

HENRY BREM, M.D.

Harvey Cushing Professor

Professor of Neurosurgery, Ophthalmology, Oncology, and Biomedical Engineering

Director, Department of Neurosurgery

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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, which are now available in clinical trials that he directs. He has investigated the 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 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.

Brem is constantly sought after as a guest lecturer across the world. In 2005 he was the E. Llewelyn Thomas lecturer at the Institute of Biomaterials and Biomedical Engineering in Toronto, Canada, as well as the Noun Shavit Memorial Lecturer at Ben-Gurion University in Beer-Sheva, Israel. In 2005 he was named the Coleman Fellow in Life Sciences from the Ben-Gurion University. Brem was the Rosomoff Visiting Professor to the University of Miami in Florida in 2007, and in 2008 he was a visiting professor at Cedars-Sinai Medical Center in Los Angeles, CA. He was the Henry A. Shenkin, MD Lecturer at Temple University in Philadelphia, PA, in 2009. In 2010, he was the Van Wagenen Professorship at the University of Rochester Medical Center in Rochester, NY.

In 2000, Brem was named director of the Department of Neurosurgery at Johns Hopkins. Since his appointment, Brem's has brought to Johns Hopkins many of nation's best neurosurgeons, who share his similar philosophy: providing the best clinical care, while pushing research boundaries to enhance patient outcomes in the field of neurosurgery. Brem strives to ensure that each patient receives the best possible, state-of-the-art care in neurosurgery from his team. In addition, patients can be assured that they will have a team of physicians and scientists who are thinking about the patients' problems and individually designing the best therapy approach across all disciplines and sciences. Patients also can be assured that the latest research, the newest technology, and the best possible therapies will be made available to them.

Brem and his team have established one of the best fellowship and residency programs in the US. His mission, which extends through his team, is to train the next generation to be cutting-edge neurosurgeons who will become academic leaders in their field. After a decade at the helm, Brem's leadership and his team were recognized with news that Johns Hopkins had been named the #1 neurosurgery program in the U.S. by *US News & World Report*.

In the last 10 years, under Brem's leadership, funding from the National Institutes of Health as well as other private sources to Johns Hopkins Neurosurgery has doubled. The Gliadel® wafer, already an FDA-approved drug for treating brain cancer and tumors, was developed in Brem's lab.

In summary, during 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®) as well as numerous additional clinical trials evolving from his laboratory that have changed brain tumor outcomes, including the OncoGel, which may be the answer to enhancing the effectiveness of medical therapy for brain tumors while simultaneously minimizing side effects. His contributions to image guidance systems have fundamentally changed neurosurgical techniques.