



# JOINT SECTION ON TUMORS

Joseph Piepmeier, MD, Editor

Spring 1997

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## CHAIRMAN'S ADDRESS

*William F. Chandler, MD*



The Joint Section on Tumors held the Second Neuro-oncology Satellite Symposium at the conclusion of the Annual Meeting of the Congress of Neurological Surgeons in Montreal this past October. The meeting was well attended and featured a large number of exciting and inspirational speakers as well as ample opportunity for the presentation of many paper presentations. Ray Sawaya was the overall scientific program chairman and we are indebted to him for an outstanding job in organizing this symposium. Jim Rutka and Mark Bernstein provided outstanding local arrangements and coordination, and Peter Black provided his usual excellent guidance as co-chairman of the event. Current plans are to have the Third Biennial Satellite Symposium in conjunction with the 1998 AANS Annual Meeting in Philadelphia.

Mitch Berger has planned an exciting and controversial program for the 1997 AANS Annual Meeting this April in Denver. Invited speakers will discuss "complications" in neurosurgical tumor procedures. There is no doubt we can all learn from these experienced speakers to prevent our own complications in the future.

The Joint Section will present the second Research Grant Award of \$15,000 this April in Denver. This money is generously donated by the National Brain Tumor Foundation in their continued effort to improve the treatment received by our patients with brain tumors.

The Nominating Committee will put forth a slate of candidates for chairman and secretary/treasurer of the Section at the AANS Annual Meeting in Denver. Election will take place by mail and the results will be announced at the Business Meeting following the Section program. I invite you all to attend the Business Meeting and to participate in this process. The election of a new chairman every two years provides the opportunity for different people to be involved in the running of the Joint Section. Please let me or Mark Bernstein know if you have a specific area of interest in the Section activities.

It has been a pleasure and an honor to serve as your chairman these past two years and I look forward to watching the Section continue to mature and grow in the future.

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## SYMPOSIUM, PROGRAM PLANNED FOR ANNUAL MEETING

**April 15, 1997**  
(2:45–6:00 PM)

### **Intraoperative Complications: Avoidance and Management in Neuro-oncology** (2:45–3:45 PM)

**Moderator:** Mitchel S. Berger

**Learning Objective:** After attending this seminar, participants will have an improved understanding of how to avoid intraoperative complications during neurosurgical procedures for tumor removal in the suprasellar, ventricular system and lateral posterior fossa. Participants will be able to describe the management of complications when operating within these common neurosurgical oncology areas. Participants will also have an increased understanding of currently available surgical technologies to avoid complications while removing tumors in these areas.

**Suprasellar Region**  
Albert Rhoton, Jr., MD

**Ventricular System**  
Johannes Schramm, MD

**Lateral Posterior Fossa**  
Peter J. Jannetta, MD

**Award Presentations**  
(3:45–4:30 PM)

**Preuss Resident's Research Award**  
[Sponsored by the Preuss Foundation, \$1,000]  
"Chromosome 11 Abnormalities Are the Most Frequent of Multiple Aberrations Detected in Pituitary Adenomas by Comparative Genomic Hybridization"  
Andrew Metzger, MD

**Mahaley Clinical Research Award**  
[Sponsored by the National Brain Tumor Foundation, \$500]  
"Safety and Efficacy of Malignant Glioma Radiosurgery: Long-term Perspective"  
Doug Konziolka, MD

**Young Investigator Award**  
[Sponsored by the American Brain Tumor Foundation, \$1,000]  
"What Describes a Benign Glioma Phenotype"  
Scott Litofsky, MD

**Open Scientific Session**  
(4:30–5:10 PM)

**Moderators:** To Be Announced

**Farber Lecture**  
(5:10–5:30 PM)

**Business Meeting**  
5:30 PM

## PREUSS RESIDENT'S RESEARCH AWARD PAPER

### NF2 Gene Transcript Mutations in Spinal Ependymomas

*Barry Birch, Jeffrey Johnson, Andrew Parsa, Rajiv Desai, Jung Yoon, Christopher Lycette, Yu Min Li, Jeffrey Bruce*

**Introduction:** Mutations of the neurofibromatosis type 2 (NF2) gene are present in 50 percent of sporadic acoustic neuromas and about one-third of intracranial meningiomas. The role of the NF2 gene in spinal ependymomas, another NF2 related tumor, is unclear. The objective of this study was to screen for NF2 mutations in sporadically occurring intramedullary spinal cord ependymomas and attempt to clarify the role of the NF2 gene in these lesions.

