

HENRY BREM, M.D.

Harvey Cushing Professor

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Henry Brem has developed new tools and techniques that have changed the field of neurosurgery. Brem carried out the pivotal clinical study that introduced navigational imaging into the neurosurgical suite. His work led to the FDA's approval of the first image guidance computer system for intraoperative localization of tumors. Furthermore, he has changed the surgical armamentarium against brain tumors by creating and developing Gliadel wafers to intraoperatively deliver chemotherapy to brain tumors. His work has shown that surgeons can deliver potent therapies directly at the tumor site.

Henry Brem, is the Harvey Cushing Professor of Neurosurgery, Oncology, and Ophthalmology and Director of Neurosurgery at Johns Hopkins. He received his undergraduate degree from New York University, his medical degree from Harvard, and trained in neurosurgery at Columbia. He has built one of the largest brain tumor research and treatment centers in the world. He reinstated the Hunterian Neurosurgery Laboratory (originally founded by Cushing) and has trained numerous researchers in brain research, in particular regarding intraoperative imaging, angiogenesis, immunotherapy, and controlled release polymers for drug delivery to the brain.

Brem has changed the surgical treatment of brain tumors by introducing new approaches for targeted therapy. He developed new classes of polymers for drug delivery that are custom synthesized for the agent being developed. The polyanhydrides, which are the first new treatments for brain tumors that the FDA has approved in 23 years, have been shown in his laboratory to be biocompatible and potent.

Brem has explored various classes of therapeutic agents including, standard chemotherapeutic drugs (such as BCNU, carboplatin, camptothecin, and steroids), new drugs (such as 4-hydroxy-cyclophosphamide and camptothecin derivatives), and chemically modified drugs for better distribution within the brain (such as dextran modified methotrexate and camptothecin derivatives). He has explored the role of antiangiogenesis agents in synergy with chemotherapeutic agents. These agents are now in clinical trials that he directs. He has explored this synergistic role of systemic and local treatments for brain tumors. Working with Bob Langer and Michael Cima at MIT he is developing microchip implants for therapeutic brain delivery.

Brem has used his laboratory experience to design and lead several novel multi-institutional clinical trials (over 700 patients) to prove the safety and effectiveness of this approach in patients with malignant brain tumors.

Funding for this research has been through the multi-institutional, National Cooperative Drug Discovery Group, of which Dr. Brem has been the Principal Investigator for over 15 years (\$20 million), as well as from laboratory support from industry and other N.I.H. grants (P20-NS31081; CIDA 5KO8-NS0105804; R24 AI-47739). Based on this work, he is the co-principal investigator of an N.I.H.-funded consortium of medical centers, centered at Johns Hopkins, carrying out clinical trials of novel agents for brain tumor therapy (NCI CA62474, CA62475) as well as the co-principal investigator of an N.I.H.-funded training program for training neurosurgeons in neuro-oncology (NCI T32 CA09574).

Brem's teaching was recognized by the Hopkins Professors Award for Excellence in Teaching in 1996. In 1998 he was elected to the Institute of Medicine of the National Academy of Sciences. In 2000 he was awarded the Grass Award by the Society of Neurological Surgeons for meritorious research; in 2001 he received the Founders Award of the Controlled Release Society; in 2004 he received the New York University Distinguished Alumni Award; and in 2005 he was co-recipient of the Society for Biomaterials Technology Innovation and Development Award.

In summary, over the past 20 years, Brem has introduced a new therapeutic approach to the treatment of brain tumors. This has led to expansion of the role of chemotherapy and biologic agents, such as antiangiogenesis and cytokines. These clinical trials are based on the outcome of his fundamental laboratory discoveries, both on the agents themselves as well as the method of their delivery to the brain. This has already led him to develop one new FDA-approved treatment for brain tumors (Gliadel^R) as well as numerous additional clinical trials evolving from his laboratory that have changed brain tumor outcomes. His contributions to image guidance systems have fundamentally changed neurosurgical techniques.