Contents

Preface ix

Acknowledgments xiii

About the Authors xv

List of Abbreviations xvii

1. Introduction 1

2. The Generation of Quantitative Radiobiology Data 9

3. Intrinsic Radiosensitivity of Proliferating and Quiescent Cells 19

4. Effects of Ionization Density and Volume 31

4.1 Ionizations along Charged-Particle Tracks 32
4.2 The ABCs of Charged-Particle Radiotherapy 40
4.3 The Frequency of Electron Track-Ends in Radiation Dose. 43

5. Impact of Fraction Size, Dose-Rate, Temperature and Overall Treatment Time on Tumor Cell Response 49

6. Ionizing Events, Molecular Targets and Lethal Lesions 59

6.1 Time-Scale of Radiation-Induced Cellular Damages and Their Expression 60
6.2 The Oxygen Effect and Oxygen Enhancement Ratio (OER) 63

6.3 Radiation Events—The Role of Energy Density and Ionization Volume 66
6.4 The Molecular Target(s) for Cell Inactivation 73
6.5 Lesions Produced in Cellular DNA by Radiation 80

7. The Radiosensitivity of Tumor Cells *In Vitro* versus *In Vivo* 85

7.1 The Radiosensitivity of Cells Irradiated in Multicellular Spheroids 86
7.2 The Radiosensitivity of Rodent Tumor Cells 87
7.3 Appropriate Inactivation Parameters for Modeling Human Tumor Response 89

8. Modern Radiobiology and the LQ Equation 95

8.1 Molecular Biology Factors of α- and β-Inactivation 96
8.2 Low Dose Hypersensitivity (LDH) 98
8.3 Bystander Effects 99

9. Normal Tissue Radiobiology 103

9.1 Information Derived from *In Vitro* Studies of Normal Tissue Cell Lines 104
9.2 Therapeutic Ratio 105
9.3 Fractionation 106
9.4 Functional Subunits (FSUs) and the Volume Effect 112
9.5 A Summary of the QUANTEC Study 116

10. Radiobiology Applied to Tumor Response Modeling 127

10.1 Surviving Fractions after Fractionated Dose Delivery 128
10.2 An LQ-Based TCP Model 129
10.3 Population Averaging 130
10.4 Incorporating Tumor Biology 133
10.5 Future Perspectives 135

Epilogue 137

References 141

Index 161