**Methods:** Reverse transcriptase-PCR followed by agarose gel electrophoresis, single strand conformation polymorphism analysis (SSCP), and automated DNA sequencing were used to screen for mutations of the NF2 gene transcript in 7 unrelated patients with sporadic intramedullary spinal cord ependymomas.

**Results:** Five of seven (71%) tumors harbored detectable mutations of the NF2 transcript occur in the majority of sporadic spinal ependymomas, are frequent in the region that is homologous to cytoskeletal proteins, and probably render the protein product inactive. This finding suggests that inactivation or modification of structural proteins may alter cellular growth characteristics. The absence of mutations in two tumors suggests that other genes may also be involved in the oncogenesis of spinal ependymomas. Our results establish that NF2 mutations have a significant function in the oncogenesis of human spinal ependymomas and add to the body of knowledge concerning the role of the NF2 gene tumorigenesis.



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## MAHALEY CLINICAL RESEARCH AWARD PAPER

### Solitary Brain Metastases: Surgery, Stereotactic Radiosurgery and/or Radiation Therapy?

Walter A. Hall, Kwan H. Cho, Andrew Lee, Bruce J. Gerbi, Chung K. Lee

**Introduction:** The most effective treatment for solitary brain metastases is uncertain as new therapies evolve. We compared the efficacy of whole brain irradiation (WBI), surgical resection with WBI and stereotactic radiosurgery (SRS) with WBI in patients with solitary brain metastases.

**Methods:** Of 231 patients with solitary brain metastases that were treated, 126 (56%) received WBI only (Group 1), 73 (32%) had surgical resection and WBI (Group 2) and 32 (14%) had SRS and WBI (Group 3). Primary cancers were lung (38%), breast (15%), unknown (12%), gastrointestinal (10%), melanoma (9%), renal cell (8%) and others (9%). The median dose of WBI was 3750 cGy (range, 2000-5000 cGy) in 15 fractions. The median radiosurgical dose was 1750 cGy (range, 1200-4000 cGy). Eighteen patients had SRS for recurrent/persistent disease and 14 patients received SRS as a boost with WBI. Actuarial survival was calculated from the date of treatment using the Kaplan-Meier method, and statistical significance was assessed with the log rank test.

**Results:** The actuarial median survivals were 3.8 months (range, 1-84 mos) for Group 1, 10.5 months (range, 1-125 mos) for Group 2 and 9.8 months (range 1-36 mos) for Group 3. The survivals at 1 and 2 years were 19% and 6% for Group 1, 47% and 19% for Group 2 and 44% and 21% for Group 3, respectively. The survival advantage for Groups 2 and 3 over Group 1 was significant ( $p < 0.0001$  by log rank) but there was no difference between Groups 2 and 3 ( $p = 0.69$  by log rank).

**Conclusions:** For patients with solitary brain metastases treated with surgery/WBI or SRS/WBI the survival is comparable but better than for WBI alone. SRS/WBI are more cost effective and can treat inaccessible lesions.



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## YOUNG INVESTIGATOR AWARD PAPER



### High-Flow Microinfusion of *c-myc* Antisense Oligonucleotides Prolongs Survival in an Animal Model of Intracranial Malignant Glioma

William Broaddus, Sujit S. Prabhu, Zhi-Jian Chen, Yue Liu, Helen L. Fillmore, George T. Gillies

**Introduction:** Antisense oligodeoxynucleotides offer the potential to block the expression of specific genes within cells. The proto-oncogene *c-myc* has been implicated in control of cellular proliferation and is abnormally expressed in human malignant gliomas. Our studies *in vitro* using antisense phosphorothioate oligonucleotides (PS-ODN) against RT2 cells (a rat glioma cell line) have shown inhibition of cellular proliferation. We tested this effect *in vivo* using the RT2 intracranial tumor model with direct intratumoral high flow micro infusion.

**Methods:** Permanent intracerebral cannulae were placed in the caudate putamen of 20 female Fischer rats. Following implantation of  $10^4$  RT2 cells on day 0, direct intraparenchymal infusions were carried out on days 3, 5, 7, and 9. Each infusion consisted of 20 microliters delivered into the tumor bed over 1 hour (0.33  $\mu$ l/min). One group was infused with artificial CSF (aCSF) and the others with PS-ODN solutions (750  $\mu$ M in aCSF) containing the 15-mer *c-myc* antisense sequence, a scrambled sequence or a scrambled sequence containing a "4G" motif (to control for a similar feature in the antisense sequence). The animals were then observed and followed for survival times.

