Oxford Textbook of

Neuro-Oncology

Edited by
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Ryo Nishikawa
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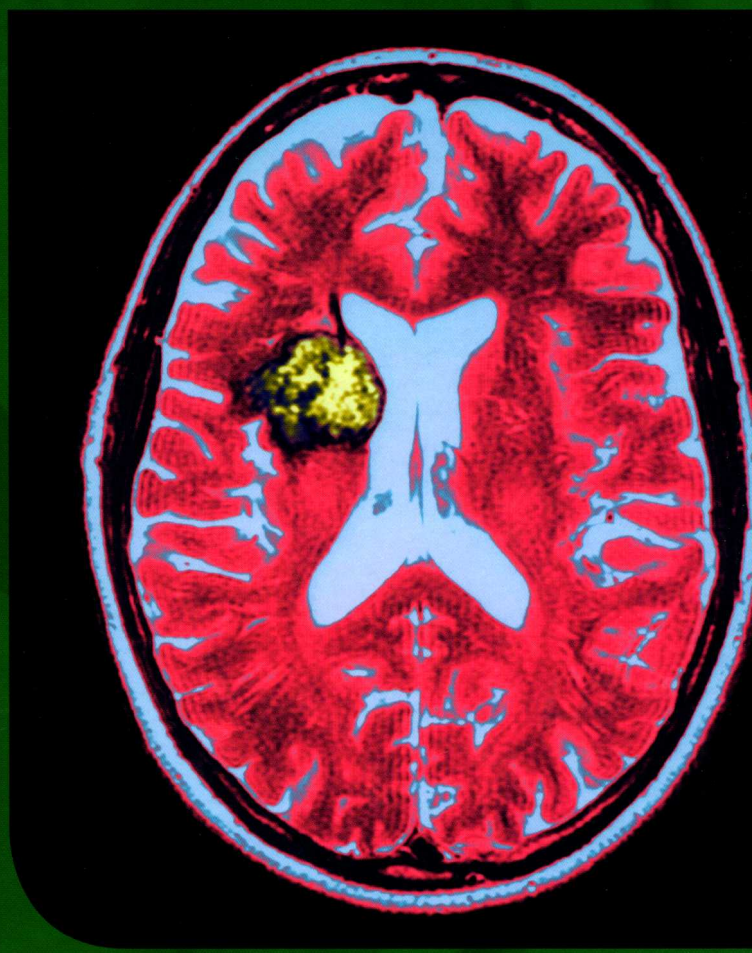

Series Editor
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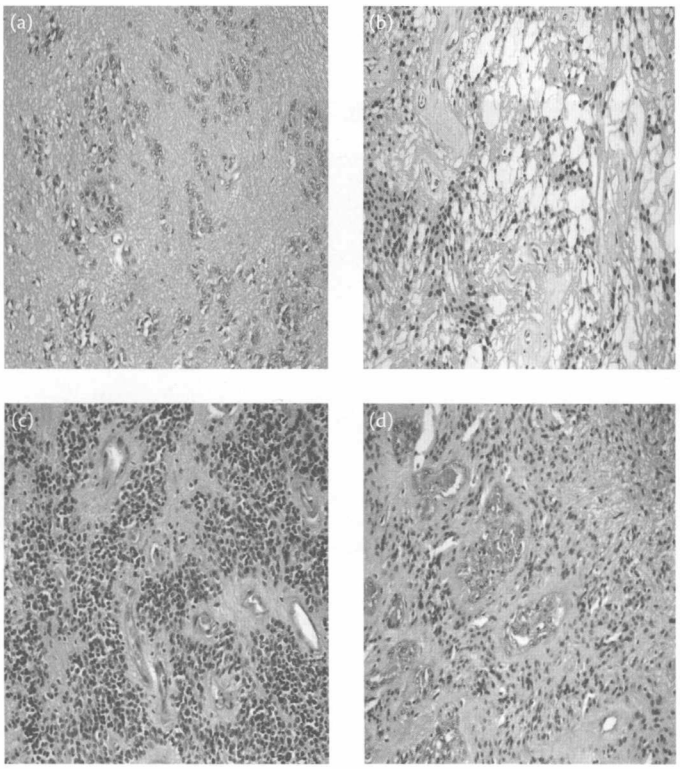

