Tumor NEWS

Fall 1999

AANS/CNS Section on Tumors

Editor: Ronald E. Warnick, MD

In This Issue...

Message From the Chair

Joseph M. Piepmeier, MD

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I want to thank the membership for offering me the opportunity to serve as Chair of the AANS/CNS Section on Tumors. It is both an honor and a privilege, and I am looking forward to working with the members of the Section over the next two years. I am particularly pleased that James Rutka, MD, will serve as Secretary/Treasurer, as he is a wonderful asset to our group.

Section Benefits

I want to remind our Section members that we have a special relationship with the *Journal of Neuro-Oncology*. As such, members of our Section can subscribe to the *Journal of Neuro-Oncology* at a 35 percent discount. Abstracts, meeting notices and announcements of our Section's activities will be published in the *Journal*. The Executive Council of our Section is well represented on the Editorial Board, and this will strengthen the *Journal* as the voice for our Section members.

Plans for CNS Meeting Underway

The Scientific Program for the 1999 CNS Annual Meeting promises to be exciting and informative. On Monday, November 1, the General Scientific Session will include a number of outstanding presentations on CNS neoplasms by international leaders from a number of disciplines related to neuro-oncology. Also on Monday, the Tumor Section Scientific Session will highlight intramedullary spinal cord tumors and include a report from Paul McCormick, MD.

On Wednesday, November 2, the second Tumor Section Scientific Session will present new information on skull base tumors, and be moderated by Ossama Al-Mefty, MD, and Thomas Origitano, MD.

Mark Your Calendars for the AANS Meeting

Plans for the 2000 AANS Annual Meeting will include a symposium on immunotherapy for gliomas. Linda Liau, MD, has prepared an outstanding presentation on this novel approach to treatment. A Satellite Symposium also is being planned and will immediately follow the AANS Annual Meeting. Ronald Warnick, MD, will serve as the Program Chair for this symposium, and I urge every Section member to make plans to attend this exciting event.

New Section Leadership

There are several new members serving on the Section's Executive Council. These individuals were selected to expand the access to our Section, introduce new ideas, and provide a forum for the future leaders of the Tumor Section. I want to thank all the members of the Executive Council who have volunteered their time and efforts to our Section. They are doing a magnificent job, and we are all open to your suggestions on how we can better serve you.

Tumor Section Highlights at the 1999 CNS Annual Meeting

Saturday, October 30, 1999
Practical Courses

8 AM–5 PM

001 Microsurgical Anatomy for Cranial Surgery
Course Director: *Albert L. Rhoton, Jr.*
Faculty: *Toshio Matsushima, Evandro de Oliveira, Ronald Smith, Antonio Mussi, Qing Liang, Tsutomu Hitotsumatus, Ryusui Tanaka, Eduardo Seoane, Hung Wen, Helder Tedeschi*

8 AM–12 PM

009 Image-Guided Cranial Surgical Navigation
Course Directors: *Robert J. Maciunas, Isabelle M. Germano*
Faculty: *John R. Adler, Jr., Gene H. Barnett, Richard D. Bucholz, Charles Joseph Hodge, Jr., Douglas Kondziolka, William D. Tobler, Haring J. W. Nauta*

015 Microsurgical Dissection Techniques
Course Director: *John Diaz Day*
Faculty: *Michael Levy, Gazi Yasargil, Christian Matula, Robert E. Harbaugh*

Sunday, October 31, 1999
Practical Courses

8 AM–5 PM

026 Temporal Bone — Acoustic Surgery
Course Directors: *Steven L. Giannotta, John Diaz Day*
Faculty: *Carl Barnes Heilman, Anil Nanda*

8 AM–12 PM

029 Functional Cerebral Mapping
Course Directors: *Nicholas M. Barbaro, Mitchel S. Berger*
Faculty: *Peter McL. Black, George A. Ojemann*

1–5 PM

041 Stereotactic Radiosurgery
Course Director: *Bruce E. Pollock*
Faculty: *William A. Friedman, Frank J. Bova, Kris Smith, John R. Adler, Jr., Allan J. Hamilton, Eben Alexander III*

Monday, November 1, 1999
Luncheon Seminars

12–2 PM

106/106R Low-Grade Gliomas: Current Treatment and Controversies
Moderator: *William C. Broaddus*
Faculty: *Mitchel S. Berger, Walter A. Hall, Robert J. Maciunas, Deborah L. Benzil, Andrew H. Kaye*

107/107R Radiation Therapy Options for Brain Tumors
Moderator: *Philip H. Gutin*
Faculty: *Christer E. H. Lindquist, Volker Strum, Jeffery A. Williams, David W. Andrews, Keith M. Rich*

108/108R Controversies in Pituitary Surgery
Moderator: *William T. Couldwell*
Faculty: *Ivan Ciric, Bruce E. Mickey, Nelson M. Oyesiku, Carl Barnes Heilman, Armando Basso*

109/109R Surgical Approaches to the Anterior Skull Base
Moderator: *Donald C. Wright*
Faculty: *Bruce M. McCormack, Linda L. Sternau, Teiji Uede, James P. Chandler, Vinko Dolenc*

110/110R Hearing Preservation in Acoustic Tumor Surgery: Practical and Technical Considerations
Moderator: *Lawrence H. Pitts*
Faculty: *Madjid Samii, Kil Soo Choi, Douglas Kondziolka, Donlin M. Long, Wolfgang Koos*

Tuesday, November 2, 1999
Luncheon Seminars

12–2 PM

207/207R Current Management of Malignant Gliomas
Moderator: *Henry Brem*
Faculty: *Kaoru Kurisu, Jeffrey J. Olson, Michael W. McDermott, Nicholas T. Zervas*

208/208R Treatment of Intracranial Meningiomas
Moderator: *Caetano Coiumbra*
Faculty: *Ossama Al-Mefty, Ghassan K. Bejjani, Mauro Loyo-Varela, Russell H. Patterson, Jr., William A. Friedman*

209/209R Complications of Pituitary Surgery
Moderator: *Martin H. Weiss*
Faculty: *Ian E. McCutcheon, Ernst H. Grote, Andrew D. Parent, Edward R. Laws, Jr., Brooke Swearingen*

210/210R Third Ventricular Tumors: Open, Stereotactic and Endoscopic Approaches
Moderator: *Harold Louis Rekate*
Faculty: *Jeffrey N. Bruce, Ivan Ciric, Takayuki Ohira, Gerard S. Rodziewicz*

211/211R **Avoidance and Management of Complications Following Cranial Base Procedures**
Moderator: *Donald P. Becker*
Faculty: *Wesley A. King, William T. Monacci, Takeshi Kawase, Thomas C. Origitano, Austin R. Colohan*

217/217R **Management of Posterior Fossa and Brainstem Tumors in Children**
Moderator: *Ian F. Pollack*
Faculty: *Liliana Goumnerova, Leslie N. Sutton, Jon D. Weingart, Herbert E. Fuchs, Jeffrey H. Wisoff*

Wednesday, November 3, 1999
Luncheon Seminars

12–2 PM

308/308R **Intracranial Metastases: Current Management Strategies**
Moderator: *Raymond Sawaya*
Faculty: *Eben Alexander III, Robert A. Fenstermaker, Robert J. Coffey, Timothy C. Ryken*

309/309R **Treatment of Craniopharyngiomas**
Moderator: *James T. Rutka*
Faculty: *Timothy B. Mapstone, Dachling Pang, Philip Harry Cogen, Bruce E. Pollock*

310/310R **Pineal Region Tumors**
Moderator: *Michael L. J. Apuzzo*
Faculty: *Gerhard Pendl, Kintomo Takakura, Gerard S. Rodziewicz*

311/311R **Tumors of the Posterior Skull Base and Tentorium**
Moderator: *Szymon S. Rosenblatt*
Faculty: *Kevin J. Gibbons, Thomas C. Origitano, Jon H. Robertson, Leonard I. Malis*

312/312R **Decision-Making for Recurrent Cranial Base Neoplasms: Observation, Reoperation or Radiation**
Moderator: *Douglas Kondziolka*
Faculty: *Hidefumi Jokura, Felix Umansky, Gail L. Rosseau*

313/313R **Treatment Strategies for Spinal Cord Tumors**
Moderator: *Kalmon D. Post*
Faculty: *Paul C. McCormick, Paul D. Sawin, Allan J. Belzberg, T. Glenn Pait*

General Scientific Session I

Monday, November 1, 1999 7:30–11:45 AM
Treatment of CNS Neoplasms and Aneurysms: The End of the Beginning

Moderator: *Joseph M. Piepmeier*
Presiding Officer: *William A. Friedman*

7:30–7:45 AM **Surgery of Cerebral Gliomas: Past, Present and Future**
Peter McL. Black

7:45–8:05 AM **Von Hippel-Lindau Syndrome: Lessons on the Origins of CNS Tumors**
Edward H. Oldfield

