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## Preface

There has been a clear-cut change in the mentality of oncologists in the last decades. Up to the end of the past century, in fact, any therapeutic approach to cancer could be assigned to one of the following two categories: treatment for definitive cure or otherwise palliation. In the former setting, the real possibility of achieving definitive healing of the disease sometimes justified treatment-related side effects or damages of not negligible severity, whereas in the latter orientation—whose intent was only a reasonable improvement in life expectancy and/or symptoms relief—a milder therapeutic conduct was more advisable. This scenario has been radically modified by the rise of more effective and safer surgical, radiation, and drug therapies, with the consequence that also in patients whose cancer could not be eradicated, it could be changed into a chronic disease in many cases with an approach more active than in the past, allowing survival times often exceeding the fateful 5-year threshold and a satisfactory quality of life.

Unfortunately, this is not the case of glioblastoma: with current therapies, one half of the affected patients die within 1 year from the diagnosis and long-term survivors are extremely rare, amounting to no more than 5 % at 5 years. But resigning to a palliation outcome is generally seen as inappropriate by the medical community and by the patients and their relatives. However, due to the frailty of the brain, surgical ablation is necessarily incomplete in most cases, and radiation therapy can be delivered only within precise dose and volume constraints. Even the most advanced radiotherapy technology scarcely impacts on tumor control, and associated chemotherapy may improve outcome only to a limited extent. Furthermore, relevant treatment-related damages may occur. So, much effort is presently made to enhance the effectiveness and safety of the available therapeutic tools.

One major determinant of therapy failure in glioblastoma, in fact, is its inherent resistance to radiation that, in light of the most recent radiobiology disclosures, can be appropriately considered as an “adaptive strategy” of the tumor against the radiation threat, which is more effective than in other cancers. The enormously improved knowledge of the natural history of glioblastoma in the fields of gene and mechanistic molecular biology, achieved in the last decades, seems to point the way to effectively cope with radiation resistance, by specifically targeting its underlying molecular determinants. However, much research is still needed, as the first clinical trials on molecular targeting agents have produced modest results. This may be due sometimes to working hypotheses not thoroughly verified in the preclinical setting

but, in general, to the great complexity of the disease and the redundancy of its biological machinery. Another cause may be the insufficient communication between preclinical and clinical researchers. There is also the need of new translational tools, besides clinical trials, such as large database collection and advanced statistical methodology.

We collected in this book authoritative information by some authors of the highest repute, giving a context to, and focusing on, clinical, laboratory, and translational radiation biology research on glioblastoma and its related pathology field. Also subjects such as particle therapy, radiation tolerance of normal brain, immunology, and nanomaterial technology are dealt with, with special reference to their respective correlated radiobiology topics. Our intent was mainly to promote the reciprocal understanding and insight among researchers and professionals in radiation and medical oncology, pathology, biology, and medical physics, in order to improve cooperation among them. Glioblastoma, although relatively rare, is in the spotlight due to the extreme complexity of its biological machinery, which represents a challenge for research, due to the necessity to disclose multiple new targets suitable for innovative therapies and unconventional approaches. These investigations might elucidate aspects of relevant interest also in other neoplasms. We hope that the efforts and the time devoted to the accomplishment of this book have obtained a useful and stimulating state-of-the-art assessment for the readers.

Siena, Italy  
L'Aquila, Italy  
Philadelphia, PA, USA

Luigi Pirtoli  
Giovanni Luca Gravina  
Antonio Giordano

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Pirtoli, L.; Gravina, G.L.; Giordano, A. (Eds.)

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