

North American Gamma Knife Consortium



STEREOTACTIC RADIOSURGERY RESEARCH, EDUCATION AND PUBLISHING FOR THE PURPOSE OF IMPROVING PUBLIC HEALTH

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NAGKC News Update: Message from the Chairman

At our recent meeting in conjunction with the American Association of Neurological Surgeons annual meeting in New Orleans in April 2013, we reviewed the status of pending applications as well as research projects currently underway. We currently have 18 participating centers in North America with pending applications from Robert Johnson in New Jersey. Activities of the consortium have continued to progress related to both retrospective clinical trials using the Gamma Knife and with the development of prospective clinical trials. The University of Pittsburgh is the current coordinating center for the consortium, and the other participating sites are noted below.

University of Pittsburgh Center for Image-Guided Neurosurgery

University of Virginia Radiosurgery Center

Mayo Clinic, Rochester MN

Cleveland Clinic Foundation

Hoag Memorial Hospital Gamma Knife Center

NorthShore University HealthSystem

Washington Hospital Healthcare System

Health Sciences Centre Winnipeg

Centre Hospitalier Universitaire de Sherbrooke

Barrow Neurological Institute

NYU Langone Medical Center

Yale New Haven Gamma Knife Center

University of Pennsylvania Gamma Knife Center

University of California, San Francisco Gamma Knife Program

Northwestern Memorial Hospital Gamma Knife Radiosurgery Center

Puerto Rico Medical Services Administration Medical Center

University of Toronto

St. Joseph's Hospital-Emory Healthcare in Atlanta

During this last six months, one center (the University of Kentucky Neuroscience Institute) became inactive. The goal of the consortium is to maintain active participation among members by submission of cases for retrospective trials or participation in and design of prospective trials.

During the last six months, several ongoing retrospective reviews have been completed. Dr. Jason Sheehan noted that the update on non-functioning pituitary adenomas is currently in press. A manuscript on parasellar and sellar meningiomas has been revised and is under repeat review at the *Journal of Neurosurgery*. Dr. Sheehan has also spearheaded a respective review of outcomes in posterior fossa meningiomas, and centers are currently submitting cases to Ms. Sharon DeCesare, our regulatory research coordinator.

Members of the consortium are asked to define a particular clinical problem of interest and to develop a de-identified patient spreadsheet based on individual center retrospective chart reviews and containing all necessary data. Members of the consortium are requested to actively participate in submission of data, since pooled data provides a much stronger study of outcomes related to Gamma Knife stereotactic radiosurgery.

Annual Meeting of the Consortium Board

The North American Gamma Knife Consortium Board invited guests and participated in the recent meeting in conjunction with the AANS meeting in New Orleans in April 2013. Participants of the board included Dade Lunsford, Doug Kondziolka, and Jason Sheehan, Kris Smith, Gail Rosseau, Gene Barnett. Dr. Igor Barani represented the University of California San Francisco. Invited guests included Ms. Katherine Gilmore-Lawless, Dr. Nicholas Barbaro from Indiana University, and Dr. Ahluwalia from Cleveland Clinic.

During the board meeting, Dr. Sheehan and Lunsford described ongoing data collection efforts related to retrospective trials of Gamma knife for hemangioblastoma and chondrosarcoma. An abstract on hemangioblastoma was presented at the AANS meeting by Dr. Kano. This was a collaborative trial between selected NAGKC and Japanese Gamma knife sites. A multicenter trial report on chondrosarcoma has been submitted for presentation at the CNS meeting in Chicago, 2013. Dr. Niranjana will present a multicenter experience with craniopharyngioma at the ISRS meeting in Toronto in June, 2013. A new retrospective clinical trial related to a repeat Gamma Knife radiosurgery for trigeminal neuralgia was presented. The latter project was designed to evaluate whether a third Gamma Knife radiosurgery procedure is of clinical value in carefully selected patients without other therapeutic options for management of their pain.

Prospective Clinical Trials

Several prospective trials are currently underway.

NAGKC 2012-1 Stereotactic Radiosurgery for Five or More Brain Metastases.

Dr. Igor Barani discussed the current status of this trial which is being funded by the consortium via a grant from AB Elekta. The goal of the study is to compare neurocognitive outcomes in patients who have Gamma knife for 5 or more brain metastases, with or without adding whole brain radiation therapy. Participating sites are currently going through the contract approval and IRB process. A data collection form is being designed and evaluated to make sure it meets study and regulatory requirements. Six centers will participate in this two-year trial with a planned accrual of 120 patients. Together with the University of Toronto, Dr. Barani will also conduct a validation study of the on line neurocognitive assessment tool used in this study.