8:05–8:25 AM **Glial Cell Ontology: The Key to Understanding Cerebral Tumors**
Mark E. Linskey

8:25–8:45 AM **Mechanisms of Glioma Invasiveness**
Susan Hockfield

8:45–9:05 AM **The Future of Pituitary Surgery**
Hae-Dong Jho

9:05–9:10 AM **Perspective on Pituitary Surgery**
Ivan Ciric

9:10–9:30 AM **The Future of Neuropathology**
Catherine Daumas-Duport

9:30–10:15 AM **Coffee Break With Exhibitors**

10:15–11:05 AM **Honored Guest Presentation: Posterior Circulation Aneurysms – A 25 Year Experience**
Duke S. Samson

11:05–11:15 AM **Introduction of the President**

11:15–11:45 AM **Presidential Address**
H. Hunt Batjer

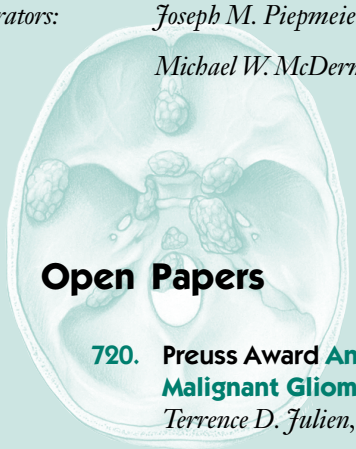
Spotlight on the Tumor Section

Scientific Session

Monday, November 1, 1999 2–5:30 PM
Section on Tumors I
Spinal Cord Neoplasms

Moderators: *Joseph M. Piepmeier*
Michael W. McDermott

2–2:25 PM	**Pathology of Intramedullary Tumors** *James Goldman*
2:25–2:50 PM	**Adjuvant Therapies for Spinal Cord Tumors** *Paul C. McCormick*
2:50–3:30 PM	**Oral Posters** *Ronald E. Warnick* *Anthony L. Asher*
3:30–4 PM	**Coffee Break With Exhibitors**
4–5:30 PM	**Open Papers (720-729)** *William T. Couldwell* *Roberta P. Glick*



Open Papers

720. Preuss Award **Antisense-mediated Inhibition of the bcl-2 Gene Induces Apoptosis in Human Malignant Glioma.**
Terrence D. Julien, Bruce M. Frankel, Sharon L. Longo, Michele Kyle, Timothy C. Ryken

721. Young Investigator Award **Regression of Glioma Growth Using a Retroviral Vector Expressing Interleukin-4.**
Quentin Malone, Andrew H. Kaye, Mary Saleh

722. **Gamma Knife Radiosurgery is Superior to Conventional Radiotherapy in the Adjunctive Management of Acromegaly.**
Mary Vance, Edward R. Laws, Jr., Ladislau Steiner, Melita Steiner, C. J. Woodu

723. **Apoptotic Signaling by Apo2L Selectively Kills Glioma Cells in Vitro and in Vivo.**
Ian F. Pollack, Melanie Erff, Avi Ashkenazi

724. **Spinal Cord Biopsies: A Review of 38 Cases.**
Ofer M. Zikel, Gary M. Miller, Bernd W. Scheithauer, William E. Krauss

725. **Hemangioblastoma (HB) of the CNS and Retina: Impact of Von Hippel-Lindau Disease (VHL) on the Outcome.**
Mika Niemela, Sebsebe Lemeta, Paula Summanen, Tom Bohling, Juha Jaaskelainen

726. **The Importance of Timing in a Two Compartment Model of Sodium Thiosulfate Protection Against Carboplatin-induced Ototoxicity in Patients With Malignant Brain Tumors.**
Edward A. Neuwelt, Nancy Doolittle, Leslie L. Muldoon

727. **Spinal Meningiomas in Patients Under Age 50: A 21-year Review.**
Ofer M.Zikel, Bernd W. Scheithauer, William E. Krauss

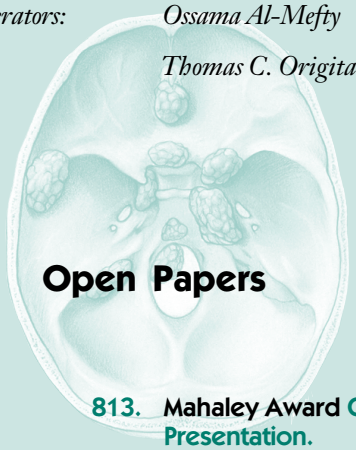
728. **Treatment of Neoplastic Meningitis With Intrathecal Temozolomide.**
Alan Villavicencio, Gary E. Archer, Roger E. McLendon, Allan H. Friedman, Darrell Bigner, Henry S. Friedman, John H. Sampson

729. **Intracranial Adenoviral Interleukin-12 Delivery Effects Potent and Long-lasting Immunity Against Glioma.**
John S. Yu, Yunhui Liu, Hua Zhang, Christopher J. Wheeler, Ken Samoto, Chenren Liu, Luis Villareal, Keith L. Black

Scientific Session

Wednesday, November 3, 1999 **2–5:30PM**
Section on Tumors II
Issues in Skull Base Surgery

Moderators: *Ossama Al-Mefty*
Thomas C. Origitano



Open Papers

2–2:20 PM	**Update on the Biology of Meningiomas and Implications for Nonoperative Treatment** *Randy Lynn Jensen*
2:20–2:40 PM	**Cranial Base Surgery for Malignant Tumors: When and When Not to Operate** *Franco De Monte*
2:40–2:50 PM	**Discussion**
2:50–3:30 PM	**Oral Posters** *James M. Markert* *Michael W. McDermott*
3:30–4 PM	**Coffee Break With Exhibitors**
4–5:30 PM	**Open Papers (813-822)** *James T. Rutka*

813. **Mahaley Award** Colloid Cysts of the Third Ventricle: Factors Associated with Symptomatic Clinical Presentation.
Bruce E. Pollock, Shawn Schreiner, John Huston III

814. MR Spectroscopy at 3 Tesla Differentiates Tumor Recurrence From Radiation Change in Patients With Astrocytomas.
James D. Rabinov, Patricia Lani Lee, Leo Ling Cheng, Frederick G. Barker, David Louis, R. Gilberto Gonzalez

815. The Middle Fossa Approach for Acoustic Neuroma: Hearing Preservation Results.
John Diaz Day, William Hitselberger, Derald Brackmann, Robert Owens

816. Safety and Efficacy of a Multi-Center Study Using Intraarterial Chemotherapy in Conjunction With Osmotic Opening of the Blood-Brain Barrier for the Treatment of Malignant Brain Tumors.
Nancy Doolittle, Michael Miner, Walter A. Hall, Tali Siegal, E. Jerome Hanson, Eva Osztie, Leslie D. McAllister, Joseph S. Bubalo, Dale F. Kraemer, David Fortin, Randal Nixon, Leslie L. Muldoon, Edward A. Neuwelt

817. Intraoperative Neurophysiological Monitoring During Surgery of Intrinsic Tumors of the Insula.
Ulrich Pechstein, Georg Neuloh, Johannes Schramm, Josef Zentner

818. Targeting Gamma 34.5-Mediated Herpes Virulence for Tumor Therapy.
Richard Y. Chung, Ennio Antonio Chiocca

819. Presurgical Motor and Somatosensory Cortex Mapping With fMRI and PET.
Richard G. Bittar, André Olivier, Abbas F. Sadikot, Frederick Andermann, G. Bruce Pike, David Reutens

820. DNA Plody, DNA Index, and S-Phase Among Secreting and Non-secreting Anterior Pituitary Adenomas: A Cytometric Study on 61 Cases With Feulgen-positive DNA Analysis.
Luciano Mastronardi, Antonio Guiducci, Cristina Spera, Franca M. Buttaro, Enrico G. Cristallini, Fabrizio Puzzilli

821. An Ultrasound-based Neuronavigation System: A Good Solution to the Brain-Shift Problem.
Geirmund Unsgaard, Atle Kleven, Steinar Ommedal, Aage Gronningsaeter

822. Hearing Preservation in Acoustic Tumor Surgery: Practical and Technical Considerations.
Wolfgang T. Koos

Ask the Experts—The Neurocrine IL-4/Pseudomonas Exotoxin Trial

Ronald E. Warnick, MD

This article was based on interviews with three investigators who are currently involved in the Phase I trial of IL-4/Pseudomonas exotoxin for the treatment of recurrent malignant glioma. The investigators recently interviewed regarding this trial include: 1)Walter Hall, MD (University of Minnesota), principal investigator in the Phase I trial and a recognized expert in the field of immunotoxin therapy; 2) Sandeep Kunwar, MD (University of California-San Francisco), co-investigator in the Phase I trial and a participant in the preclinical studies of the IL-4/Pseudomonas exotoxin; and 3) Steven Marcus, MD, Senior Vice President of Clinical and Regulatory Affairs at Neurocrine Biosciences.

