

# STEREOTACTIC RADIOTHERAPY OF RECURRENT MALIGNANT GLIOMAS

Clinical White Paper

Tumors of the central nervous system (CNS) represent approximately 175,000 newly diagnosed cases worldwide per year, with an estimated annual mortality of 125,000<sup>1,2</sup>. Malignant gliomas comprise 30% of all primary CNS tumors and remain one of the greatest challenges in oncology today, despite access to state-of-the-art surgery, imaging, radiotherapy and chemotherapy<sup>3</sup>.

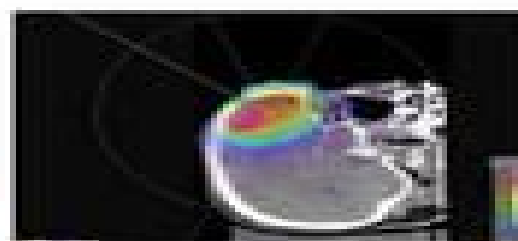
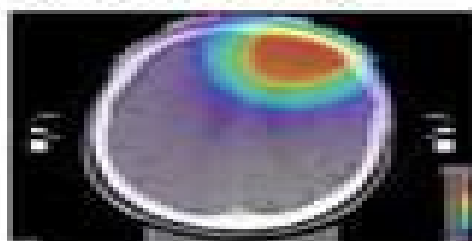
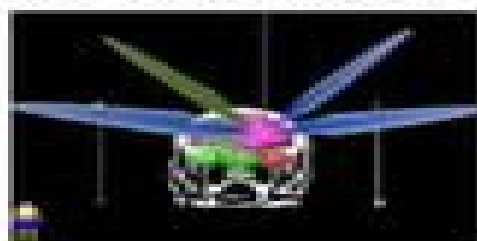


Figure: Details of a typical malignant glioma treatment plan

Signs and symptoms of malignant gliomas depend on the location, size and growth of the tumor and may include headaches, seizures, focal neurologic deficits and changes in mental status<sup>4</sup>. Both the tumor and its treatment often result in profound quality of life changes. Early failure of local treatment is common with this disease and relapse occurs in form of continuous growth close to the margin of the original lesion in approximately 80% of all cases<sup>5</sup>.

The World Health Organization classification system is predominantly used for naming and grading malignant gliomas; within this system, grade III astrocytomas and grade IV glioblastoma multiforme (GBM) are the most prevalent types with poor prognosis<sup>6</sup>. For glioblastoma, median survival time is limited to approximately 12 – 17 months<sup>7</sup>.

Although malignant gliomas are incurable in the vast majority of patients, surgery and radiotherapy are the traditional cornerstones of initial therapy protocols and provide palliative survival benefit<sup>8,9</sup>. Surgical techniques remain an important tool for glioma management, with complete surgical resection as the goal<sup>10</sup>.

Regardless of the degree of resection, adjuvant radiotherapy is administered after surgery. In early randomized studies, significant increases in survival were achieved in patients with high-grade gliomas with the administration of 50 – 60 Gy of whole brain radiotherapy following surgery<sup>11,12</sup>. Adjuvant chemotherapy is also used in the initial treatment of high-grade gliomas, with increased survival recently demonstrated in clinical trials<sup>13,14</sup>.

The vast majority of gliomas recur within or adjacent to the original tumor bed<sup>15</sup>. Treatment options for recurrent gliomas are limited because most therapeutic alternatives have already been performed, including neurosurgery and a full course of radiotherapy and chemotherapy. Optimal surgical resection might be possible in a subgroup of patients; however, it is accompanied by a high risk of morbidity because of the infiltrative nature of the tumor<sup>16</sup>. Conventional radiotherapy alternatives are often limited with respect to dose prescription because radiotherapy is already a component of first-line therapy in most patients.

Stereotactic radiosurgery (SRS) is appealing because of its ability to precisely deliver high doses of irradiation to a defined target volume in a single fraction with less treatment-associated morbidity compared with surgery<sup>17</sup>. However, SRS is limited to smaller lesions and low doses, as the risk of radiation-induced side effects rises with increasing treatment volume and dose<sup>18</sup>. Fractionated stereotactic radiotherapy (FSRT) enables the precise application of radiotherapy to a defined target volume while exploiting the radiobiologic advantage of fractionation and minimizing the risk for severe radiation-induced side effects<sup>19,20</sup>.

Combining FSRT with chemotherapy further increases high-grade recurrent glioma treatment efficiency. For recurrent GBM, temozolomide has been shown to improve quality of life and progression-free survival<sup>21</sup>.

An overview of the recent literature on hypofractionated FSRT treatments for recurrent malignant gliomas is presented in the table below.

# Radiotherapy Of Malignant Disease

**Wolfgang Guggemos**

A red circular graphic with a gradient, appearing as a partial circle or a stylized 'C' shape, located to the right of the author's name.

## **Radiotherapy Of Malignant Disease:**

**The Radiotherapy of Malignant Disease** E.C. Easson, R.C.S. Pointon, 2012-12-06 Radiotherapy or radiation therapeutics as the name suggests is a branch of general therapeutics. In this case the therapeutic agent is ionising radiation which induces specific and predictable biological changes. Radiotherapy is sometimes described as therapeutic radiology because historically the earliest X ray machines were used both for diagnostic and therapeutic purposes. Diagnostic radiology has since become a very complex and time consuming speciality requiring the undivided care and attention of the diagnostic radiologist. Similarly radiotherapy now embraces both X ray beams and the radiations from radium and various artificial radium substitutes. This too requires the full time attention of the radiotherapist. In recent years radiotherapy has sometimes been described as radiotherapeutic oncology to indicate the involvement of the radiotherapist in oncological management and indeed in all aspects of oncology from prevention and early detection to the treatment after care and for those who need it terminal care of the patient. The radiotherapist by total commitment to the cancer problem is in truth the epitome of the oncologist. In the same way as the medical physician or internist requires a proper understanding of the pharmacology of the therapeutic agents he or she employs the nature metabolic biochemistry and biological effects of any administered drug so also the radiotherapist needs to understand the nature biological effects and therapeutic potentialities of ionising radiations. The radiotherapist's pharmacology involves an understanding of the relevant physics and radiobiology. **The**