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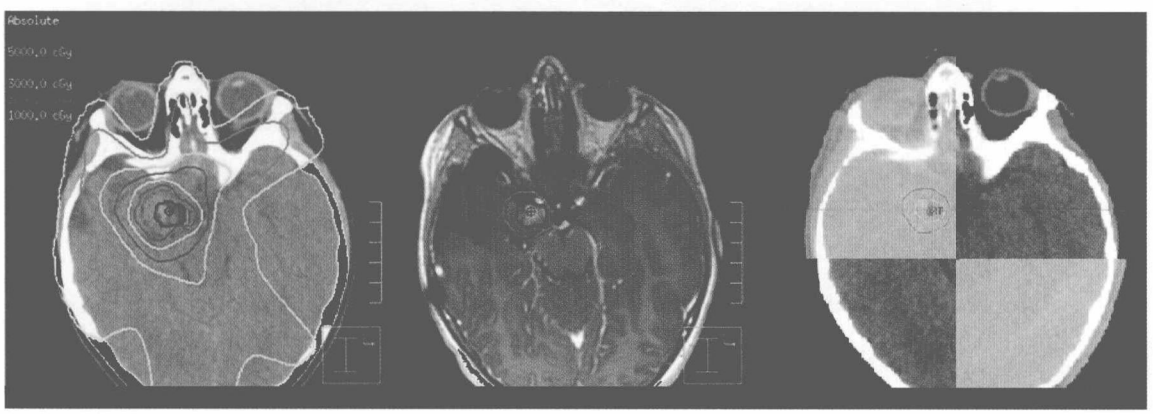

Fig. 8.3 Radiation plan for a 12-year-old boy with recurrent ganglioglioma, prescription dose was 5400 cGy in 30 fractions (left panel). Fusion of the diagnostic MRI (middle panel) allows the delineation of the gross tumour volume (GTV, blue line) and planning target volume (PTV, green line) that incorporates a safety margin for tumour infiltration and daily setup variation. CT acquisition on the linear accelerator (right panel) allows co-registration and comparison of the 'CT of the day' (light grey checker) with the planning CT (dark grey checker) to detect and correct positioning variation with millimetre accuracy.

Foreword

During my 50 years of laboratory research and caring for patients with central nervous system (CNS) tumours, I have witnessed and participated in many developments that at first seemed promising, but dead-ended in disappointing blind alleys; fortunately, others resulted in greater knowledge and clarity about CNS diseases as well as improved outcomes.

Over the years, books published on CNS cancer and its treatment were met with mixed reviews by small audiences, but, nonetheless, helped educate multiple generations of physicians and scientists. When I began my career, I was one of very few in the world willing to focus on CNS cancer research and treatment. Learning from books and experts in other fields helped in that process. Book chapters, being less constrained than articles, can provide more contextual information for the reader than a single article can provide. In my view, a book is frequently the best vehicle for educating others. After moving to Houston, Texas, United States, to become Chair of the Department of Neuro-Oncology at The University of Texas MD Anderson Cancer Center, I wanted to write a textbook, which became *Cancer in the Nervous System* (1996, 2002, Oxford University Press), to educate a new generation of neuro-oncologists and address problems in treatment as well as concerns about symptom management for tumour- and treatment-related effects.

