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Current and Future Management of Brain Metastasis

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Foreword

It has long been considered that brain metastases are the terminal stage of cancer progression and their management had mostly been focused on the palliative aspects of treatment. However, taking quality of life into account, the treatment of brain metastases, the most common intracranial solid tumors identified in adults, needs to be reconsidered. Moreover, the incidence of brain metastasis is on the increase thanks to advances in diagnostic imaging tools, easy-available opportunities of screening for metastasis, population growth of cancer survivors, and extension of survival period in cancer patients. Radiation therapy, surgery, radiosurgery and conservative management have been the mainstay of brain metastasis management only to reveal that not a single modality is perfect. Recent advances in management strategies combining multiple modalities and development of their appropriate indications has opened a new field of brain metastasis management focusing on disease control. The current purpose of the management of brain metastasis is no longer confined to palliation. Moreover, the management of brain metastasis in modern times not only requires prolonged survival but also preservation of quality of life. To meet those requirements, radiosurgery has become a key modality in the management of brain metastasis. Many new guidelines and protocols of multidisciplinary approaches have been tried and suggested during last two decades. While plenty of data have accumulated on the knowledge and promising outcomes of brain metastases there is still confusion and impulse decision-making in clinical practice. So, this book is most opportune to wrap up the erstwhile knowledge on brain metastasis management in order to provide clinicians with the currently best management strategies and to encourage researchers to take a new leap forward.

Current and Future Management of Brain Metastasis offers the most up-to-date guidelines. In this comprehensive volume, almost every aspect of brain metastasis management is covered and practical points on difficult situations in daily clinical practice are suggested. Each chapter encompasses extensive reviews and broad perspectives on specific topics. The contributors to this comprehensive volume are the most renowned personages in this rapidly progressing field who, due to their devotion and hard work, have continuously shown their excellence. I would like to
thank Professor L. Dade Lunsford for his valuable advice and for taking the initiative to realize the publication of this book. I would also like to express my gratitude to Dr. Dan Leksell for his dedicated support. I hope this volume will be of help to all clinicians who are involved in the management of cancer patients regardless of their major field.

Dong Gyu Kim
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Introduction

Come writers and critics
Who prophesize with your pen
And keep your eyes wide
The chance won't come again
And don't speak too soon
For the wheel's still in spin
And there's no tellin' who
That it's namin'
For the loser now
Will be later to win
For the times they are a-changin'.
Bobby Dylan, *The times they are a changin'*
Second Stanza

It is likely that no new technology has had a greater impact on the management of metastatic brain cancer than stereotactic radiosurgery (SRS). The use of cross-fired and precisely focused radiation to achieve a tumor controlling response without the need to open a patient's head has been revolutionary. Most often done in a single procedure as an outpatient, and associated with both a strong therapeutic window – tumor control and satisfactory risk profile – reproducibility, and ever-increasing evidence-based medicine outcome analysis, SRS has changed the entire paradigm of care of patients when cancer spreads to the brain.

In prior years, metastatic brain cancer was in essence the beginning of the end. Patients, treating physicians, and families all realized that such an ominous event started the time clock. Most patients could expect only a few months if no additional treatment was offered. Those who opted for conventional management with fractionated external beam radiation therapy might average 6 months for responsive cancers such as lung or breast, and even fewer months for more resistant cancers such as renal cell or melanoma. The pursuit of aggressive systemic treatments – newer surgical, chemotherapeutic, or immunological therapies – was thought to be of little value once the clock started ticking. Withdrawal of active treatment and conversion to palliative care became the routine.
Whole-brain radiation became a standard management, based in part because of the limited benefit of systemic chemotherapy, and in part because of the lack of value of other options. In the absence of widely available and beneficial alternatives, most research looked at fractionation schemes, sensitizers, or brain protection strategies. Whole-brain radiation therapy became the standard of care supported by a distinct reimbursement stream in most societies. Over the years we came to recognize that most patients who survive for more than 6 months after fractionated whole-brain radiation therapy begin to pay a significant price. Concomitant with the emerging development of progressive white matter leukoencephalopathy, patients and their families began to see a gradual deterioration in cognitive skills. Executive decision making and recent memory abilities gradually worsened. These changes can be explained not only on the impact of radiation therapy on the relatively radiation-sensitive oligodendroglia critical for white matter function, but also on the effective annihilation of periventricular progenitor cells that might be the source of brain repair mechanisms.

Surgical removal of metastatic tumors proved to have limited impact because many cancer patients were already ill and poor candidates for craniotomy. Many tumors were recognized in deep-seated locations unsuitable for even image-guided approaches. Of the 200,000–400,000 patients in the United States newly diagnosed with metastatic brain cancer, probably less than several thousand per year were reasonable candidates for craniotomy. Most had solitary brain tumors associated with significant mass effect in surgically reachable lobar locations. Magnetic resonance imaging facilitated the revolution in thinking. Earlier recognition coupled with a reliable diagnostic imaging technique that sorted out solitary from multiple tumors required an effective therapeutic partner. SRS filled that requirement and was applicable to many more patients than craniotomy could provide.

This monograph is designed to review the evidence based medicine that supports the firm integration of radiosurgery into the treatment paradigm of metastatic brain cancer. At the same time we want to provide evidence for the appropriate use of fractionated radiation therapy and surgery in properly selected patients. We have enlisted the talents of well known authorities in cancer to review our understanding of brain metastases, the histopathologic nature of such tumors, and their potential radiobiological response. The various current management strategies including surgery, radiation therapy, chemotherapy, and radiosurgery are reviewed. The results of SRS for selected tumor types and using various technologies are discussed. The recognition of treatment related side effects and their management are pursued. Finally, the role of SRS after craniotomy or after failure of radiation therapy or prior SRS, and emerging strategies for SRS are analyzed. At the end I and my colleagues will attempt to summarize the past, present, and future management of metastatic brain cancer. By the appropriate use of radiosurgery, we believe that cancer that spreads to the brain can become a chronic disease. Oncologists can pursue more effective treatment of the systemic disease. Patients and their families will no longer need to push the time
clock. Radiosurgery, performed once or many times, can end the concept that metastatic brain cancer is always the cause of fatality. Instead we can control such disease in more than 80% of patients. Quality of life is maintained. Radiosurgery has only a brief impact on the patient’s life and allows the oncologist to pursue ever more successful treatment for the primary disease.

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