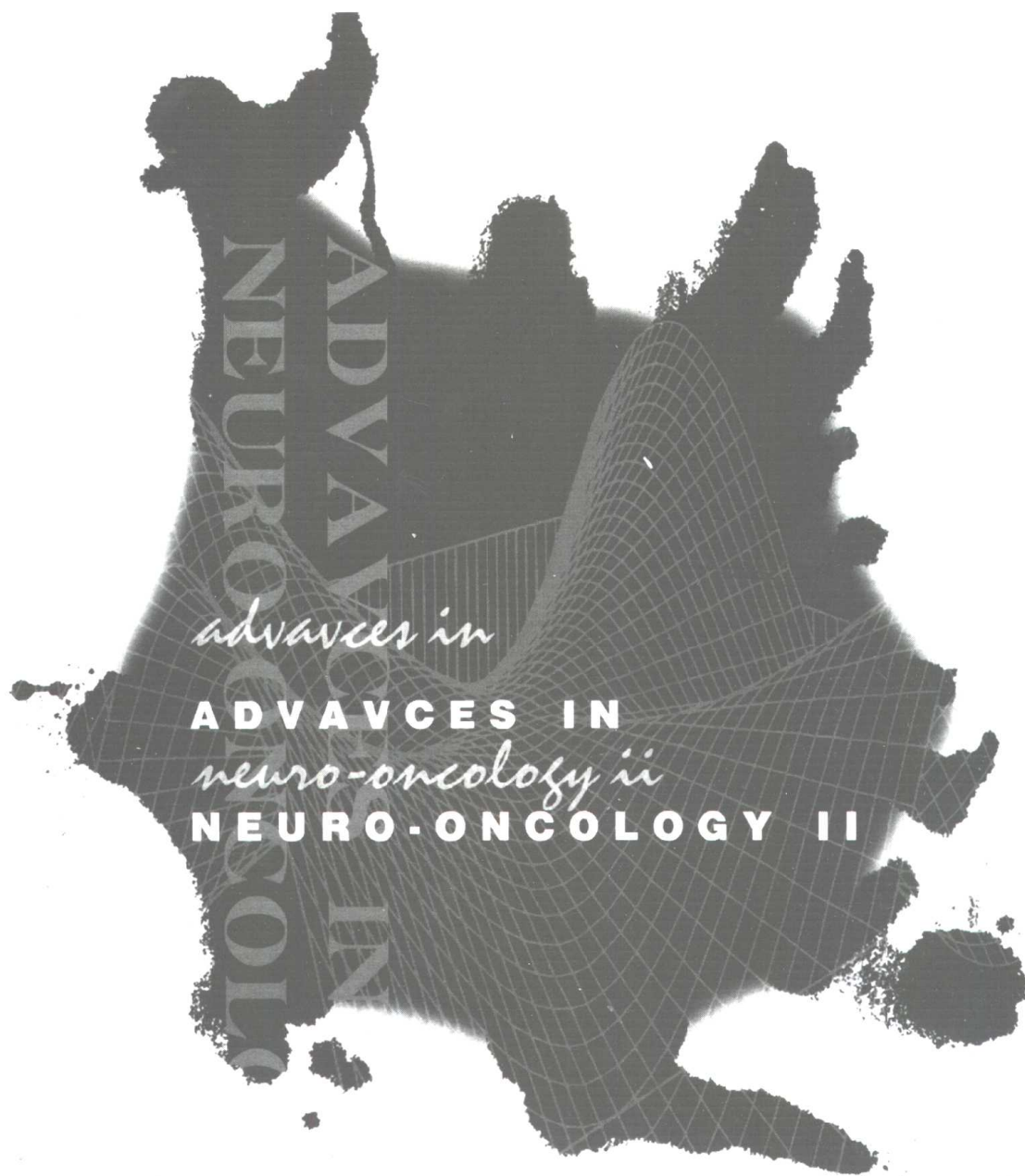


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ADVAVCES IN NEURO-ONCOLOGY II

ADVAVCES IN  
NEURO-ONCOLOGY II

# 神经肿瘤学最新进展



SCIENCE  
&  
CULTURE



EDITED BY

PAUL L.KORNBLITH,MD

MICHAEL D.WALKER,MD

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# ADVANCES IN NEURO-ONCOLOGY II