Q. Can you describe the IL-4/Pseudomonas exotoxin that is currently in Phase I testing in the U. S. and Germany?

Dr. Hall: The targeted toxin is a recombinant chimeric fusion protein composed of circularly permuted interleukin-4 and a mutated form of the Pseudomonas exotoxin (termed IL-4 toxin).

Q. What preclinical work formed the basis for this approach?

Dr. Kunwar: This class of targeted toxins was developed in the laboratory of Ira Pastan, MD, at the National Institutes of Health. The cDNA of a mutant form of the Pseudomonas exotoxin was fused to the cDNA of the targeting moiety, in this case IL-4. This ligand was somewhat difficult to use since the binding domain of the recombinant toxin was partially "hidden."

Therefore, Robert Kreitman, MD, and Raj Puri, MD, developed a permuted form that exposed the IL-4 receptor binding domain. This recombinant protein was produced in large quantities and then purified. It specifically binds to glioblastoma cells that express the IL-4 receptor, which leads to internalization and translocation into the cytoplasm. The enzymatic toxin reverses the ADP-ribosylate elongation factor-2, which inhibits protein synthesis and ultimately results in cell death. The potency of this targeted toxin is evident by cytotoxicity at nano-to-picomolar concentrations with a steep dose-effect curve. The cytotoxic effect of the IL-4 recombinant toxin against glioblastoma cell lines was the real evidence that these tumors, do in fact, express some level of IL-4 receptors.

Further experiments in glioblastoma xenografts confirmed the clinical efficacy of local IL-4 toxin delivery. In non-human primates, there was no evidence of significant toxicity with intrathecal doses of the IL4-toxin, consistent with the fact that normal brain tissue does not express detectable levels of the IL-4 receptor.

Q. Is this the first clinical trial for this targeted toxin?

Dr Marcus: A Phase I trial of the IL-4 toxin was conducted by Robert Rand, MD, at the John Wayne Cancer Institute. Nine patients with recurrent glioblastoma were treated with intratumoral infusion of the IL-4 toxin (maximum dosage=6ug/ml, maximum volume=170ml). There was radiographic evidence of a biologic effect in five patients who received dosages greater than 2ug/ml. Four patients required post-infusion craniotomy for debulking of tumor necrosis. Only one patient remains progression-free (18 months). This preliminary study documented the biologic activity of the IL-4 toxin and supported the initiation of a more definitive clinical trial.

Q. What type of patients are eligible for the current Phase I clinical trial?

Dr. Hall: Patients must be over the age of 18, with recurrent anaplastic astrocytoma or glioblastoma multiforme and a Karnofsky Performance Status of 60 percent or greater. Patients must have received external beam radiation therapy and have a tumor volume of less than 100 cc. Patients cannot have multifocal disease or leptomeningeal dissemination.

Q. Can you describe the protocol treatment regimen?

Dr. Hall: This is a Phase I trial to determine the maximum tolerated dose of the IL-4 toxin for human use. Three patients will be entered at each dose level (6 ug/ml, 9 ug/ml, 15 ug/ml, and 24 ug/ml). Appropriate candidates will undergo a biopsy to confirm recurrent tumor, at which time one to three ventricular catheters will be placed stereotactically into the tumor for infusion of the targeted toxin. The intratumoral infusion will begin 24 hours later. Patients will receive 40 ml continuously over a 96-hour period via a microinfusion pump. After the infusion, the catheter(s) will be removed and a MR scan will be performed to assess the degree of edema and document any early biologic effect. Subsequent MR scans will be obtained one month after surgery and then at eight-week intervals.

Q. Does the study escalate toxin concentration, infusate volume, or both?

Dr. Hall: This study escalates toxin concentration while keeping the volume of infusion constant. Once the maximum tolerated dose of the IL-4 toxin is reached, an additional 12 patients will be treated at that dose level.

Q. What are the advantages of convection delivery?

Dr. Kunwar: Drug delivery has been a constant problem in the treatment of brain tumors and a significant reason why therapies that are effective in small animal models often fail in humans. Convection-enhanced delivery involves the slow infusion of fluid into the extracellular space. The system has several advantages: 1) homogeneous distribution of large macromolecules over long distances using a pressure gradient rather than a concentration gradient (diffusion); 2) avoidance of high concentration peaks seen with diffusion; 3) circumvention of the blood-brain barrier; 4) limited systemic toxicity; 5) reversible tissue changes similar to cerebral edema with few permanent histological changes; and 6) treatment of infiltrating tumor cells within normal tissue without damaging that tissue.

Q. Is there a concern that delivery of this volume of fluid could lead to edema in patients with pre-existing mass effect?

Dr. Kunwar: Exacerbating the effects of cerebral edema in these patients is a definite concern. However, with the extremely slow infusion rates needed for bulk-flow microinfusion, as well as the selective use of corticosteroids and mannitol, patients appear to tolerate this form of delivery.

Q. What are the endpoints of the study?

Dr. Hall: The primary objective of the study is to determine the safety and maximum tolerated dose of IL-4 toxin that can be delivered into a recurrent astrocytoma via an intratumoral catheter, using an external microinfusion pump. A secondary objective is to determine whether there is any therapeutic effect of the IL-4 toxin in the treatment of recurrent malignant astrocytoma.

Q. What is the current accrual status?

Dr. Marcus: To date, 20 patients have been treated at doses of 6 ug/ml (9 patients), 9 ug/ml (6 patients), and 15 ug/ml (5 patients) in the two ongoing Phase I trials in the United States and Germany. Dose limiting toxicity was not identified at the two lower dose levels. One patient at the 15 ug/ml dose level exhibited a grade IV serious adverse event and further assessment of this patient is in progress.

Q. Are there any plans for a Phase II trial?

Dr. Marcus: Upon identification of a maximum tolerated dose, a Phase II study will be initiated to evaluate the anti-tumor effect of the IL-4 toxin in 15 patients with recurrent glioblastoma. The primary endpoint will be progression-free survival.

Q. What do you believe will be the limiting factor for the success of the IL-4/Pseudomonas exotoxin?

Dr. Hall: The limiting factor will be the ability to treat the entire tumor volume using present catheter designs. Because of the irregular shape of these tumors, particularly when a surgical resection has been performed, it is difficult to distribute the targeted toxin to the entire tumor.

Dr. Kunwar: The challenge is to distribute the toxin to the entire volume of brain containing tumor cells. This may require multiple dosing or the use of long-term infusion systems. In such a scenario, development of antibodies against the protein may alter the efficacy of the toxin. In addition, there may be selection of a sub-population of tumor cells that do not express the IL-4 receptor and, therefore, are resistant to the therapy.

Q. Do you have any final thoughts on the prospects of targeted toxin therapy?

Dr. Hall: This therapy is extremely promising for the treatment of malignant astrocytoma because of its extreme potency. These agents selectively target tumor cells and should have little effect on normal brain cells. If this agent is selective for these tumors, it may revolutionize the treatment of malignant gliomas. In the best case scenario, future patients may require only a biopsy for tissue diagnosis followed by infusion of the IL-4 toxin. There may be no need for radiation therapy or chemotherapy. Questions regarding single treatment versus repeat infusion will need to be answered. Chronic low dose infusion may be the most effective strategy.

Dr. Kunwar: Targeted toxins take advantage of extremely potent, naturally occurring protein toxins. These toxins function by a very different mechanism than most chemotherapeutic agents and radiation therapies. Since they are enzymes, there is no need for a large number of molecules to gain entry into the cell to achieve a cytotoxic effect. The future of these toxins will be the ability to find the best targeting moiety; one that will selectively target all the tumor cells and not the normal tissue. This may not be possible with a single toxin and may require a combination of targeted proteins that is based on the patient's particular tumor.

Minutes From the Executive Council Meeting

James T. Rutka, MD

AANS/CNS Section of Tumors
April 26, 1999 ■ New Orleans, Louisiana

The Executive Council meeting of the AANS/CNS Section on Tumors was called to order at 1 PM by Chairman, Mark Bernstein, MD. In attendance were Joseph Piepmeier, MD; Raymond Sawaya, MD; Michael McDermott, MD; Jack Rock, MD; William Couldwell, MD; Ronald Warnick, MD; Paul Kornblith, MD; Mitchel Berger, MD; Anthony Asher, MD; Peter Black, MD; James Rutka, MD; Roberta Glick, MD; Nicolas DeTribolet, MD; David Thomas, MD; and William Chandler, MD.

Committee Reports

Secretary/Treasurer's Report

The minutes from the Executive Council's meeting on October 5, 1998, in Seattle, were accepted by Dr. Black, and seconded by Dr. Berger without change. The financial report for the Section was presented by Dr. Piepmeier. Assets are approximately $240,000, and $2,500 stems from accrued interest on a $50,000 long-term investment policy. Some issues arose surrounding the Statement of Financial Position from the AANS National Office in that approximately $11,000 appeared as a liability, and instead should have been reported as an asset.