**Results:** All animals tolerated the infusions well, with no evidence of toxicity. The animals infused with aCSF, scrambled and "4G" ODN's succumbed to tumors at 16.5, 17.3 and 16.3 days (mean) respectively. In the antisense group, one animal survived until day 20 and the remainder survived without morbidity until they were sacrificed on day 28. Histological studies of the brains of animals sacrificed on day 28 showed no evidence of tumor.

**Conclusions and Discussion:** This data suggests that high flow microinfusion of *c-myc* antisense PS-ODN prolongs survival of animals with malignant glioma. The infusions appear to be well tolerated and allow delivery of these agents into the CNS despite their inability to cross the blood-brain barrier. This new application of a novel delivery technique suggests that antisense oligonucleotide therapy in the CNS holds great promise for clinical applications.

# MINUTES OF THE EXECUTIVE COUNCIL MEETING

Joint Section on Tumors  
September 30, 1996 ❖ Montreal, Quebec

The Executive Council of the Joint Section on Tumors was called to order at 6:35 AM by Chairman Bill Chandler. Also present were Mark Bernstein, Mitch Berger, Peter Black, Bill Couldwell, Roberta Glick, Ed Laws, Paul Kornblith, Nelson Oyesiku, Joe Piepmeier, Jack Rock, Mark Rosenblum, Jim Rutka, Ray Sawaya, and Ron Warnick.

## Minutes:

The minutes of the Executive Council Meeting held at the AANS Meeting in Minneapolis, Minnesota, April 29, 1996 were accepted as written.

## Treasurer's Report:

The Section continues to be in stable financial condition with total assets of \$167,566.00 as of June 30, 1996. The proposed budget for 1997 was briefly presented. Graphs showing the Section's revenues, expenses, and net assets since 1990 were presented. A discussion of potential new projects to fund with our healthy bank account resulted in Dr. Laws' explanation that Section-specific costs of running the web site will now be billed to the specific Section. Drs. Rutka and Ellenbogen will continue to work on behalf of the Joint Tumor Section's initiatives in this area including communication with Dr. William Friedman, the editor of **Neurosurgery: On-Call**. Dr. Black raised the issue of financial support for the AACR Satellite Symposium, June 7-9, 1997, which our Section is co-sponsoring. Dr. Laws indicated that an "up-front" commitment might be frowned upon by the AANS, although helping with a short-fall would be acceptable. It was re-iterated that the Council had made the decision to support this Symposium and is integrally involved in the abstract review process and other aspects of the Symposium.

## Awards Committee:

The winner of the Mahaley Award at the 1996 CNS Meeting was Dr. Walter Hall. The winner of the Preuss Award was Dr. Barry Birch. The Young Investigator Award was given to Dr. William Broaddus. Dr. Chandler reported that persistent efforts to obtain reimbursement from the Preuss Foundation for past and future Preuss Award recipients have resulted in a recent correspondence from the Foundation indicating their commitment.

## Bylaws Committee:

Dr. Rock asked for clarification on who would vote on an issue like the Low-Grade Glioma Practice Parameters and the response was that it would be the Executive Council (as opposed to the membership at large). Dr. Black asked Dr. Rock to re-examine the Bylaws to see any amendments requisite to our Section's remaining in compliance with the Bylaws guidelines described by the parent organizations and used by other Joint Sections.

## Education Committee:

Dr. Alexander was not in attendance and no report had been submitted.

## International Committee:

No international representative was in attendance but correspondence had been received by Dr. Bernstein from Dr. de Tribolet and Mr. Thomas indicating they had no news to report.

## Membership Committee:

Dr. Lillehei was unable to attend, but had submitted a report indicating that currently we have 505 Active, 51 International, 9 Resident, 14 Associate/Retired, 3 Honorary, and 58 Adjunct members. There are 2 new resident members and 1 adjunct member for consideration. A graph showing membership since 1990 revealed that growth in the Section seems to have plateaued over 1995 and 1996. Items to remedy this situation were discussed including a letter to be sent to all North American neurosurgery residents inviting them to join.

## Membership Services Committee:

Dr. Rutka continues to research discounts for members on certain books and discounts for residents taking special courses related to Neuro-oncology. Dr. Rutka was asked to place an advertisement on the Internet to increase the visibility of the Section and inviting others to join.