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## Dedication

*The editors would like to dedicate this book to our wives, Judy and Kate, who have encouraged us to continue this work for these many years.*

# Special Dedication

*Dr. Harry M. Zimmerman, 1901–1995*

---

There is one significant element that was intended for this volume which is unfortunately missing. It was our request that Dr. Harry M. Zimmerman provide us with an introduction to this volume. He had agreed and was in the process of preparing his contribution when this formidable and seemingly indestructible figure was taken from us by cancer.

Dr. Zimmerman was as vigorous at 94 years old as can be imagined. He lived in the present and for the future. Yet what a past he had! Dr. Zimmerman worked with Harvey Cushing at Yale and regaled me with stories of how Dr. Cushing and he went to baseball games, shared a common backyard area in their adjoining homes, and worked together to define basophilic adenomas of the pituitary gland. Dr. Zimmerman proudly displayed an autographed photograph of Dr. Cushing, addressed to him, "with basophilic regards—Harvey Cushing."

Upon leaving Yale, he joined the Navy, rose to the rank of Commander, and worked with Dr. Albert Sabin on viral diseases and vaccines. During this time, he was close to Admiral Chester Nimitz and a photograph of these two figures also graced the wall of his office. Admiral Nimitz was extremely interested in medical issues and apparently had really wanted to become a physician but could not afford the cost.

After the Navy, Dr. Zimmerman was asked to join a new enterprise, which was to become the Albert Einstein College of Medicine in New York. Dr. Zimmerman

was a leader of this enterprise, convincing Albert Einstein to allow his name to be used and serving as the foundation for the establishment of an academic program.

At the Montefiore Hospital, which became an Einstein affiliate, Dr. Zimmerman was a legend. He and Dr. Leo Davidoff formed the nucleus of an outstanding program in clinical and basic neuroscience. In neuro-oncology, Dr. Zimmerman made monumental contributions. He developed the "Zimmerman ependymblastoma," one of the first reproducible chemically induced experimental CNS tumors in mice. This model became the testing ground for early studies of chemotherapy as well as giving insight into the etiology of human glial tumors. His work as a neuropathologist was instrumental in establishing the entire field.

Perhaps his most lasting achievements were as a teacher. It is hard to find a neuropathologist anywhere in the world who did not know him. It is remarkable how many in the fields of neuropathology, neurosurgery, and neurology spent at least some time under his tutelage. Major figures such as Dr. Lucien Rubenstein and Dr. Joseph Ransohoff were among Dr. Zimmerman's students.

In his later years, rather than retiring, Dr. Zimmerman remained active, chairing the Research Committee, evaluating pathology slides sent to him from all over the world, and serving as a pillar of the institution that he so magnificently developed. In his last several years he even was able to direct a large sum of money to help

support his beloved Montefiore Hospital. Both Yale University and Einstein/Montefiore have endowed chairs in his honor.

I had the privilege of working directly with Dr. Zimmerman and was constantly amazed by his vigor and youthful outlook. Two years ago he was Visiting Professor in Pittsburgh and was honored in Japan. Although I am saddened that he was un-

able to complete his contribution for this book, I know that all of us who work in the field of neuro-oncology have, in fact, built upon the foundation that he helped to establish.

Therefore, it is with great affection and respect that this special dedication is made.

Paul L. Kornblith, MD

# Introduction

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It is now over 100 years since the first modern successful brain tumor operations were carried out and close to 100 years since Harvey Cushing made his first clinical observations pertaining to brain tumor treatment. As we reflect on a century of progress, it is quite clear that two very different tracks have been followed. For benign or surgically removable lesions, the picture is of spectacular improvement in outcomes. Advances in microsurgery, anesthesia, and perioperative care have been coupled with incredible diagnostic technology to provide early diagnosis and safe surgical treatment of virtually all surgically accessible lesions. Tumors such as acoustic schwannomas, which were lethal, are now routinely removed with complete safety.