We are now at another crossroads in information because of the explosion of molecular and genetic studies that affect the way we classify tumours and, in turn, how we treat the considerable number of rare benign and malignant tumours of the CNS. I believe this novel paradigm was why so many senior international authors from the multiple specialties essential to our field took the time to create this well-structured and highly informative book. This book brings together the changing neuropathology landscape, important molecular–genetic drivers of these tumours, and provides thoughtful discussions by experts on how best to treat and manage patients afflicted with these rare tumours. Each generation must strive to educate the next generation of clinicians and scientists if we are to make progress in the care of our patients. This requires a book, such as the *Oxford Textbook of Neuro-Oncology*, to bring together the relevance of pathology, molecular–genetic associations, prospective clinical trials, and the experiential insights gained by experts who have treated the very rare tumours absent from formal clinical trials. This panoply of knowledge is well conveyed in this textbook. Taken together, it informs and affects how these tumours are understood today and how best to approach their diverse treatments.

This 21-chapter book, modeled after the World Health Organization classification of central nervous system tumors, takes a 'meet the professor' approach. It provides a framework to assist the reader prepare to understand how we treat and inform patients with respect to treatment options and prognosis when new molecular–genetic knowledge is revealed. Is this textbook the last word? Certainly not, but it is the current word and, as such, deserves a special place in the library of those who care for individuals with CNS tumours and those who research possibilities for improving their survival.

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Preface

The practice of neuro-oncology entails the management of many different types of tumours of the nervous system by a multidisciplinary team of healthcare providers. These tumours represent a diverse spectrum of underlying molecular biological subtypes, prognostic categories, age distributions, and treatment recommendations. The World Health Organization (WHO) classification of central nervous system tumours is the foundation for the categorization and, by extension, clinical management and treatment of patients with all types of nervous system tumours. The WHO classification has traditionally been based on light microscopic description of the cellular elements of tumours in the brain, spinal cord, nerves, and meninges. The 2016 WHO classification of central nervous system tumours for the first time incorporates molecular markers into the categorization of some types of nervous system tumours, particularly gliomas. This revised classification will serve as the basis for future clinical trials and, ultimately, management recommendations for these newly recognized pathological-molecular subsets of central nervous system tumours. Current management guidelines are derived, however, from clinical trials and studies utilizing earlier versions of the WHO classification system. This book is intended for clinicians as a complement to the WHO classification system with a focus on clinical management of nervous system tumours in adults and children. Each chapter is co-authored by a multidisciplinary, international group of leading authorities in adult and paediatric neuro-oncology. The book is organized according to the 2007 WHO classification of central nervous system tumours and each chapter follows a similar framework. The introductory chapter reviews the 2016 revision of the WHO classification of central nervous system tumours and how these changes may influence future clinical trials, clinical practice, and subsequent editions of this book.

Tracy T. Batchelor
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Abbreviations

