

Contents

Foreword ix
Contributors xi

I

INTRODUCTION TO DIFFUSION MRI

1. Introduction to Diffusion MR 3

PETER J. BASSER AND EVREN ÖZARSLAN

- 1.1. What is Diffusion? 3
- 1.2. Magnetic Resonance and Diffusion 5
- 1.3. Diffusion in Neural Tissue 7
- 1.4. Concluding Remarks 8
 - Acknowledgments 9
 - References 9

2. Pulse Sequences for Diffusion-Weighted MRI 11

JIM PIPE

- 2.1. MRI Pulse Sequence Primer 11
- 2.2. Adding Diffusion Weighting to a Pulse Sequence 17
- 2.3. Bulk Motion Sensitivity 21
- 2.4. Single-Shot Echo Planar Imaging Methods 23
- 2.5. Parameter Optimization 26
- 2.6. Other DWI Pulse Sequences 29
 - References 34

3. Diffusion Acquisition: Pushing the Boundaries 35

KARLA L. MILLER

- 3.1. The Modular Nature of Diffusion Sequences 35
- 3.2. Improving Image Quality 38
- 3.3. Improving Diffusion Contrast 49
- 3.4. Conclusions 58
 - Acknowledgments 58
 - References 58

4. Geometric Distortions in Diffusion MRI 63

JESPER L.R. ANDERSSON

- 4.1. Introduction 63
- 4.2. Echo Planar Imaging 64
- 4.3. Where Does the Off-Resonance Field Come From? 68

- 4.4. Modified Imaging Techniques that Yield Less-Distorted Images 70
- 4.5. Imaging Techniques that Acquire Information about the Off-Resonance Field 72
- 4.6. Image Registration-Based Methods for Correcting Distortions 77
- 4.7. Recent Work at the FMRIB 79
 - References 84

5. Gaussian Modeling of the Diffusion Signal 87

DEREK K. JONES

- 5.1. Introduction 87
- 5.2. Diffusion Basics 88
- 5.3. Basic Modeling and Quantification 90
- 5.4. Data Acquisition Strategies 96
- 5.5. Artifacts 99
- 5.6. What is a Model? 102
 - References 102

6. Multiple Fibers: Beyond the Diffusion Tensor 105

KIRAN K. SEUNARINE AND DANIEL C. ALEXANDER

- 6.1. Introduction 105
- 6.2. Multiple Fibers: What's All the Fuss About? 106
- 6.3. Model-Based Approaches 108
- 6.4. Nonparametric Algorithms 111
- 6.5. Derived Information 118
- 6.6. Applications and Exploitation 119
- 6.7. Summary 120
 - Appendix A. Qball implementation 121
 - Appendix B. Spherical Deconvolution Implementation 121
 - Acknowledgments 121
 - References 121

II

DIFFUSION MRI FOR QUANTITATIVE MEASUREMENT

7. White Matter Structure: A Microscopist's View 127

JULIA M. EDGAR AND IAN R. GRIFFITHS

- 7.1. Introduction 127
- 7.2. Cellular Components of the CNS White Matter 130
- 7.3. Water Content of White Matter 145