## Newsletter:

Dr. Piepmeier explained that the newsletter will be a little late this fall. It was recommended that the mailing of the newsletter be expanded to include all North American neurosurgery residents. If possible, an advertisement for the NBTF Research Grant Award will be included in the mailing for the newsletter.

## Nominating Committee:

Dr. Black requested the Council's permission to recruit some other members to the Committee. A number of names were suggested and Dr. Black was requested to proceed. This will require a change in the Bylaws, which Dr. Rock will attend to. It was also decided that in the mail vote by the membership at large, only one name should be put forward for each of the positions of Chairman and Secretary-Treasurer. The next new term of office will commence after the AANS Meeting in April, 1997.

### Program Committee:

Dr. Couldwell was thanked for his efforts on the session on Pituitary Tumors at the present meeting. Dr. Berger will be responsible for the Session at the AANS Meeting in April, 1997 and indicated that he was interested in having a session on complications, an idea which was endorsed by the Council. Dr. Keith Black is responsible for the Tumor Session at the CNS Annual Meeting in 1997 and Dr. Berger, who is the Annual Meeting Chairman for that Meeting, indicated that a new format of having two afternoon sessions for each Section will likely be adopted. For the Tumor Section, it will be recommended to have keynote speakers each day, and also about 20 brief poster/platform presentations in which participants will have perhaps 3 minutes and 3 slides to present their work.

### Research Committee:

Dr. Glick prepared a detailed research report outlining a number of issues related to government grants, alternate (i.e., industry collaboration) funding, and the issue of scientific misconduct. She presented an outline of an NCI meeting on Surgical Issues in Cancer Research, which she recently attended. Dr. Warnick presented the questionnaires on neuro-oncology research opportunities, which will be mailed out to all North American neurosurgery residents and Program Directors in the near future. Hopefully a follow-up report will be available for the AANS Meeting in April, 1997.

### Task Forces:

#### 1. Guidelines

Drs. Rock and Bernstein updated the group on the progress with the Low-Grade Glioma Guidelines. Dr. Ed Shaw had presented the first draft of the guidelines on low-grade glioma in Minneapolis and was in the process of revising them when Dr. Walters indicated to him that the entire process had to be revisited with the view of preparing a document similar to that prepared for the Severe Head Injury Guidelines. Dr. Bernstein pointed out that to date, the preparation of the low-grade glioma practice parameters has cost the Section \$0.00 and that a brief update of the progress will be presented in his talk on Wednesday morning at this CNS Meeting.

#### 2. Multidisciplinary Neuro-oncology Effort

Dr. Chandler had corresponded with the various subspecialty societies and has been given the names of representatives by all groups except ASTRO. This will probably not go further at a formal level at the present time but we all feel we should continue to provide support and act as a "role model" for other subspecialty groups. The Society of Neuro-oncology (SNO) was discussed vis a vis their upcoming meeting in November and it was urged that efforts be continued for our Section to work complementarily with SNO.

### CNS Satellite Symposium:

Dr. Sawaya reported that the final programs have been received in Montreal and everything is in place for the Symposium. There are 98 registrants to date, 22 platform papers (of which one was withdrawn),

and 50 posters (of which one was withdrawn). Dr. Sawaya was thanked for his excellent efforts.

### Journal of Neuro-oncology:

Dr. Laws indicated the AANS was interested in buying and running *The Journal of Neuro-oncology*, noting that the product is good but the price a little high. Dr. Kornblith presented the merits of maintaining the *Journal* as is, as currently it is attracting about 10 new manuscript submissions per week and has grown to 15 issues per year. If a neurosurgical organization were to buy it, the many submissions from non-neurosurgeons might decline and weaken the *Journal's* appeal and distribution.

### Central Brain Tumor Registry:

Ms. Carol Kruchko was invited and presented the First Annual (1995) Report. She indicated that CBTRUS' funding (approximately \$200,000/year budget) was being discontinued after 1998 and invited the Joint Tumor Section to become more formally involved, including financial support after 1998. Dr. Chandler asked Ms. Kruchko to formalize her thoughts and requests in writing. It was articulated by a number of Council members that the data CBTRUS generates is only fair and of limited use and that the Section would probably not be very interested in sinking funds into this kind of research.

### Young Neurosurgeon's Committee:

Dr. Nelson Oyesiku was invited to the Meeting in his role as Liaison from the Young Neurosurgeon's Committee of the AANS to the Joint Section on Tumors. This provides an opportunity to introduce the advantages of membership to a number of neurosurgeons early on in their career. We will welcome Dr. Oyesiku at our Executive Council Meetings and invite him to liaison with our Membership Committee Chairperson.