5-ALA	5-aminolevulinic acid
AED	antiepileptic drug
ASCT	autologous stem cell transplantation
CBTRUS	Central Brain Tumor Registry of the United States
CBV	cerebral blood volume
CCG	Children's Cancer Group
CHOP	cyclophosphamide, doxorubicin, vincristine, and prednisone
CI	confidence interval
CNS	central nervous system
COG	Children's Oncology Group
CPC	choroid plexus carcinoma
CPP	choroid plexus papilloma
CPT	choroid plexus tumour
CR	complete response
CSF	cerebrospinal fluid
CSI	craniospinal irradiation
CSRT	craniospinal radiotherapy
CT	computed tomography
DI	diabetes insipidus
DIA	desmoplastic infantile astrocytoma
DIG	desmoplastic infantile ganglioglioma
DIPG	diffuse intrinsic pontine glioma
DLBCL	diffuse large B-cell lymphoma
DNET	dysembryoplastic neuroepithelial tumour
EANO	European Association for Neuro-Oncology
EBRT	external beam radiotherapy
ED	Erdheim–Chester disease
EFS	event-free survival
EGFR	epidermal growth factor receptor
EMA	epithelial membrane antigen
EOR	extent of resection
EORTC	European Organization for Research and Treatment of Cancer
ESCC	epidural spinal cord compression
ETMR	embryonal tumour with multilayer rosettes
FAP	familial adenomatous polyposis
FLAIR	fluid-attenuated inversion recovery
GC	gangliocytoma
GFAP	glial fibrillary acidic protein
GG	ganglioglioma
GH	growth hormone
GTR	gross total resection
HAART	highly active antiretroviral therapy
HAR	hyperfractionated accelerated radiotherapy
HDT	high-dose therapy
HFRT	hyperfractionated radiotherapy
HIV	human immunodeficiency virus
HL	Hodgkin's lymphoma
HNPCC	hereditary nonpolyposis colorectal cancer
IARC	International Agency for Research on Cancer
IDH	isocitrate dehydrogenase
IELSG	International Extranodal Lymphoma Study Group
iGCT	intracranial germ cell tumour
IPCG	International PCNSL Collaborative Group
ISCM	intramedullary spinal cord metastasis
JXG	juvenile xanthogranuloma
KPS	Karnofsky performance score
LDD	Lhermitte–Duclos disease
LEAT	long-term epilepsy-associated tumour
MB	medulloblastoma
MGMT	O^6-methylguanine-DNA methyltransferase
MPNST	malignant peripheral nerve sheath tumour
MRI	magnetic resonance imaging
MRS	magnetic resonance spectroscopy
mTOR	mammalian target of rapamycin
NCCN	National Comprehensive Cancer Network
NF	neurofibromatosis
NGGCT	non-germinomatous germ cell tumour
NHL	non-Hodgkin's lymphoma
NIH	National Institutes of Health
NK	natural killer
NM	neoplastic meningitis
NOA	Neuro-Onkologische Arbeitsgemeinschaft/German Neuro-Oncology Group
NSCLC	non-small cell lung cancer
NSE	neuron-specific enolase
ONG	optic nerve glioma
ONSM	optic nerve sheath meningioma
OS	overall survival
PA	pilocytic astrocytoma
PCNSL	primary central nervous system lymphoma
PCV	procarbazine, CCNU (lomustine), and vincristine
PET	positron emission tomography
PFS	progression-free survival
PNET	primitive neuroectodermal tumour
PPT	primary parenchymal tumour
PTEN	phosphatase and tensin homologue

PXA	pleomorphic xanthoastrocytoma
RDD	Rosai–Dorfman disease
RGNT	rosette-forming glioneuronal tumour
RTOG	Radiation Therapy Oncology Group
SBRT	stereotactic body radiotherapy
SEER	Surveillance, Epidemiology and End Results
SEGA	subependymal giant cell astrocytoma
SFOP	Société Française d'Oncologie Pédiatrique/French Pediatric Oncology Society
SFT	solitary fibrous tumour
SIOP	International Society of Paediatric Oncology
SRS	stereotactic radiosurgery
SRT	stereotactic radiotherapy
TSC	tuberous sclerosis complex
UKCCSG	United Kingdom Children's Cancer Study Group
VAD	ventricular access device
VPS	ventriculoperitoneal shunt
WBRT	whole-brain radiotherapy
WHO	World Health Organization