NAGKC 12-02 Stereotactic Radiosurgery for Glioblastoma

This is a multicenter phase II study of border zone stereotactic radiosurgery with or without Avastin chemotherapy in patients with recurrent or progressive glioblastoma multiforme. This trial will be funded by a combination of support from Genentech, Elekta, and the consortium. Doctors Niranjana, Kano, and Lunsford have finalized the protocol for this study. UPMC/University of Pittsburgh will be the coordinating center for this trial and Dr. Ajay Niranjana is the PI. The primary endpoint is overall survival at six months after radiosurgery. Although board participants suggested that other primary endpoints might be appropriate for this study, in view of extensive prior negotiation with corporate sponsors, it was felt that changing the primary endpoint was not feasible at this time. This trial will include 40 patients. Twenty-five are planned to be accrued at the UPMC/University of Pittsburgh and five each would be accrued at NYU, the Barrow Neurological Institute, and UVA.

NAGKC 13-01 Phase I/II Studies to Optimize the Outcomes of Large AVMs Using Radiosurgery Followed by Embolization

Dr. Kano at the University of Pittsburgh Center for Image-Guided Neurosurgery presented an extensive AVM followed by adjuvant embolization protocol and has asked members to review the protocol and provide additional feedback. This proposed study looks at large-volume AVMs (greater than 15 cc) which may have improved outcomes when prospectively staged radiosurgery is followed by endovascular embolization after completion of the second radiosurgical procedure. The goal would be to see whether safety and increased efficacy (obliteration and bleed risk reduction) can be obtained. Potential funding of such a project will require outreach to manufacturers of embolic agents such as Onyx.

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NACKG 13-02 Phase I Trial of Afatinib for Stereotactic Radiosurgery for Brain Metastases for Patients with HER2-Positive Breast Cancer and EGFR Positive Lung Cancer with One to Four Brain Metastases.

Representing the Cleveland Clinic, Dr. Ahulwalia, a neuro-oncologist, described the rationale and design for this study. The use of molecular targeting approaches related to the receptor status of tumors will continue to expand. The FDA approval for such a study is pending, and the NAGKC would be a potential active participant in this trial.

NAGKC 13-3 Radiosurgery or Open Surgery for Epilepsy (ROSE) Trial Continuation

Dr. Nick Barbaro from Indiana University, the prior primary investigator for this trial at the University of California San Francisco, provided an update related to the ROSE trial. This trial was recently closed by NIH because of difficulties with patient accrual. AB Elekta has agreed to fund the continuation of the study in order to accrue the final 40 patients. Data from these 40 patients could be combined with those of the NIH trial. Dr. Barbaro noted that centers in India and Great Britain have been important contributors to this trial. This NAGKC trial would be funded by AB Elekta. Dr. Mark Quigg of the University of Virginia would be co principal investigator of the trial. Dr. Barbaro agreed that Indiana University would need to join the NAGKC and likely would develop a contract with NAGKC to perform the trial.

Secretary/Treasurer Report

The secretary/treasurer report indicates that the NAGKC continues to maintain a satisfactory fund balance. The NAGKC budget is based on initial membership fees of \$5000 and annual dues of \$2000 from participating sites. The slim administrative infrastructure of the NAGKC consists of part-time assistance from Rebecca Shapiro, Sharon DeCesare (who handles regulatory affairs), and Paul Stanick who helps to organize the NAGKC website. The NAGKC website is now on an independent server. Future research funding support to the NAGKC will need to include an indirect cost payment to support the need for a growing infrastructure of the consortium.

Spotlight: Cleveland Clinic Gamma Knife Center

The Cleveland Clinic Gamma Knife Center® established in 1997, has treated more than 4,000 patients. The center was the second in the United States to start using Elekta's Leksell Gamma Knife Perfexion™ and was one of the first centers to perform Gamma Knife as an almost exclusively outpatient experience. In 2012, the center acquired the Extend system for the Gamma Knife Perfexion, which allows for safe treatment of larger brain tumors situated in more critical areas by performing the treatment over a few days instead of a single day. Cleveland Clinic's Gamma Knife Center is also one of only a few centers worldwide certified by Elekta, to train physicians and physicists in this precise form of stereotactic cranial radiosurgery.

The Gamma Knife Center is part of Cleveland Clinic's Rose Ella Burkhardt Brain Tumor and Neuro-Oncology Center. The Burkhardt Brain Tumor Center is one of the largest and most comprehensive programs in the country and is dedicated to providing exceptional patient care including surgery, radiation, chemotherapy and clinical research trials for brain tumor patients. It is also dedicated to advancing novel treatment options emerging from the institute's extensive basic and translational research programs. The Burkhardt Brain Tumor Center enrolled over 200 patients in research trials in the last five years and is active in 25 trials currently.

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Cleveland Clinic Gamma Knife Center faculty and staff.



The Burkhardt Brain Tumor Center is part of Cleveland Clinic's Neurological Institute, which is ranked by *U.S. News & World Report* among the best neurology and neurosurgical programs nationwide. We also hold top ranking for these programs in Ohio. The center works closely with Cleveland Clinic Taussig Cancer Institute, recognized by *U.S. News & World Report* among the country's leading cancer hospitals and also top ranked for cancer care in Ohio.

Surgeons:

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Mark Bain, MD
Erin Dyer, MD
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Kambiz Kamian, MD
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Sean Nagel, MD (Metrohealth neurosurgeon)
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