- 7.4. Changes in White Matter due to Abnormalities in Myelin 145
- 7.5. The Ultrastructural Effects of Demyelination and Axonal Damage in Humans 147
- 7.6. Plasticity in White Matter 148
- 7.7. Summary 148
Acknowledgments 148
References 149
- 8. The Biological Basis of Diffusion Anisotropy 155**
CHRISTIAN BEAULIEU
- 8.1. Utility of Microscopic Water Motion 155
- 8.2. Relationship of Water Diffusion Anisotropy to Tissue Microstructure 158
- 8.3. Role of the Apparent Diffusion Coefficients for Interpreting Anisotropy 171
- 8.4. Issues Related to Diffusion Anisotropy Measurements in Tissue by MRI 175
- 8.5. Summary 178
Acknowledgments 178
References 178
- 9. Inferring Microstructural Information of White Matter from Diffusion MRI 185**
YANIV ASSAF AND YORAM COHEN
- 9.1. The Morphological Features of White Matter 185
- 9.2. Diffusion MRI and Tissue Microstructure 186
- 9.3. Diffusion Tensor Imaging—A Tool for White Matter Microstructural Mapping 187
- 9.4. Diffusion Tensor Imaging—A Tool for White Matter Microstructural Mapping? 188
- 9.5. Types of Diffusion Processes in the Tissue 189
- 9.6. Q-Space Analysis 191
- 9.7. Models of Diffusion in White Matter 195
- 9.8. Towards Virtual Biopsy of White Matter With Diffusion MRI 199
- 9.9. Summary 204
References 205
- 10. Cross-Subject Comparison of Local Diffusion MRI Parameters 209**
STEPHEN M. SMITH, GORDON KINDLMANN, AND SAAD JBABDI
- 10.1. Introduction 210
- 10.2. Cross-Subject Registration (Image Alignment) 210
- 10.3. Voxel-Based Morphometry—Overview and Application to Diffusion Data 212
- 10.4. Problems of Interpretability in VBM-Style Analyses 212
- 10.5. Region-of-Interest and Tractography-Based Strategies for Localizing Change 214
- 10.6. Tract-Based Spatial Statistics 215
- 10.7. Other Skeleton-Based Work 218
- 10.8. Statistical Modeling, Thresholding, and Multivariate Approaches 219
- 10.9. Alternative Diffusion Measures to Test 223
- 10.10. Interpretation Issues: Partial Volume Effects and Complex Tract Structure 226
- 10.11. Standard Space Templates and Atlases 229
- 10.12. Empirical Studies of Gaussianity and Repeatability in Diffusion MRI Data 230
- 10.13. Example Multi-Subject Studies 231
- 10.14. Conclusions 236
References 236
- 11. Diffusion MRI in Neurological Disorders 241**
BENEDETTA BODINI AND OLGA CICCARELLI
- 11.1. Introduction 241
- 11.2. Brief Overview of Methods for Clinical Research 242
- 11.3. Clinical Applications 243
- 11.4. Conclusions 252
References 252
- 12. Diffusion Tensor Imaging in the Study of Aging and Age-Associated Neural Disease 257**
DAVID H. SALAT
- 12.1. Introduction 257
- 12.2. Typical Diffusion Metrics Utilized in the Study of Tissue Microstructure Across the Lifespan 258
- 12.3. Diffusion in Aging 261
- 12.4. Associations Between DTI Metrics and Gray Matter Morphometry 270
- 12.5. Caveats to the use of Diffusion Imaging in the Study of Aging and Age-Associated Disease 271
- 12.6. Future Directions 274
Acknowledgments 275
References 275
- 13. Diffusion Imaging in the Developing Brain 283**
SERENA J. COUNSELL, GARETH BALL, ANAND PANDIT, AND A. DAVID EDWARDS
- 13.1. Changes in Diffusion Measures with Increasing Gestational Age 283
- 13.2. Abnormal White Matter and Cortical Gray Matter Development in Preterm Infants at Term 285
- 13.3. Assessing the Connectome in the Developing Brain 286
- 13.4. DTI in Preterm Brain Injury 288
- 13.5. Diffusion MRI Studies of the Developing Preterm Brain and Association with Neurodevelopmental Outcome 292
- 13.6. MRI in the Term Infant with Perinatal Brain Injury 294
- 13.7. Future Directions 296
- 13.8. Conclusions 297
References 297

14. Individual Differences in White Matter Microstructure in the Healthy Brain 301

JAN SCHOLZ, VALENTINA TOMASSINI, AND HEIDI JOHANSEN-BERG

- 14.1. Introduction 301
- 14.2. Gender and Handedness 303
- 14.3. Changes in White Matter Microstructure with Development and Aging are Associated with Development or Deterioration in Cognitive Skills 305
- 14.4. Age-Independent Variation in Brain Structure Reflects Inter-Individual Variation in Behavior 306
- 14.5. Are Individual Differences in White Matter due to Nature or Nurture? 312
- 14.6. Conclusion 313
References 314

15. Diffusion Tensor Imaging and its Application to Schizophrenia and Related Disorders 317

M. KUBICKI, C.F. WESTIN, O. PASTERNAK, AND M.E. SHENTON

- 15.1. Introduction 317
- 15.2. Review of DTI Findings in Schizophrenia 321
- 15.3. Future Directions: What are we Missing and How Can we Fill in the Gaps? 327
References 330

III

DIFFUSION MRI FOR *IN VIVO* NEUROANATOMY

16. Mapping Connections in Humans and Non-Human Primates: Aspirations and Challenges for Diffusion Imaging 337

DAVID C. VAN ESSEN, SAAD JBABDI, STAMATIOS N. SOTIROPOULOS, CHARLES CHEN, KRİKOR DIKRANIAN, TIM COALSON, JOHN HARWELL, TIMOTHY E.J. BEHRENS, AND MATTHEW F. GLASSER

- 16.1. Introduction 338
- 16.2. Neuroanatomical Fundamentals 338
- 16.3. Approaches to Imaging Human Brain Connectivity 341
- 16.4. Imaging Structural Connectivity: The HCP Strategy 342
- 16.5. The Fiber Architecture of Gyral Blades and Deep White Matter 346
- 16.6. Discussion 355
Acknowledgments 356
References 356