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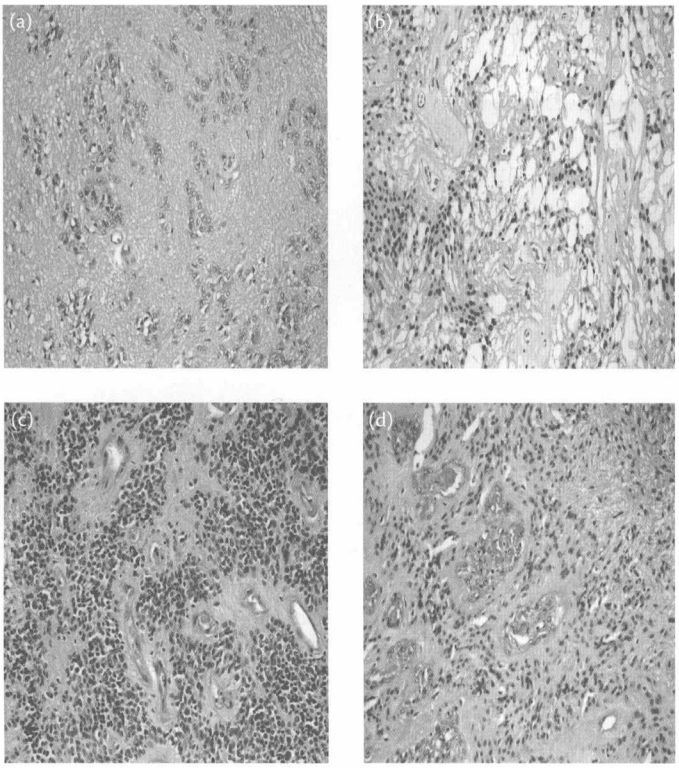

Fig. 5.1 Histology of ependymoma. (a) Ependymoma (WHO grade II). (b) Anaplastic ependymoma (WHO grade III). (c) Subependymoma (WHO grade I). (d) Myxopapillary ependymoma (WHO grade I).

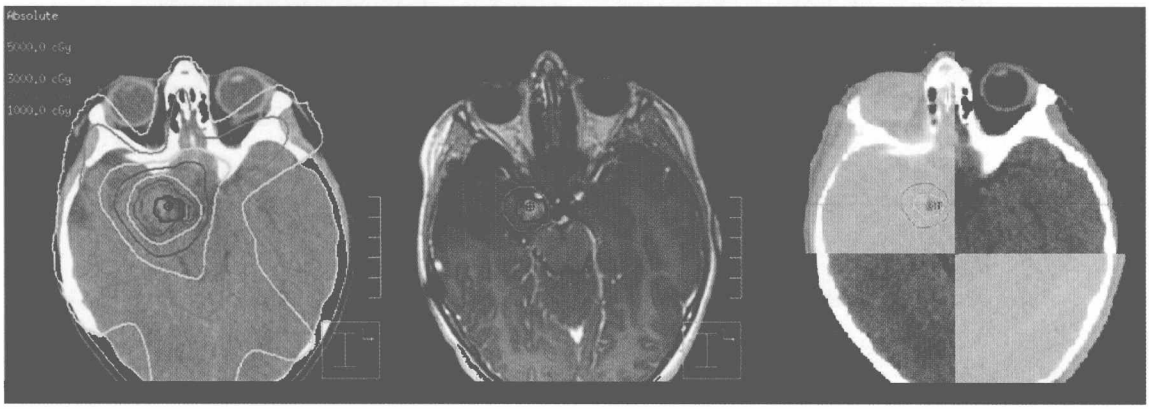

Fig. 8.3 Radiation plan for a 12-year-old boy with recurrent ganglioglioma, prescription dose was 5400 cGy in 30 fractions (left panel). Fusion of the diagnostic MRI (middle panel) allows the delineation of the gross tumour volume (GTV, blue line) and planning target volume (PTV, green line) that incorporates a safety margin for tumour infiltration and daily setup variation. CT acquisition on the linear accelerator (right panel) allows co-registration and comparison of the 'CT of the day' (light grey checker) with the planning CT (dark grey checker) to detect and correct positioning variation with millimetre accuracy.