Awards Committee

Award winners at the 1999 AANS Annual Meeting were:

Preuss Award	Sandeep Kunwar, MD
Mahaley Award	Doug Kondziolka, MD
Young Investigator Award	Walter Stummer, MD
National Brain Tumor Foundation Translational Research Award	Adam Mamelak, MD
Farber Award	Edward Oldfield, MD

A question was raised concerning the future of the Farber Award. It was decided that contact would be made with Dr. Wilson to determine if there would be changes in the presentation of this lectureship. Dr. Sawaya announced that investigators can now indicate on the online abstract form which award they are competing for; this has helped when tracking prospective applicants.

Bylaws Committee

Dr. Rock reported that the bylaws were approved by the AANS/CNS. He also reported that Guidelines were being written regarding the case of an 18-year-old with a single metastatic brain lesion. To prepare these Guidelines for acceptance, Dr. Rock noted there were at least seven class I and II papers in medical literature, and nearly 25 class III papers. It is hoped that a draft of these Guidelines will be available by the next Section meeting in Boston. Of note, the Low Grade Glioma Guidelines were published in *Neurosurgical Focus* in June 1998.

Education Committee

Dr. Couldwell submitted a document from Vincent Traynelis, MD, which summarized standards for the resident curriculum. Dr. Couldwell is actively engaged in establishing standards for fellowship training in Neuro-Oncology. It is expected that the Residency Review Committee will oversee these standards, which will eventually lead to the accreditation, but not the certification, of a neurosurgeon in neuro-oncology. It was suggested that a similar skull base surgery accredited fellowship will evolve as well.

Drs. DeTribolet and Thomas reminded the Executive Council that the International Brain Tumor Conference is slated to take place October 3-5 1999 in Sapporo, Japan.

Dr. Berger announced that the European Association of Neuro-Oncology, the Society of Neuro-Oncology, and the Japanese Neuro-Oncology Group will meet for the first time at the World Federation Meeting in Washington, D.C., in fall 1999.

Membership Committee

Dr. McDermott announced that following the Section mailing to residency program chairmen, there were ten responses for resident membership. Dr. McDermott described the use of the NEUROSURGERY://ON-CALL® Web site to promote membership within the Section. In addition, a list was circulated with the names of nine new members who had applied. Dr. Black moved that they be accepted into the Section; Dr. Piepmeier seconded this motion.

Membership Services

Dr. Asher announced that the online journal club was progressing nicely. Unfortunately, the previous aide Allison Casey, has left the AANS organization. There was discussion as to whether Allison Casey should be retained as a consultant to establish the online journal club, or whether a different individual within the AANS should be identified. It was decided that the AANS National Office would be notified of the issue, and that they should advise the Executive Council as to the best route to take.

Newsletter

Dr. Warnick was congratulated for the outstanding spring 1999 newsletter. It was suggested that extra copies of the newsletter be prepared and sent to all neruosurgical residents throughout North America. Dr. Piepmeier brought to the attention of the Executive Council the possibility of the Congress of Neurological Surgeons publishing a membership magazine titled, "Neurosurgery News." It was suggested that, if developed, a Section newsletter be published in this communication vehicle as well.

Nominating Committee

Dr. Chandler reported that he received several nominations for the positions of Tumor Section Chair and Secretary. Dr. Piepmeier was appointed as the new Chair of the AANS/CNS Section on Tumors and Dr. Rutka was named Secretary.

Program Committee

At the AANS Annual Meeting in New Orleans, the main Neuro-Oncology session was comprised of speakers providing updates on intraoperative MRI. Dr. Warnick organized this event and Dr. McDermott will be organizing the program for the 1999 CNS meeting. Special sessions will be held on spinal cord neoplasms and skull base surgery.

Research Committee

Dr. Glick gave an update on research funding opportunities. She brought to the attention of the Executive Council special funding for clinical trials involving lower socioeconomic groups.

Leadership Conference

Dr. Piepmeier attended the Leadership Conference on January 23-24, 1999 in Chicago. During the conference, it was proposed that Larry Chin, MD, a member of the Tumor Section, serve as the Section's representative on the AANS/CNS Washington Committee. It also was suggested that he report directly to the Executive Council before decisions are made.

Dr. Piepmeier moved that the Tumor Section give $25,000 to the Washington Committee so that they can continue to represent neurosurgeons on a wide range of issues.

Other Business

Satellite Symposium

Dr. Warnick is in charge of organizing the 1999 Satellite Symposium, which will immediately follow the AANS Annual Meeting in San Francisco. The local arrangements person for the event will be Dr. McDermott, and the preliminary design and structure of the Satellite Symposium was discussed.

Localized Therapy

Dr. Bernstein has written a letter on behalf of the AANS/CNS Section on Tumors to Mark Hadley, MD, concerning a document circulated to the Section on localized therapy for gliomas.

Genetic Vector Registry

Dr. Bernstein has written a letter of response to Dr. Ryken, stating that the AANS/CNS Section on Tumors is in support of the genetic vector registry.

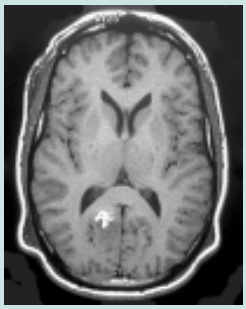
You Make the Diagnosis

Ronald Warnick, MD

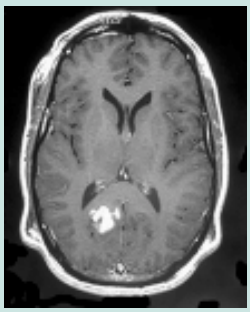
This article represents a new feature for the *Tumor Section newsletter*. A clinical case history will be presented along with pertinent imaging studies. After you formulate a differential diagnosis, turn to page 12 to read more about the case.

Case History

A 33-year-old previously healthy man presented with a one-month history of visual scotomata. These consisted of flashing lights and movements in the left visual field that were progressive in frequency and intensity. Neurological examination was significant only for a partial left inferior quadrantanopsia. A magnetic resonance (MR) scan revealed a signal abnormality located in the medial right occipital lobe characterized by subacute hemorrhage and gadolinium enhancement.



Non-contrast T1-weighted MR scan demonstrates a focal area of subacute hemorrhage located in the right medial occipital lobe without significant edema.



T1-weighted MR scan with gadolinium shows a heterogeneous area of contrast enhancement in the same region.

Issues to Consider

1) What is a reasonable differential diagnosis for this hemorrhagic, enhancing lesion?

2) Would you recommend any other diagnostic or imaging studies?

3) What are some treatment options for this patient?

4) What intervention would you recommend based on the available information?

To see the diagnosis, turn to page 12

Researchers to be Recognized at the 1999 CNS Annual Meeting

Preuss Award

Antisense-mediated Inhibition of the bcl-2 Gene Induces Apoptosis in Human Malignant Glioma.

Terrence D. Julien, Bruce M. Frankel, Sharon L. Longo, Michele Kyle, Timothy C. Ryken

The bcl-2 proto-oncogene represses a number of apoptotic pathways and is expressed in increasing amounts in glial tumors of higher malignancy. We tested whether antisense oligonucleotides to the bcl-2 gene would affect glioma cell viability. Antisense oligonucleotides directed to the first six codons of the human bcl-2 gene were transfected into malignant glioma cells. Two human Bcl-2 positive glioblastoma cell lines from our tumor bank were transfected in vitro with bcl-2 antisense (AS) and nonsense (NS) oligonucleotides at 1uM and 5uM concentrations for 5 and 24 hours. Cell viability was assessed at 2, 4, 5, and 7 days by cell counting using a hemocytometer. There was up to a log-fold decrease in cell growth of the bcl-2 AS treated cells compared to the NS transfected cells for both Roc (p= 0.007 and p=0.004) and Jon52 (p=0.02 and p=0.004) at 5 and 24 hours of transfection. There was up to 50 percent decreased survival in both cell lines at 1uM and 5uM concentrations after 24 hour transfection with anti-bcl-2 oligonucleotides (all p<0.01). Western blot analysis demonstrated a decrease in Bcl-2 protein expression in one cell line, while there was a statistically significant increase in the apoptotic index of both cell lines (p< 0.05).

Our results suggest that transfection of human glioma cells with AS bcl-2 results in increased apoptotic death. This provides evidence that Bcl-2 plays a role in tumor progression by acting as an oncogene, and inhibiting the bcl-2 gene could have a therapeutic effect.

Young Investigator Award

Regression of Glioma Growth Using a Retroviral Vector Expressing Interleukin-4.