The other route involves the treatment of malignant tumors of the brain and spinal cord. The same advances that have improved the outcomes for patients with benign tumors have provided for a safer diagnostic and operative care environment for malignant tumor patients. Overall, however, outcomes have been at best limited because of the biological and anatomical effects of these aggressive lesions.

This book, the second in the series, is intended to provide an overview of certain selected major scientific and clinical areas in which advances can be and are being made. Some of the areas, such as the treatment of malignant pediatric tumors, have shown dramatic, almost revolutionary, improvement in the clinical outlook for patients. Other areas have been more progress at the basic research level, and exciting new aspects of fundamental research importance are evolving.

The book is divided into three sections. Each section is preceded by a brief overview. Basic research advances in the first section cover a group of particularly active areas of study. The field of basic research has truly expanded in almost logarithmic fashion. One of the most gratifying changes is that basic scientists now consider malignant brain tumor research a fertile field for their efforts and are using model systems of human and animal brain tumors for their investigations.

Neuropathology has become a molecular rather than purely histopathological area; diagnostic neuroradiology is now extremely sophisticated. These two fields are described in the second section.

Although many of the modalities that have made neurosurgery so much safer have applicability to virtually all intracranial procedures, there are certain technologies that find their primary applicability in improving the clinical outcomes for patients with brain tumors. These are reviewed in the third section along with a description of the current status of the management of malignant disease of the spine.

Radiation therapy has been a mainstay of treatment for malignant CNS tumors and even for certain benign lesions. The radiobiology of these tumors helps us understand the limits of radiotherapy. The contrasting and yet often complementary roles of external beam radiotherapy and focused (stereostatic) radiosurgical approaches comprise the clinical portion of this section.

The use of chemotherapy is becoming increasingly relevant and its role in adult and pediatric tumors is presented. Two



new approaches to improving the use of this modality include chemosensitivity testing and the use of biodegradable polymers.

Immunobiology and the corresponding immunotherapeutic modalities are also described. This field provides useful insights and the basis for new potential therapies.

It is hoped that this focused view of the advances in the field of neuro-oncology will serve to present the current and future aspects of how to understand and better manage the continued challenges. It is our plan that this be the second in an ongoing series of books describing the advances in the field.

In 1988, the first volume in this series was published. MRI had not yet had its full impact, radiosurgery was implant-oriented, chemotherapy was the saga of one old standby drug and its variable means of delivery.

In this volume, the new advances in basic science are described, along with improvements in diagnosis and in the conventional modes of therapy. New and promising approaches to therapy are detailed. It is the intent of the editors that this volume will serve to summarize some of the more intriguing advances in neuro-oncology and will be merely the second in a series of volumes that chronicle the evolution of this ever-evolving, exciting, and yet perpetually challenging field.

The editors wish to express their appreciation to the authors of the chapters who have put such effort into their work and to the publisher, Mr. Steven Korn, who has been devoted to this effort and provided his full and enthusiastic support.

Paul L. Kornblith, MD  
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# Section I

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## Basic Science

Primary human central nervous system tumors represent an incredibly difficult clinical challenge. At one time the obstacles to clinical treatment seemed so overwhelming that there were many who felt that basic research into the biology of human brain tumors was likely to be unrewarding.

In the past decade there has been a gradual appreciation for the fact that although human brain tumors are a clinical challenge, they offer the scientist unique opportunities to gain insights into basic mechanisms of tumor growth and progression. The widespread acceptance of brain tissue models in tissue culture and animals provide the cancer researcher with the necessary tools for research.

The fact that human astrocytic tumors have a biologically based grading scale is of particular interest. Such a biological

grading permits the researcher to compare the properties of low, intermediate, and high levels of malignancy in cells of the same lineage. The mechanisms that underlie the progression from normal astrocytes to highly aggressive glioblastoma have been excellent subjects for research.

The advent of knowledge of tumor growth factors and their myriad effects as opened a new field of important research. Again brain tumors serve as a fine model.

In this section we now can appreciate the type of insights that are now available through the efforts of an outstanding group of scientists. The chapters represent some of the most exciting and intriguing observations currently being investigated. It is our plan that this section will serve to stimulate further interest in the remarkable scope and depth of the research efforts in neuro-oncology.