### Next Satellite Symposium:

Dr. Laws, who will be the 1997-98 President of the AANS, has suggested the Section have its next Satellite Symposium in conjunction with the AANS Meeting in Philadelphia in April, 1998. The Council thanked Dr. Laws for this endorsement and felt this is an excellent idea for a number of reasons and plans to go forward.

### Voynick Fellowship in Neuro-oncology:

Yale University has received a donation from a grateful family and is establishing the Voynick Fellowship in Neuro-oncology, which will be a yearly event including a visit by a prominent neuro-oncologist. Dr. Piepmeier has asked the Executive Council to play a role in the selection of this individual and the Council is pleased to be involved in this way.

The Meeting was adjourned at 8:50 AM.

Respectfully submitted,

Mark Bernstein MD, FRCSC  
Secretary-Treasurer  
AANS and CNS Joint Section on Tumors

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# NEWS ITEMS

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## American Brain Tumor Association Town Hall Meetings

The American Brain Tumor Association has a new educational Sunday afternoon program for brain tumor patients and their families entitled *Town Hall Meetings*. You may want to participate in one of these programs as a sponsor or a speaker.

The intent of this regional activity is to offer patients/families an opportunity to hear a panel of clinicians present state-of-the-art treatment information in his/her own specialty. Each clinician makes a brief presentation and then responds to written questions from the audience.

We extend grateful appreciation to the doctors who volunteered their time and expertise for the two successful meetings held last year:

Detroit — 180 patients/families:

Kanta Bhambani, MD, Children's Hospital of Michigan  
Larry Junck, MD, University of Michigan Hospital  
Lisa Rogers, DO, Harper Hospital  
Mark Rosenblum, MD, Henry Ford Health Sciences Center  
Howard Sandler, MD, University of Michigan Hospital

Los Angeles — 230 patients/families

Michael L.J. Apuzzo, MD, University of Southern California  
Keith Black, MD, University of California, Los Angeles  
Timothy Cloughesy, MD, University of California, Los Angeles  
W. Michael Shea, MD, Hoag Cancer Center  
Stuart Siegel, MD, Children's Hospital Los Angeles

Plans are currently underway to host the third and fourth *Town Hall Meetings* in Baltimore, March 16th, and Philadelphia, April 6th, respectively.

If you would like to help plan a meeting in your area, please contact the office of the American Brain Tumor Association, 847/827-9910.

## National Brain Tumor Foundation Patient and Health Professional Conference March 14–15, 1997 in Houston, Texas

The National Brain Tumor Foundation and the M.D. Anderson Cancer Center are pleased to announce the second regional brain tumor conference in Houston, Texas. This day-and-a-half conference will feature the latest information on topics such as state-of-the-art developments in science and treatment; the effects of brain tumors on physical and cognitive functioning; wellness strategies for physical and mental health; and special issues pertaining to pediatric patients. For additional information about registration, call M.D. Anderson Conference Services at 713-792-2222.

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## National Brain Tumor Foundation and Joint Section on Tumors Neuro-oncology Research Grant

The Second Annual Neuro-oncology Prize, sponsored by the National Brain Tumor Foundation and awarded through the Joint Tumor Section, will be awarded this Spring at the 1997 AANS Meeting. This \$15,000 prize is awarded for research that has demonstrated promise in the laboratory and is now applicable in clinical trials.

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Look for the  
*Pituitary Tumor Removal*  
episode of  
"The Operation"  
on  
The Learning Channel  
Saturday, April 19th  
8 PM & 11 PM

# JOINT SECTION COMMITTEE REPORTS

## Education Committee Report

*Eben Alexander III, MD*

The project to develop a CD-ROM on neuro-oncology continues to be a goal. Ideally, it would provide neurosurgical and neuro-oncological investigators with basic clinical and scientific literature concerning brain tumors in an easily accessible format. There are many issues to be resolved including copyrights, royalties and making this CD-ROM affordable to potential buyers. Communication with the Executive Committees of both the CNS and the AANS to gain support for this venture continues.