**Radiotherapy of Malignant Disease** R.C.S. Pointon, 2012-12-06 Radiotherapy as practiced at the renowned Christie Hospital and Holt Radium Institute is brought up to date in this new second edition of *The Radiotherapy of Malignant Disease*. The contributions are all written by current or former members of the hospital staff. The opening chapters provide the necessary background information basic physics and radiobiology principles of chemotherapy and mould room practice. The main part of the book represents the very essence of the Manchester school of thought. It is designed to show in detail how to treat by X rays and radium malignant tumors in various anatomical sites. The book thus gives practical guidance on clinical techniques necessary in all disciplines involved in the management of malignant disease. From the reviews of the first edition. It should be in the library of every radiotherapy department and in the hands of every trainee. *British Medical Journal* 1 This book should be an important and interesting reference book on the shelves of any medical library or radiotherapist's office. *American Journal of Roentgenology* 2 There can be few established radiotherapists described by the editors as the epitome of the oncologist who did not read the earlier versions of the Manchester textbook and may still use it for reference. This latest edition is costly but it should continue to be read by all trainees aspiring to the DMRT and FRCR wherever they may be in training and whatever the philosophy of their teachers. *Journal of the Royal Society of Medicine* 3 **The Radiotherapy of Malignant Disease** R. C. Pointon, Robert Charles Snow Pointon, 1991 1E 1985 Scientific basis of radiation therapy functions of a mould room principles of radiotherapy clinical application *The Radiotherapy of Malignant Disease* R. C. S.

Pointon,2014-09-01      **The Treatment of Malignant Disease by Radiotherapy** Ralston Paterson,1963      Radiotherapy for Non-Malignant Disorders Michael Heinrich Seegenschmiedt,Hans-Bruno Makoski,Klaus-Rüdiger Trott,Luther W. Brady,2009-04-15 Non malignant or benign diseases can be successfully treated using ionizing radiation technologies It was first proposed in 1898 by Sokoloff who reported the analgesic effects of radiotherapy for painful rheumatoid arthritis Since then the use of these techniques for painful muscle skeletal diseases has gained acceptance particularly in Europe but is still carried out actively in the United States Non malignant diseases that are amenable to radiotherapy can be classified as inflammatory degenerative hyperproliferative functional or other disorders However the topographic and morphologic considerations are more relevant Even though radiation therapy for benign diseases has not been pursued actively since the 1950s more recent interest has dictated that it can be a very effective treatment modality The use of radiotherapy can be justified for invasive and aggressive growth such as that seen with desmoids for cosmetic deformations and functional loss as seen with keloids or endocrine orbitopathy or for life threatening complications such as hepatic hemangiomas or juvenile angiofibromas that occur in children or adolescents Many of the non malignant diseases can have a major and lasting effect on quality of life by causing pain or other serious symptoms particularly when other methods of treatment are unavailable have failed or may induce more side effects It is not generally the first choice of therapy in these non malignant diseases but it is acceptable as defined The book edited by Seegenschmiedt et al      The Treatment of Malignant Disease by Radiotherapy James Ralston Kennedy Paterson,Ralston Paterson,1963      **Research Awards Index** ,      **Nuclear Science Abstracts** ,1966      **Index-catalogue of the Library of the Surgeon-General's Office, United States Army** National Library of Medicine (U.S.),1972      **Quarterly Cumulative Index to Current Medical Literature** ,1922      *Quarterly Cumulative Index to Current Medical Literature. V. 1-12; 1916-26* ,1923      Subject Index of Current Extramural Research Administered by the National Cancer Institute National Cancer Institute (U.S.),1974      Research Grants Index National Institutes of Health (U.S.). Division of Research Grants,1975      **International Medical and Surgical Survey** ,1922      **Malignant Tumors of the Lung** Jean-Paul Sculier,Willard A. Fry,2012-12-06 Lung cancer is the neoplastic disease with the highest mortality numbers in the world The disease is very common in industrialized countries This textbook synthesizes the basic science of lung cancer with state of the art accounts of diagnosis and treatment Written by a distinguished panel of experts from Europe Asia and North America it covers all of the most important fields biology pathology epidemiology screening diagnosis therapy supportive care and prognosis All physicians caring for patients with lung cancer especially surgeons chest physicians radiation oncologists and medical oncologists will find a wealth of information that meets their needs Whenever possible the principles of evidence based medicine are followed by providing data from systematic reviews meta analyses methodology based guidelines and randomized clinical trials      The Causation and Clinical Management of Pelvic Radiation Disease Philip F. Schofield,Eric W. Lupton,2012-12-06 Material for this book was gathered in the early 1980 s in Manchester

where a higher incidence than usual of complications in the gastro intestinal and urinary tract was observed Part I describes the principles and methods of radiotherapy for pelvic tumours pathological features and radiological analysis of bowel and urinary tract changes Parts II and III are devoted to clinical assessment and management where the need for a multidisciplinary approach is emphasized      *Cumulated Index Medicus* ,1970      *Combined Subject and Author Indexes to Radiobiology Bibliographies* U.S. Atomic Energy Commission. Division of Technical Information,1967      *The Treatment of Malignant Disease by Radiotherapy* Ralston Paterson,1963

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