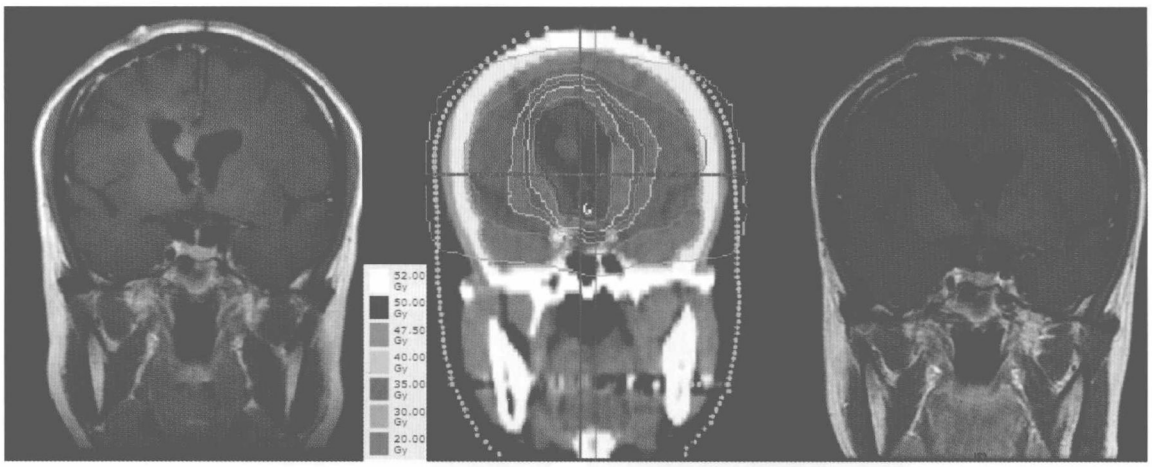

Fig. 8.5 Pre-radiation coronal T1-enhanced MRI of a 38-year-old woman with recurrent central neurocytoma (left panel) treated with image-guided conformal radiotherapy (middle panel) and with a near total radiographic response to treatment and subsequently stable disease 5 years post radiation (right panel).

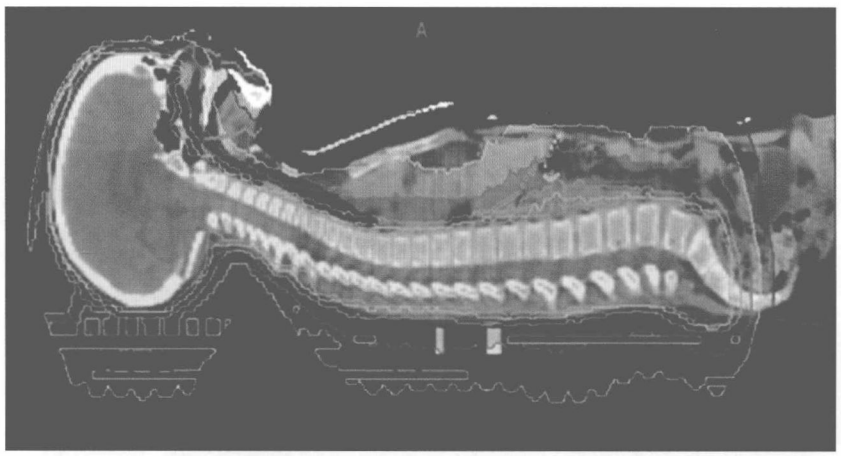

Fig. 9.4 Tomotherapy plan for craniospinal radiotherapy.