17. Classic and Contemporary Neural Tract-Tracing Techniques 359

ROBERT J. MORECRAFT, GABRIELLA UGOLINI, JOSÉ L. LANCIEGO, FLORIS G. WOUTERLOOD, AND DEEPAK N. PANDYA

- 17.1. Introduction 360
- 17.2. A Brief Historical Perspective of the Development of Experimental Tract Tracing 360

- 17.3. Contemporary Application of Experimental Tract Tracing in Non-Human Primates 365
- 17.4. Conclusions 394
References 394
Further Reading 399

18. The Human Connectome: Linking Structure and Function in the Human Brain 401

OLAF SPORNS

- 18.1. What is the Connectome? 401
- 18.2. Modes of Brain Connectivity 402
- 18.3. Defining Network Nodes of the Connectome 405
- 18.4. Graph Analysis of Brain Connectivity 409
- 18.5. Mapping the Network of Structural Connections of the Human Brain 415
- 18.6. Relating Structural Connections to Functional Interactions 419
- 18.7. Brain Connectivity and Network Disease 422
- 18.8. The Future of the Connectome 423
Acknowledgments 423
References 423

19. MR Diffusion Tractography 429

TIMOTHY E.J. BEHRENS, STAMATIOS N. SOTIROPOULOS, AND SAAD JBABDI

- 19.1. Introduction 429
- 19.2. Streamline Tractography 430
- 19.3. Probabilistic Tractography 435
- 19.4. Global Tractography Approaches 441
- 19.5. Choice of Local Description of Diffusion in Tractography 443
- 19.6. Designing a Diffusion Tractography Study 444
- 19.7. Future Advances in Diffusion Tractography 445
- 19.8. Summary and Conclusions 448
References 448

20. Validation of Tractography 453

PENNY L. HUBBARD AND GEOFFREY J.M. PARKER

- 20.1. Introduction 453
- 20.2. Validation of Fiber Orientation Information 455
- 20.3. Validation of Tractography 460
- 20.4. Summary 476
References 477

21. Connectivity Fingerprinting of Gray Matter 481

JOHANNES C. KLEIN, TIMOTHY E.J. BEHRENS, AND HEIDI JOHANSEN-BERG

- 21.1. Introduction 481
- 21.2. Application to Subcortical Gray Matter 488

- 21.3. Application to Cortical Gray 494
- 21.4. Validation 500
- 21.5. Conclusions 506
References 506
- 22. Contribution of Diffusion Tractography to the Anatomy of Language 511**
MARCO CATANI AND SANJA BUDISAVLJEVIĆ
- 22.1. Introduction 511
- 22.2. The Anatomy of the Arcuate Fasciculus: From Blunt Dissections to Tractography 512
- 22.3. Lateralization of the Arcuate Fasciculus 514
- 22.4. Comparative Anatomy of Perisylvian Language Network 516
- 22.5. Functional Correlates of Perisylvian Language Network 517
- 22.6. Beyond the Arcuate Fasciculus: Ventral and Frontal Networks 518
- 22.7. Application of Tractography to Language Disorders 519
- 22.8. Summary and Future Directions 524
Acknowledgments 525
References 525
- 23. Presurgical Tractography Applications 531**
ANDREAS J. BARTSCH, ARMIN BILLER, AND GYÖRGY A. HOMOLA
- 23.1. Introduction 531
- 23.2. Presurgical Applications, Tract Latitudes, and Tracking Failures 535
- 23.3. Potential Surgical Targets and Intentions 545
- 23.4. Presurgical Tractography 553
- 23.5. Summary and Conclusions 560
Acknowledgments 561
References 561
- 24. Comparing Connections in the Brains of Humans and Other Primates Using Diffusion-Weighted Imaging 569**
MATTHEW F.S. RUSHWORTH, JÉRÔME SALET, ERIC D. BOORMAN, AND ROGIER B. MARS
- 24.1. Introduction 569
- 24.2. Comparing Tractography with Tract-Tracing Techniques 570
- 24.3. Using Tractography to Examine the Connections of Human Ventral Frontal Cortex 571
- 24.4. Language and the Arcuate Fascicle in Humans and other Primates 573
- 24.5. Tractography Suggests Basic Similarities in Frontal Cortex Organization in Humans and other Primates 573
- 24.6. Premotor Cortex 578
- 24.7. Comparing the Parietal Cortex in Humans and other Primates 579
- 24.8. Conclusions 581
References 581
- 25. Imaging Structure and Function 585**
SAAD JBABDI
- 25.1. Introduction 585
- 25.2. Structural Imaging and Brain Morphometry 586
- 25.3. Combining Sources of Data 591
- 25.4. Imaging Anatomic-Functional Networks 597
- 25.5. Conclusions 602
References 602
- Index 607**