Quentin Malone, Andrew H. Kaye, Mary Saleh

Vascular endothelial growth factor [VEGF] is over expressed in virtually all glioblastomas and has a potent angiogenic effect. Using a gene therapy protocol, the mechanism of action of IL-4 down regulation of VEGFR and its efficacy as a treatment for glioma were examined. A polycistronic IRES-containing retroviral vector was constructed which expressed IL-4 and beta-galactosidase. The purified vector was transfected into an ecotropic packing cell line with individual clones being isolated and cultured. IL-4 production was determined by immunoassay. Athymic mice used for subcutaneous rat C6 glioma inoculation and immunocompetent CBA strain mice for intracerebral implantation of tumor cells. Both co-injection of tumor and treatment cell lines and delayed injection of treatment line into established tumors were undertaken. Tumor volume and vascularity were determined and histopathological analysis of the tumor was undertaken. Tumor growth was significantly retarded in treated athymic animals with both co-injection and delayed injection experiments. Vascular density of the tumor was significantly reduced in treated animals. Intracerebral experiments confirmed a similar significant reduction in tumor volume and vascular density with co-injection. In animals which underwent delayed stereotactic implantation of the packaging cell line expressing IL-4, regression of established C6 intracerebral tumors occurred with tumor eradication achieved. A marked peritumoral eosinophilic infiltration was noted. Beta-galactosidase activity was present in peritumoral endothelium only.

In immunocompetent mice eradication of established intracerebral tumor can be achieved using interleukin-4 mediated down regulation of VEGF receptors. The retroviral vector utilized in these experiments successfully induced local endothelial cell expression of interleukin-4.

Mahaley Award

Colloid Cysts of the Third Ventricle: Factors Associated With Symptomatic Clinical Presentation.

Bruce E. Pollock, Shawn Schreiner, John Huston III

Patients with third ventricular colloid cysts typically are diagnosed when they develop CSF obstruction at the foramen of Monro. The clinical and neuroimaging characteristics related to symptom development are poorly understood.

From January 1974 to June 1998, 155 patients with newly diagnosed colloid cysts were managed at our center. Eighty-seven patients (56%) were felt to have tumor related symptoms and underwent surgery (resection=74; VPS=11; stereotactic aspiration=2. Sixty-eight patients (44%) had colloid cysts believed to be incidental and observation with serial neuroimaging was recommended.

Univariate analysis comparing the two patient groups found four factors associated with symptomatic clinical presentation: younger patient age (44 yr vs 57 yr, P<0.001), cyst size (13 mm vs 8 mm, P<0.001), ventricular dilatation (83% vs 31%, P<0.001), and increased signal on T2-weighted MRI (44% vs 8%, P=0.001). All four variables remained significant in a multivariate logistic regression model: patient age (P=0.04, odds ratio=1.0), cyst size (P=0.04, odds ratio=1.2), ventricular dilatation (P=0.02, odds ratio=7.2), and increased signal on T2-weighted MRI (P=0.04, odds ratio=2.7). Recursive partitioning of the patients based on age (>50 yr=0 pts; <50 yr=1 pt), cyst size (<10 mm=0 pts; >10 mm=1 pt), and ventricular dilataion (no=0 pts; yes=1 pt) demonstrated four relative risk groups for symptomatic presentation. Group I (0 pts)3/34 patients, 9%; Group II (1 pt) 19/45 patients, 42%; Group III (2 pts) 47/57 patients, 83%, Group IV (3 pts) 18/19 patients, 95%. Multivariate analysis including the patient groups resulted in removal of the other variables from the model, whereas the patient groups remained signficant (p<0.001, odds ratio=6.4) to predict symptomatic presentation.

Third ventricular colloid cysts that enlarge more rapidly cause CSF obstruction and symptoms of increased intracranial pressure. However, some cysts enlarge more gradually allowing the patient to accomodate to the enlarging mass without disruption of CSF flow and the patient remains asymptomatic. Consequently, incidental colloid cysts are more frequently discovered in older patients and may not require neurosurgical intervention.

In Brief...

National Brain Tumor Foundation Designates New Grant

To honor one of our nation's premier brain tumor researchers and clinicians, the National Brain Tumor Association (NBTF) is designating a special research grant in the name of Charles B. Wilson, MD. "Dr. Wilson's contribution to brain tumor treatment, whether through his own research or the successful training of hundreds of young physicians, is unmatched," said Donald R. Share, Board member and Chair of NBTF's Research Committee. "Our greatest hope is for this grant to inspire other investigators to emulate Dr. Wilson and keep searching until a cure for brain tumors is found," Mr. Share said.

The grant will be offered annually to an investigator pursuing brain tumor treatments and cures. The grant will be available to all North American brain tumor researchers and reviewed by NBTF's Scientific Advisory Committee. For more information, contact the NBTF by phone at (800) 934-CURE or via e-mail at nbtf@braintumor.org

1999 Midwest Regional Brain Tumor Conference

The NBTF, in conjunction with the Neuroscience Institute at the University of Cincinnati Medical Center, the Mayfield Clinic and Rhone-Poulenc Rorer Pharmaceuticals, is hosting the 1999 Midwest Regional Brain Tumor Conference. The event is slated to take place October 1-2, 1999 at the Northern Kentucky Convention Center in Covington, Kentucky.

The conference, designed especially for brain tumor patients, their families and friends, and health professionals with a special interest in neuro-oncology, will feature presentations and demonstrations on the latest treatments, such as gene therapy, biological therapies, radiotherapies, computer-assisted surgical techniques, and alternative therapies. The program also will include workshops on heredity and genetics, hospice care, working with HMOs, support groups, and communicating about brain tumors, as well as consultation rooms, internet resources, and luncheon roundtables.

In addition, the program will feature internationally-renowned neuroscientists from such prominent institutions as Johns Hopkins, University of Cincinnati, Children's Hospital Medical Center in Boston, Children's Hospital Medical Center in Cincinnati, and many more. Representatives from community resource groups, support groups, and many brain tumor patients are working hard to make this program one of the most unique and exciting events of its kind.

For more information or a copy of the program, contact Sheila Stuckey, Conference Coordinator, at (800) 325-7787, ext. 5251, via e-mail at Sstuckey@mayfieldclinic.com or visit the Neuroscience Institute Web site at www.health-alliance.com\tni.

RTOG Continues to Grow

The Radiation Therapy Oncology Group (RTOG) is an international organization that sponsors research in the treatment of tumors. It was organized in 1968 with funding from the National Cancer Institute. During its tenure, it has activated 300 protocols and accrued a total of 60,000 patients to cooperative group studies. One of its goals is to further refine standards of treatment for brain tumors.

There are two meetings each year to review and discuss new and ongoing protocols. These meetings are open to all neurosurgeons at participating institutions. Currently, there are six active glioma protocols and one active brain metastasis protocol. At the current rate of accrual, it is estimated that the RTOG will need two new glioma protocols and one to two new metastatic protocols each year.

Over the past two years, the RTOG has clearly seen that the presentation of concepts by individual neurosurgeons can evolve to become active multicenter protocols. The Neurosurgical Committee meeting has become very active in the RTOG, sponsoring symposiums on basic and clinical science concerning primary and metastatic brain tumors. Many of the members of the AANS/CNS Section on Tumors are already affiliated with RTOG sites. The RTOG, and specifically the Brain Tumor and Neurosurgical Committees, are very receptive to new ideas from the neurosurgical community.

The RTOG actively encourages submissions of translational studies. An example would be the evaluation of genetic or biochemical changes during treatment modalities. This provides a potential research opportunity for neurosurgeons interested in establishing a wider patient base for their research, and potentially allowing neurosurgeons to obtain primary or increased funding. The RTOG also allows neurosurgeons to submit their ideas to an international group for open discussion, which helps share information and resources. Anyone interested in becoming more involved should contact Dennis Bullard, MD, at Debullard@msn.net.

Annual Meeting Plans Underway

The 4th Annual Meeting of the Society for Neuro-Oncology (SNO) will be held November 18-21, 1999 in Scottsdale, Arizona. An optional Educational Day on November 18 will feature an overview of neuro-oncology basic science, CNS lymphoma and germ cell tumors. Breakout sessions will focus on neuro-imaging, epidemiology, surgical advances, radiosurgery and novel therapeutics. Formal meeting presentations have been drawn from the latest basic, translational and treatment research for neuro-oncology. For more information, contact Jan Esenwein via e-mail at jesenwei@notes.mdacc.tmc.edu or by fax at (713) 349-8788.

You Make the Diagnosis continued from page 9

Ronald Warnick, MD

Clinical Course

The differential diagnosis in this case was quite broad including hemorrhagic tumor, arteriovenous malformation with subacute hemorrhage, cavernous malformation, subacute infarct, infection or inflammation. The patient underwent cerebral angiography and this study did not show vascular malformation, tumor stain or vascular occlusive disease. Therefore, a vascular etiology seemed unlikely although a cavernous malformation was not ruled out by this study.