## Membership Services Committee Chair Report

*James Rutka, MD*

**Neurosurgery://On-Call™** is now linked with our Web site. These items were added with the help of Allison Casey, Interactive Communications Specialist at the AANS, ([avc@aans.org](mailto:avc@aans.org)). The following information is now available:

- Important news and research
- Tumor Section Meetings
- Awards for the Tumor Section (Preuss, Mahaley, Farber)
- Current brain tumor protocols across North America
- Guidelines for the practice of neurosurgery
- Research opportunities for residents and fellows
- Grant opportunities

A Tumor Section logo is being developed. It will be on display at the next Section Meeting in Denver.

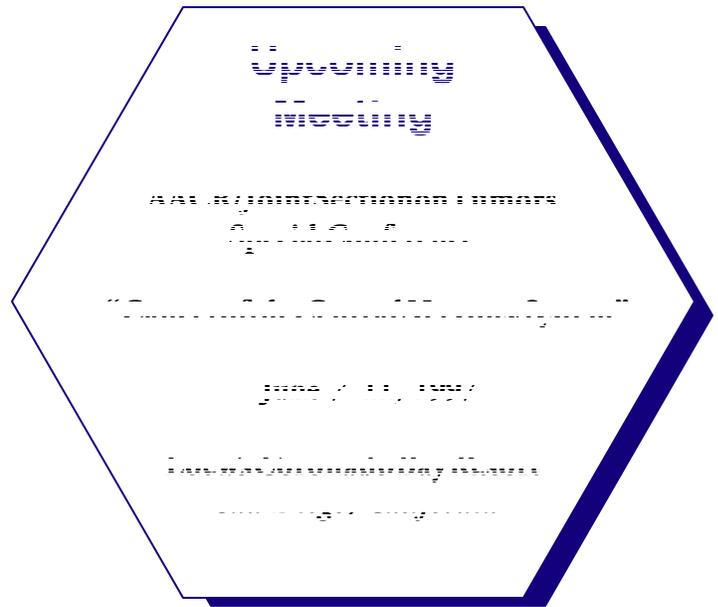
## Membership Committee Report

*Kevin O. Lillehei, MD*

The current membership for the Joint Section on Tumors is:

Active Members .....	505
International Members .....	51
Residents .....	12
Associated/Retired .....	14
Honorary Members .....	3
Adjunct Members .....	59

With the recent mailing to Program Chairs, we received a good response from Resident applicants. This will be reflected at our next Executive Committee Meeting.



## Michael S. Voynick Neuro-oncology Visiting Fellow

The Section of Neuro-oncology at Yale is pleased to announce the First Annual Michael S. Voynick Visiting Fellow in Neuro-oncology. This Fellowship was created to recognize those individuals who have spent their careers making significant contributions in research and the treatment of brain tumor patients. Nominations for the Voynick Fellow will be solicited from the Executive Committee of the Joint Section on Tumors. The award recipient will be invited to visit Yale's Neuro-oncology Section in the Department of Neurosurgery, participate in the multi-disciplinary tumor board, engage in teaching and deliver the keynote address at the Annual Voynick Neuro-oncology Symposium. The first Symposium is planned for the Fall of 1997.

**AANS/CNS Section on Tumors**  
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The American Association of Neurological Surgeons

## 1997 Course Schedule

### Socio-Economic Courses

#### 1997 Reimbursement Update for Neurosurgeons

**Chairman:** Richard A. Roski, MD, FACS

August 22-23 – Chicago, IL

October 24-25 – Philadelphia, PA

November 16-19 – Maui, Hawaii

#### A Proactive Approach to Managed Care: Strategies & Solutions

**Chairman:** John A. Kusske, MD

June 21-22 – Cleveland, OH

November 7-8 – Palm Beach, FL

#### Surgical Management of Movement Disorders

**Chairmen:** William T. Couldwell, MD, PhD

Robert G. Grossman, MD

June 27-29 – Orlando, FL

New  
Course!

### Clinical Skill Courses

#### Neurosurgical Critical Care for Neurosurgeons, Neuroscience Nurses & Physician Assistants

**Chairman:** Michael J. Rosner, MD

June 5-7 – Philadelphia, PA

#### Interactive Image-Guided Neurosurgery (Frameless Stereotaxy)—Hands-On

**Chairmen:** Robert J. Maciunas, MD

Kevin T. Foley, MD

November 21-22 – Memphis, TN

#### Minimally Invasive Neurosurgery: Neuroendoscopy—Hands-On

**Chairman:** Alan R. Cohen, MD

November 14-15 – Cleveland, OH

#### Stereotactic Neurosurgery

**Chairman:** Philip L. Gildenberg, MD, PhD

November 7-8 – San Francisco, CA