and in a fibrosarcoma (FSaII) model. In addition, RSR13 combined with radiation therapy decreased the spread of metastases in the Lewis lung cancer model. Decreased tumor cell survival after radiation therapy was seen with RSR13 and oxygen breathing in the EMT6 breast cancer model and with RSR13 and carbogen breathing in the FSaII fibrosarcoma model. The radio-enhancement effect of RSR13 was shown to be oxygen-dependent, with no direct cytotoxic effect on the tumor, bone marrow or skin.

### Q: Can you describe the results of the Phase II trial?

**Liard:** A Phase II study in glioblastoma multiforme showed that RSR13 plus RT increased median survival 27 percent compared to NABTT historical controls (*Int. J. Rad. Oncol. Biol. Phys.*, Vol. 48(3):182, 2000). RSR13 has also been used as a radioenhancer in patients with brain metastases and with NSCLC and has shown promising results in both indications. Human studies in

more than 300 cancer patients have shown the side effects to be acceptable. Adverse events observed in association with RSR13 include a tingling sensation of the mouth and lips during infusion, nausea and vomiting, headache, rash and fatigue. Some patients had an allergic reaction after receiving RSR13, which included a skin rash, fever and decreased blood pressure. Others have developed a temporary decrease in blood oxygen levels. Additional possible side effects are a temporary decrease in kidney function and fluid retention.

### Q: Which patients are eligible for the current Phase III clinical trial?

**Liard:** Eligibility criteria cannot be listed in detail here, but the trial will be conducted in patients with newly diagnosed GBM with no prior treatment except for surgery and corticosteroids. Patients must have a KPS  $\geq$  60, arterial oxygen saturation on room air  $\geq$  90% by pulse oximetry, adequate hematologic, hepatic, and renal function as defined by clinical laboratory values, and no planned further treatment (e.g., radiosurgery, chemotherapy) until progression.

### Q: Can you describe the protocol treatment regimen?

**Liard:** Patients with newly diagnosed GBM will receive a six-week course of cranial RT (2 Gy x 30 = 60 Gy). Patients in Treatment Arm A will receive RSR13, 75 or 100 mg/kg, administered IV over 30 minutes through a central venous access device with concurrent administration of O<sub>2</sub> (4 L/minute). RT will be given as soon as possible after end-infusion, but must be within 30 minutes after end-infusion. Patients in Treatment Arm B will receive the same course of cranial RT as given to patients in Treatment Arm A, but without RSR13 or concurrent administration of O<sub>2</sub>.

### Q: What are the endpoints of the study?

**Liard:** Primary endpoint is overall survival. Secondary endpoints are: (1) time to tumor progression assessed by both clinical and radiographic criteria and (2) quality of life assessed by Spitzer Questionnaire and KPS.

### Q: What is the current status of the Phase III trial?

**Liard:** The trial will be conducted as Study RSR13 RT-011 and is scheduled to begin this summer. Its design has been discussed with the Division of Oncology Drug Products of the FDA. The trial will be a phase III, randomized, open-label, comparative study of cranial radiation therapy, with or without RSR13 and supplemental oxygen, in patients with newly diagnosed glioblastoma multiforme. When the protocol is finalized, interested

Since hypoxia is believed to be a major cause of radiation treatment failure, RSR13 may facilitate the tumor killing effect of radiation therapy through its capacity to increase tumor oxygenation.

investigators will be identified. An investigators meeting will be organized within the next few months.

**Q: What do you believe will be the limiting factor for the success of RSR13?**

**Liard:** RSR13 will be successful insofar as it offers the medical community and patients a clinically significant survival benefit in a life-threatening condition with an unmet medical need, without presenting unacceptable risks and toxicities. Should the benefit-to-risk ratio be favorable, the issues associated with the administration of RSR13 should not be a major obstacle to its use. These issues include the need to insert a PICC line or a central catheter, oxygen administration, monitoring oxygen saturation for 30 to 120 minutes after radiation therapy and interactions with certain medications commonly used in this patient population such as aromatic anticonvulsants and corticosteroids.

**Q: Do you have any final thoughts on the prospects of RSR13 for glioblastoma or other tumor types?**

**Liard:** RSR13 is a small molecule that increases the efficacy of radiation therapy (RT) through a unique and well-understood mechanism of action. A phase II study in glioblastoma multiforme showed RSR13 plus RT increased median survival 27 percent compared to NABTT historical controls. Preliminary Phase II results in NSCLC show an 87 percent response rate in patients treated with RSR13 plus RT following induction with paclitaxel and carboplatin. A pivotal Phase III trial in treatment of brain metastases was initiated in March 2000. Data from 12 completed Phase I and II trials and over 400 patients show a favorable safety profile over traditional cytotoxic drugs. We are confident that RSR13 has the potential to be an important addition to radiation therapy in a variety of indications.

**Q: Who should the reader contact to obtain more information on this Phase III trial?**

**Liard:** Please contact the medical director of this Phase III trial:  
Jean-Francois Liard, MD, PhD  
Sr. Director, Clinical Development  
7000 N Broadway, Suite 400  
Denver, CO 80221  
Phone: (888) 255-6702, ext. 129  
Cell: (303) 881-7939  
E-mail: liard@allos.com

## Wanted: Contributions to *Tumor News*

In the next issue of *Tumor News*, we will once again publish the columns "You Make the Diagnosis" and "Ask the Expert." If you have an interesting clinical case, as well as pertinent imaging studies, that you would like to publish in the "You Make the Diagnosis" column, please let us know. Or, if you are involved in an interesting and ground-breaking clinical trial and would like to share the progress or results of that trial with your fellow Section members in the "Ask the Expert" column, please contact:

Ronald E. Warnick, MD  
222 Piedmont Ave., #3100  
Cincinnati, Ohio 45219  
Fax: (513) 558-0886 • E-mail: nsgymd@aol.com

## Information at the Click of a Mouse

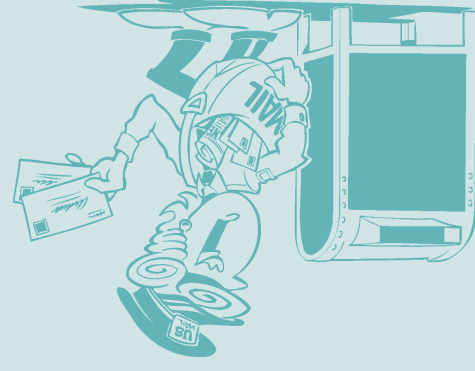
Information abounds on the Tumor Section area of **NEUROSURGERY://ON-CALL®**, including the *Select Review in Neuro-Oncology*, the new Genetic Vector Registry, and links to various research and funding opportunities. To view this section of the site, visit [www.neurosurgery.org/sections/tumor/summary.html](http://www.neurosurgery.org/sections/tumor/summary.html).

**AANS/CNS Section on Tumors**  
5550 Meadowbrook Drive  
Rolling Meadows, Illinois 60008

# We Want to Hear From You

The Editor of *Tumor News* is interested in hearing your comments and queries on this issue of the newsletter, as well as your ideas for future issues. Please send your feedback to:

Ronald E. Warnick, MD  
222 Piedmont Ave., #3100  
Cincinnati, Ohio 45219  
Fax: (513) 558-0886  
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