Prior to any intervention, the patient underwent positron emission tomography that demonstrated the right occipital lesion to have low uptake of 18-fluorodeoxyglucose and moderate accumulation of C11-labeled methionine. This pattern of uptake was thought to be consistent with a low-grade glioma, in spite of MR characteristics more typical of a maligant neoplasm (e.g., hemorrhage, enhancement).

The patient's visual symptoms were progressive and a repeat MR scan performed four weeks after the initial study showed an interval increase in the volume of hemorrhage, enhancement and edema. Various treatment options were discussed but the patient ultimately underwent a MR-guided stereotactic biopsy using the Cosman-Roberts-Wells stereotactic system. An area within the enhancing portion of the lesion was targeted via a parieto-occipital approach and multiple tissue samples were obtained.

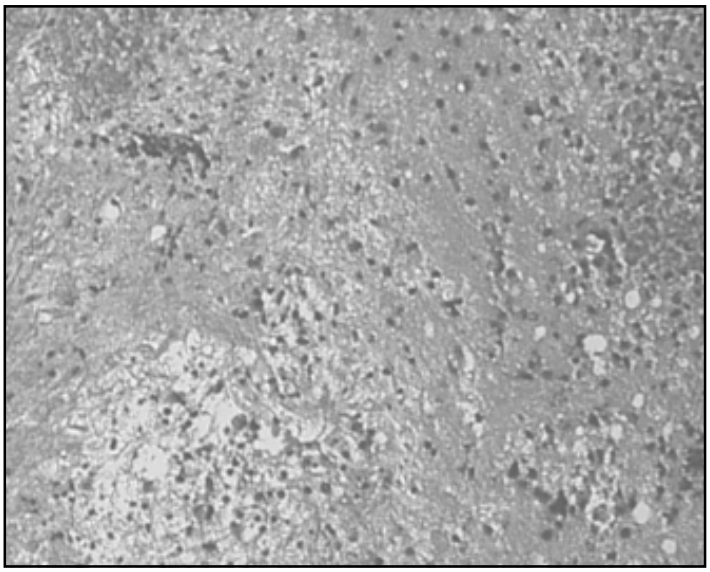
Routine histology showed no overt neoplasm. There were extensive reactive changes including focal necrosis, perivascular cuffing, and parenchymal infiltration by T-lymphocytes and macrophages. An extensive workup for bacteria, mycobacteria, fungi and toxoplasmosis was negative. There were no viral inclusion bodies and immunohistochemistry for Herpes simplex was negative. Ultimately, fluorescence in situ hybridization (FISH), using a commercially available kit, confirmed the diagnosis of Herpes encephalitis.

The patient was maintained on steroids (Prednisone 80mg qd) and started on Acyclovir (1 gram po tid). Six weeks later, a repeat MR scan revealed a dramatic reduction in the mass effect and volume of the hemorrhagic/enhancing mass. He was neurologically intact except for a residual left inferior quadrant visual field defect. Therapy was continued for a total of three months.

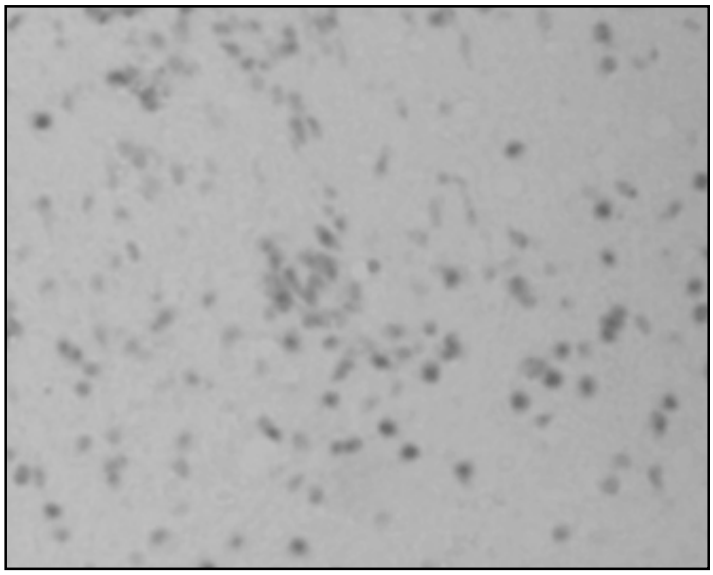
Comments

This is a unique case of Herpes encephalitis occurring outside the temporal lobe masquerading as a hemorrhagic tumor. Herpes encephalitis is generally confined to the temporal lobes and adjacent structures (e.g., inferior frontal lobe, insular cortex) and only rarely encountered as a focal mass outside the temporal lobe. The MR characteristics of edema, hemorrhage and blood-brain barrier disruption can easily mimic a maligant neoplasm. Brain biopsy provides adequate tissue for both routine histology and specialized tests for the Herpes virus. As seen in this patient, immunohistochemistry for Herpes proteins is less sensitive than fluorescence in situ hybridization and are able to detect RNA or DNA expressed during active Herpes infection. Most patients will show clinical and radiographic improvement after initiation of acyclovir therapy.

If you have any comments regarding this case study, or would like to contribute an interesting case to "You Make the Diagnosis," please e-mail Ronald Warnick, MD, Newsletter Editor, at NSGYMD@aol.com.



H & E histologic section reveals focal necrosis, perivascular cuffing, and parenchymal infiltration by reactive cells.



Fluorescence in situ hybridization shows positive cells indicative of active Herpes infection.

Application for Membership

AANS/CNS Section on Tumors

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 847-692-9500 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@neuro.ucsf.edu

A Close Look at Section Membership

Michael W. McDermott, MD

The AANS/CNS Section on Tumors came into existence in 1984, under the direction of Mark Rosenblum, MD, who successfully promoted the Section and doubled its membership during his 6-year tenure. Since the Section's humble beginning, our membership has continued to grow under the guidance of our Section Chairs.

This year, Joseph Piepmeier, MD, took over the Section with an enthusiastic Executive Council and sound finances, thanks to the hard work of former Chair, Mark Bernstein, MD. In the spirit of encouraging new, younger members, Dr. Piepmeier has appointed Fred Lang, MD, as our Section's young neurosurgeon representative.

Membership Continues to Grow

Membership levels in the Tumor Section have continued to grow over the years — remaining consistent with increasing membership in the AANS and CNS, as well as the AANS/CNS Sections. The most significant increase in our Section's membership occurred between 1989-90, when total membership grew 73 percent (Figure 1). Apart from two minor declines, total membership has increased between 2.6-4.8 percent each year.

The two levels of membership with the biggest growth between 1994 and 1999 are Associate and Resident membership, up 500 percent and 262 percent, respectively (Figure 2). In the future, we hope that the youngest and brightest minds in neuro-oncology and related research/clinical fields also will join the ranks of our Section.

This year, we will be sending another reminder to all Resident members of the AANS and CNS, inviting them to become members of the Tumor Section. For the first time, the Section also plans to host a small reception at the CNS Meeting in Boston, allowing interested residents and young neurosurgeons to meet other members and find out first-hand about the Section's activities.

Compared to the other AANS/CNS Sections, the Tumor Section boasts the third largest membership (Figure 3). In particular, it ranks second in terms of resident membership.

Membership Levels

Currently, there are six levels of membership in the AANS/CNS Section on Tumors including Active, International, Associate, Honorary, Adjunct and Resident. Membership application forms, as well as a description of each membership category, can be found on the official Web site of the AANS and CNS — **NEUROSURGERY://ON-CALL**® (www.neurosurgery.org). Please consider one of your colleagues for membership and help expand the depth and breadth of expertise in the Section.

The future poses many challenges for the field of neuro-oncology and it is sure to be an exciting time. If you are not already a member of our Section, and have an interest in the field of neuro-oncology, please consider joining!