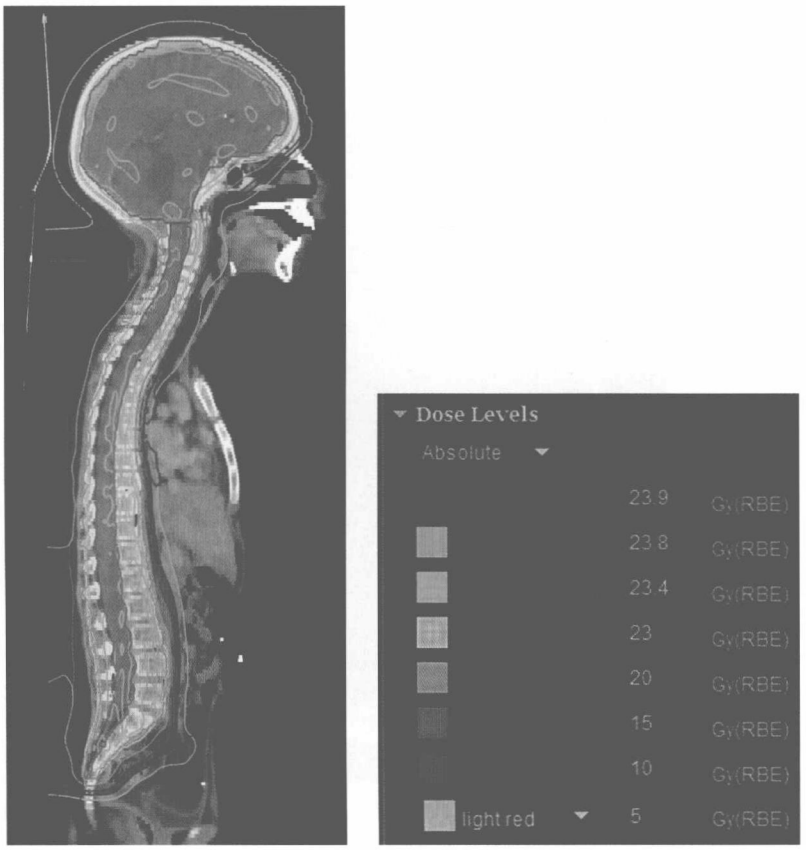

Fig. 9.5 Pencil beam scanning dose distribution for craniospinal irradiation in a child with medulloblastoma.

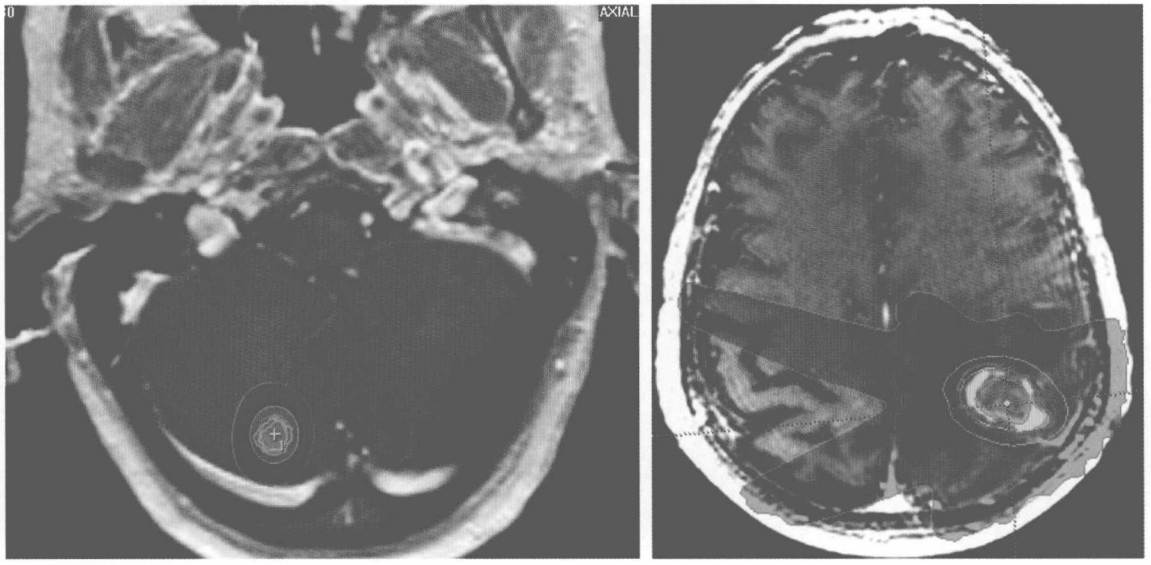

Fig. 19.1 Example of stereotactic radiosurgery (left) with an arc technique applied, and stereotactic radiotherapy (right) for a larger metastasis with multiple fixed convergent beams. Light blue colour: high-dose area, purple colour: low-dose area.