Figure 1

Membership Profile of the AANS/CNS Section on Tumors

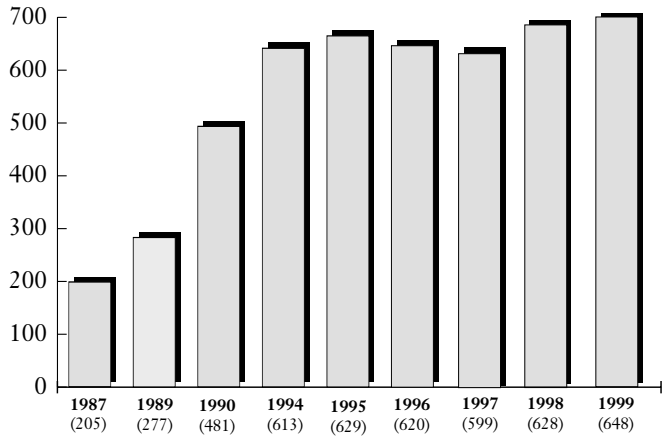


Figure 2

AANS/CNS Section on Tumors Resident Membership Levels

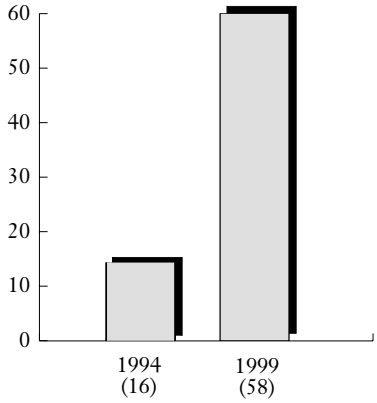
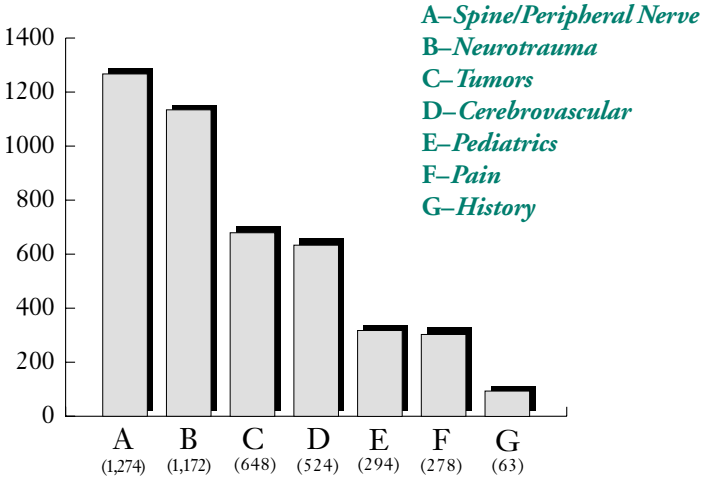


Figure 3

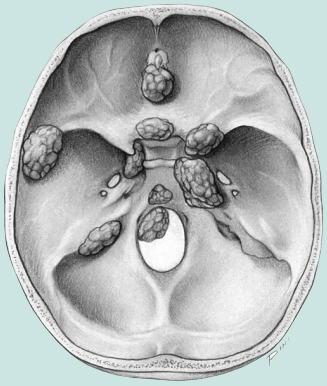
Current Membership Levels



Spectacular Scientific Program

Planned for the 2000

AANS/CNS Section on Tumors
Fourth Biennial Tumor Satellite Symposium



San Francisco Hilton and Towers
San Francisco, California
April 13-14, 2000

Meeting highlights include:

- Conveniently held at the conclusion of the 2000 American Association of Neurological Surgeons Annual Meeting.
- **SCIENTIFIC SESSIONS** on exceptional educational topics, including:
  - Novel Delivery Strategies for Anti-tumor Agents
  - Skull Base Meningioma Treatment Paradigms
  - Craniopharyngioma–Point/Counterpoint
  - Translational Strategies for Pediatric Brain Tumors
- **SPECIAL LUNCHEON SEMINAR** on "How to Build a Brain Tumor Center".
- **PRESENTATION** of scientific papers and scientific posters.
- **SPECIAL LECTURE** by Darell Bigner, MD, PhD, on "Targeted Toxins for Gliomas Based on their Genetic Pathogenesis".
- **RECEIVE** up to 12 credit hours of Continuing Medical Education toward the AMA Physician's Recognition Award.

Abstract submission begins September 9, 1999 for the Fourth Biennial Tumor Satellite Symposium. For your convenience, the online abstract form is available through NEUROSURGERY://ON-CALL® at www.neurosurgery.org.

ABSTRACT DEADLINE
DECEMBER 1, 1999

Specific details of the scientific program, hotel reservation, and registration forms will be included in the AANS Preliminary Program mailing in December.

Contact Ronald Warnick, MD, at nsgymd@aol.com for questions regarding the scientific program.

For further information contact:

Tumor Section Annual Meeting Office
Phone: 847.692.9500 • Fax: 847.692.2589
www. neurosurgery.org

The American Brain Tumor Association's Dedication to Research

The American Brain Tumor Association's (ABTA) Board of Directors recently committed funding to 13 researchers through its fellowship program. Following is a list of the clinicians recognized.

1999-2001 Fellowship Awards

($60,000 fellowship stipend, payable over two years)

Researcher: James J. Evans, MD
Sponsors: Joung H. Lee, MD, and John K. Cowell, PhD
Institution: Cleveland Clinic Foundation
Research: *Differential Expression of Genes in Meningothelial Meningiomas*

Researcher: Daphne Haas-Kogan, MD
Sponsor: Mark A. Israel, MD
Institution: University of California (San Francisco)
Research: *The Role of PTEN and the P13K/PKB Signaling Pathway in Malignant Gliomas*

Researcher: Anna Marie Kenney, PhD
Sponsor: David H. Rowitch, MD, PhD
Institution: Dana-Farber Cancer Institute
Research: *In Vivo Antagonism of Sonic Hedgehog-Induced CNS Precursor Cell Proliferation by Cholesterol Biosynthesis Inhibitors*

Researcher: Peter Y. Kim, MD, PhD
Sponsor: James E. Goldman, MD, PhD
Institution: Columbia-Presbyterian Neurological Institute
Research: *Development of an Animal Glioma Model*

Researcher: Ali H. Mesiwala, MD
Sponsor: Daniel Silbergeld, MD
Institution: University of Washington
Research: *Blood-Brain Barrier Disruption Using High Intensity Focused Ultrasound*

Researcher: Andrew E. Sloan, MD
Sponsor: John Kamholz, MD, PhD
Institution: Wayne State University/Karmanos Cancer Institute
Research: *Characterization of Gene Expression in Human Glial Cells and Neoplasms by Serial Analysis of Gene Expression (SAGE) Technique*

Researcher: Edward R. Smith, MD
Sponsor: E. Antonio Chiocca, MD, PhD
Institution: Massachusetts General Hospital
Research: *Characterizing the Interaction Between Oncolytic Viruses and Tumors*

Researcher: Mingjian You, MD, PhD
Sponsor: Ronald A. DePinho, MD
Institution: Dana-Farber Cancer Institute
Research: *Identification of Genes Cooperating With the Null Mutation of INK4a/ARF Tumor Suppressor Locus in Gliomagenesis*

1998-2000 Continuing Fellows:

Researcher: Karen Chong, MD, PhD
Sponsor: Allan Bradley, PhD
Institution: Baylor College of Medicine
Research: *Identification & Characterization of Tumor Suppressor Genes in Medulloblastoma*

Researcher: Charles Cobbs, MD
Sponsors: Joseph S. Beckman, PhD, and Harold Sontheimer, PhD
Institution: University of Alabama
Research: *The Role of Nitric Oxide and Peroxynitrite in the Inhibition of p53 and MnSOD Activity in Gliomas*

Researcher: Sydney Gary, PhD
Sponsor: Susan Hockfield, PhD
Institution: Yale School of Medicine
Research: *Regulation of a Brain-specific Extracellular Matrix Protein in Glioma*

Researcher: Martha Simmons, MD, PhD
Sponsor: Kenneth D. Aldape, MD
Institution: University of California (San Francisco)
Research: *Prognostic Markers in Glioblastoma*

Researcher: Xiso-Yang Wang, PhD
Sponsor: C. David James, PhD
Institution: Mayo Foundation
Research: *Study of Epidermal Growth Factor Receptor Amplicon in Glioblastomas*

Translational Research Grants

This year, the ABTA proudly awarded two $50,000 one-year translational research awards to the following researchers.

Researcher: Benham Badie, MD
Institution: University of Wisconsin
Research: *Evaluation of Microglia as a Novel Glioma Delivery System*

Researcher: John Y. H. Kim, MD, PhD
Institution: Children's Hospital and The Dana–Farber Cancer Institute
Research: *Neurotrophin-3 Treatment of Medulloblastoma in PATCHED Knock-out and Nude Mouse Models*

Applications for next year's ABTA Fellowships and Translational Grants can be obtained from the ABTA office. Phone (847) 827-9910 or e-mail your request to info@abta.org.

Medical Student Summer Research Fellowships

This unique research program provides the means for seven medical students to spend a summer in a renowned research laboratory working with leading-edge clinicians. Below are this year's fellows.