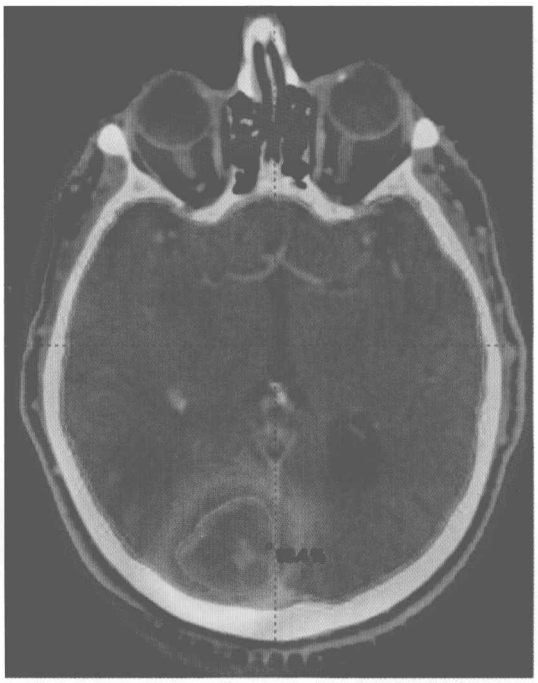

Fig. 19.2 Example of simultaneous integrated boost technique with whole-brain radiotherapy (WBRT). Green colour: dose for WBRT, red colour: a higher dose delivered at the same time as WBRT during the same daily radiotherapy session, for example, a total dose of 30 Gy for the whole brain and 60 Gy to the metastases.

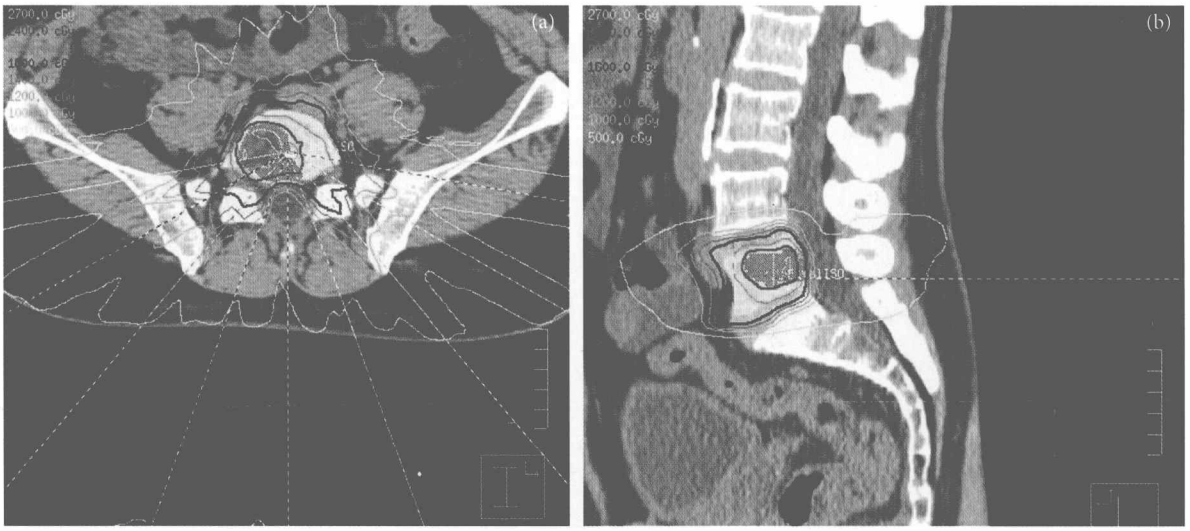

Fig. 20.2 Axial (a) and sagittal (b) MRI views of a L5 metastasis from renal cell carcinoma. The SBRT treatment plan is included. Note the rapid dose fall-off from the 24 Gy isodose line (red) to the 10 Gy isodose line (light blue) at the anterior edge of the spinal canal.

Contents