1999 Medical Student Summer Fellows

Student: Grant Su
Sponsors: Eric Wong, MD, and Julian Wu, MD
Institution: Beth Israel Deaconess Medical Center/Harvard Medical School
Research: *Detection of Matrix Metalloproteinase Expression in Patients With Medulloblastoma*

Student: C. Ryan Miller
Sponsor: G. Yancey Gillespie, PhD
Institution: University of Alabama at Birmingham
Research: *Retargeting Adenovirus Vectors to Human Malignant Gliomas*

Student: Steven Sykes
Sponsor: Tim Cloughesy, MD
Institution: University of California
Research: *Comparative Study of Peripheral Blood DNA to Brain Tumor DNA*

Student: Nathan Walker
Sponsors: Keith Crutcher, PhD, Ronald Warnick, MD, and Robert Brackenbury, PhD
Institution: University of Cincinnati Medical Center
Research: *The Use of Brain Tissue Sections for Analysis of Glioblastoma Invasion*

Student: Ute Gawlick
Sponsor: Edward J. Roy, PhD
Institution: University of Illinois at Champaign–Urbana
Research: *Immunotherapy Using Tumor–Targeted Costimulation*

Student: Peter J. Nicholls
Sponsor: Donald A. Ross, MD, and Phillip Kish, PhD
Institution: University of Michigan
Research: *Determining the Expression and Activity of Cyclo-Oxygenase–2 in Brain Tumor Cells In Vitro and In Vivo*

Student: Dale Yu
Sponsor: Paul G. Fisher, MD
Institution: Stanford University Medical Center
Research: *Carboplatin Hypersensitivity in Children With Brain Tumors*

Department chairs interested in this program, or researchers wishing to mentor a student during the summer of 2000, should contact the ABTA office at (847) 827-9910.

Young Investigator Grants

The ABTA, in conjunction with the AANS/CNS Section on Tumors and the Society for Neuro-Oncology, offers several awards to outstanding young investigators in recognition of their contributions to the field of brain tumor research.

This year, the ABTA is pleased to announce a special $15,000 grant to the Society for Neuro-Oncology to encourage the inclusion of young investigators in this multidisciplinary brain tumor forum.

Epidemiology Research Award

This newly-created award, given through the Society for Neuro-Oncology (SNO), will recognize outstanding contributions to the field of brain tumor epidemiology, and will be presented at the SNO Annual Meeting in November 1999. For more information, contact the SNO office at (713) 745-2344.

Central Brain Tumor Registry of the United States Grant

Founded by ABTA to establish a registry where all brain tumors — benign and malignant — will be recorded, the ABTA continues to support this organization. This year, a $25,000 grant which is part of a multi-year commitment to the registry, conveys the ABTA's understanding of the urgent need for statistical data documenting the incidence and prevalence of this disease.

Development of Neuro-Oncology Fellowship Guidelines

William T. Couldwell, MD, PhD

Recently, there has been interest from several fronts to develop more rigid criteria for fellowship training in medical specialties, such as neurosurgery. The reasons for this interest are threefold:

- Ensure an adequate academic environment in the training institution prior to offering fellowship training.
- Enable minimum guidelines and ensure adequate training and uniformity of experience between programs.
- Develop universal criteria that will allow individuals to adequately compare various fellowship training programs.

Given the current trend to establish guidelines for fellowship training, the AANS/CNS Section on Tumors is working to create guidelines that reflect the educational mission of the AANS, CNS and the respective Sections. This process enables our members to be involved in the development of guidelines at a grass roots level, instead of having guidelines developed and enforced by an alternative administrative body.

To this end, our Section has developed guidelines for neuro-oncology fellowship training following a review of the existing programs in the United States and Canada (recently published in the *Journal of Neuro-Oncology* 41:89-94, 1999). The criteria have been submitted to the AANS and CNS Education Committees and will be used to ensure adequate fellowship training in accordance with the Neurosurgical Residency Review Committee (RRC) of the Accreditation Council for Graduate Medical Education (ACGME). Although there has been disagreement and concern regarding regulation of fellowship training, the process of ensuring an adequate training environment within individual fellowships is a desirable one, and should be endorsed.

Following are the sample guidelines submitted by our Section to the AANS and CNS.

Prerequisite Training

Accredited residency in Neurological Surgery (accredited program through the RRC of the ACGME or the Royal College of Surgeons in Canada).

Definition of Discipline

Neuro-oncology is a medical and surgical discipline that provides the operative and non-operative management (prevention, diagnosis, evaluation, treatment, critical care and rehabilitation) of patients with central and peripheral nervous system tumors (both benign and malignant).

Duration and Scope of Education

1. The educational program must be diversified and well balanced. The exact mix of clinical and basic science activity may depend upon the particular fellow and program; however, all programs should offer substantial opportunity to pursue both basic scientific and clinical (medical and surgical) training and research.

2. Length of fellowship training must be at least one-year, up to a maximum of two years.

3. The program must provide the fellow with experience in direct patient management during his or her fellowship training. The fellow must have major or primary responsibility for patient management with faculty supervision.

4. The fellow also should have administrative responsibility, as designated by the Fellowship Director.

5. Fellows must be introduced to the practice of neuro-oncology in an outpatient setting where non-emergency patient care is directed for evaluation before and after surgical and medical treatment. The fellow must be involved in the decision-making process regarding the nature and timing of treatment, and participate in follow-up care.

6. Prior to entry into the program, the fellow must be informed, in writing, as to the length of the proposed training. The length of training must not be changed without mutual agreement between the Fellowship Director and the fellow.

Institutional Organization

Sponsoring Institution

A fellowship training program in Neuro-Oncology must have one sponsoring institution within a single geographic location with primary responsibility for the entire program.

Appropriate institutions include medical schools, hospitals and medical foundations. The institution must demonstrate commitment to the program in terms of financial and academic support.

Participating Institutions

Participating institutions include the sponsoring institution and other integrated and/or affiliated institutions approved by the RRC for training purposes. Participating institutions must promote the educational goals of the program rather than simply enlarge the program.

Number of Fellows

Where there is demonstrated excellence in providing educational experience for the residents, a program may be authorized to enroll more than one fellow per year. This decision should be monitored by the RRC, in consideration of a faculty of national and international stature in neuro-oncology, the quality of the educational program, the quality of clinical care, the number and distribution of cases, and the quality of clinical and basic science research.

Faculty Qualifications and Responsibilities

The Fellowship Director and teaching staff are responsible for the general administration of the fellowship program, including recruitment, selection, instruction, supervision, counseling, evaluation, the advancement of fellows and the maintenance of records related to program accreditation.

Fellowship Program Director Responsibilities

1. There must be a single neurosurgical Program Director for the fellowship.
2. The Program Director must be a practicing neurosurgeon who possesses and practices the necessary administrative, teaching and clinical skills, and has experience to conduct the program.
3. The Program Director must be certified by the ABNS or its equivalent and deemed satisfactory by the RRC.
4. The Program Director must be licensed to practice medicine in the state or province where the institution that sponsors the program is located. The Program Director must have an appointment in good standing to the medical staff of an institution participating in the program.
5. The Program Director must prepare a written statement outlining the educational goals of the program with respect to knowledge, skill and other attributes necessary to satisfactorily complete the fellowship training. This must be distributed to other faculty and the prospective fellow.
6. There must be regular evaluation of the fellow's knowledge, skills, and overall performance, including professional attitude.
7. The Program Director must provide a final written evaluation for each fellow completing the program.
8. The Program Director must prepare an accurate statistical and narrative description of the program, as requested by the RRC.
9. The Program Director must provide an atmosphere of true scholarship with promotion of significant scholarly activity by all faculty members involved in fellowship training:
   - A faculty recognized by peer-review to be active contributors to the field of Neuro-Oncology;
   - Participation in research, particularly in projects that are funded following peer review and/or result in publication or presentations at regional and national scientific meetings;
   - Participation in journal clubs and research conferences;
   - Offer guidance and technical support (e.g., research design, and statistical analysis) for fellows involved in research; and
   - Provision of support for resident participation in scholarly activities.

Interaction with Approved Neurosurgical Residency Training

A volume of training will significantly enable adequate exposure to neuro-oncological cases without interfering with residency training, if a training program exists in the same institution. The requisite case volume and supervision will be approved by the RRC.

Salary Support

Salary support available through the institution or faculty satisfactory to support the fellow should be at least $35,000 (U.S.) per year. In addition, other expenses necessary for the fellow to provide clinical services (malpractice insurance, attending staff hospital fees and dues) should be covered by the institution.

Other Program Personnel

1. The program must be provided with the additional professional, technical, and clerical personnel needed to support the administration and educational conduct of the program

2. Support and ancillary staff (physician extenders: i.e. nurse practitioners or physician assistants), to provide clinical support to satisfy the regulations currently in place to ensure adequate rest periods for clinicians in training.

Tumor Highlights at the 2000 AANS Annual Meeting

Plans are well underway for the 68th AANS Annual Meeting, which will take place April 8-13, 2000 in San Francisco, California. Some of the Meeting highlights include the following Breakfast Seminars:

- Novel Treatments for Malignant Brain Tumors
- Management of Brain Stem Tumors
- Low-Grade Gliomas: Current Treatment and Controversies
- Recurrent Pituitary Tumors
- Current Management of Glioblastoma
- Third Ventricle Tumors
- Advanced Techniques in the Treatment of Pituitary Tumors
- Neurosurgical Management of Neurocutaneous Syndromes
- Management of the Difficult Meningioma
- Surgical Adjuncts for Neuro-Oncology
- Contemporary Management of Craniopharyngiomas

AANS/CNS Section on Tumors
22 South Washington Street
Park Ridge, Illinois 60068-4287

Section on Tumors Officers