INDEX

Actinium-225
Properties, 74
Renal toxicity, 233
Use in acute myelogenous leukemia (AML), 222, 233
Activated tin ester (ATE). See Radiohalogen labeling - ATE
Acute myeloid leukemia (AML)
Selection of radionuclide for radioimmunotherapy, 221
Targets for radioimmunotherapy, 220
Treatment with 188Re-anti-CD66 antibodies, 231
Treatment with 131I-BC8 antibodies, 230
Treatment with 131I-M195 and 131I-lintuzumab, 227, 327
Treatment with 131I-p67 antibodies, 230
Treatment with 213Bi-lintuzumab, 232
Treatment with 225Ac-lintuzumab, 233, 327
Treatment with 90Y-lintuzumab, 230
Affibodies, 21
(ZHER24)2, 22
Radiobromination, 52
Staphylococcus protein A Z-domain, 22
Albumin binding, 26
Effect on pharmacokinetics, 26
Trastuzumab Fab, 27
Alpha (α)-Emitters
Penetration distance and LET, 46
Use for treatment of acute myeloid leukemia (AML), 222, 232
Use for treatment of brain tumors, 141, 154

Animal models of cancer
OncoMouse™, 409
Predictive utility for subsequent human studies, 409
Transgenic mouse models, 406, 408
Xenograft mouse models, 406, 408
Astatine-211. See Radiohalogen labeling:
Astatine radionuclides
ATM. See DNA strand breaks: ATM protein
Atomic nanogenerator. See Actinium-225: Properties
Auger electrons
111In-labeled 4D5 antibodies, 421
111In-labeled EGF, 311
111In-labeled exendin-4, 322
111In-labeled M195 and HuM195 (lintuzumab), 328
111In-pentetreotide, 303, 305
123I/125I-mTc, 300
125I/111In/99mTc-labeled LL1 antibodies, 324
125I/123I-IUdR, 299
125I-labeled daunorubicin analogues, 331
125I-labeled mAb A33, 320
125I-labeled mAb CO17-1A, 322
16-α-125I-iodo-17-β-estradiol (125I-E2), 329
67Ga/125I/111In-labeled 1F5 antibodies, 326
Anti-EGFR monoclonal antibodies labeled with 111In or 125I, 316
Bystander effects, 293
Comparison of different radionuclides, 294

Monoclonal Antibody and Peptide-Targeted Radiotherapy of Cancer, Edited by Raymond M. Reilly
Copyright © 2010 John Wiley & Sons, Inc.

613
Auger electrons (Continued)
- Cross-dose effect, 298
- DNA strand breaks, 292
- History, 289
- Microdosimetry, 296
- Penetration distance and LET, 46
- Physics principle, 289
- Relative biological effectiveness (RBE), 291

BAD. See DOTA: Use for labeling with 90Y

BAT. See TETA: Use for labeling with 67Cu

Bax. See Radiation: Induced apoptosis

Bcl-2. See Radiation: Induced apoptosis

Bcl-xL. See Radiation: Induced apoptosis

Beta (β)-Particles
- Penetration distance and LET, 46

Bexxar, 177
- Administration procedure, 173, 177
- Chemotherapy following radioimmunotherapy, 195
- Comparison with unlabeled tositumomab in clinical trials, 189
- Dosimetry, 178, 183
- High dose with stem cell support, 197
- History, 170
- Phase 1 trial, 180
- Phase 2 trials, 183
- Pivotal trial with comparison to chemotherapy, 184
- Radioimmunotherapy following chemotherapy, 195
- Rationale for administration of unlabeled antibody pre-dose, 175
- Response in indolent non-Hodgkin’s lymphoma, 190
- Response in non-Hodgkin’s lymphoma, 180
- Response in rituximab refractory patients, 190
- Response in transformed lymphoma, 192
- Response to retreatment, 200
- Side-effects, 185
- Treatment in patients with >25% marrow involvement, 202

Bismuth-213
- Use for treatment of leukemia, 232

Bombesin receptor 2 (BB2). See Gastrin releasing peptide receptor (GRPr)

Brain tumors, 139
- Combination of radioimmunotherapy, external radiotherapy and chemotherapy, 151
- Loco-regional therapy, 140
- Outcome following 131I-81C6 treatment, 149
- Phase II trial of 131I-81C6, 149
- Pre-targeted radioimmunotherapy using the avidin-biotin system, 156
- Prognosis, 139
- Targeted radiotherapy, 141
- Targets for radiotherapy, 142
- Treatment with 125I-mAb 425, 417
- Treatment with 131I-ch81C6, 153
- Treatment with 131I-labeled BC-2 and BC-4 antibodies, 144
- Treatment with 90Y-DOTATOC, 156
- Treatment with 90Y-labeled BC-2 and BC-4 antibodies, 145
- Treatment with locoregional 131I-labeled 81C6, 147
- Use of 211At-81C6 for treatment, 154

Breast cancer
- Cell culture models, 404
- Expression of sodium iodide symporter (NIS), 364
- Molecular phenotypic properties, 403
- Transgenic mouse models, 407

Bromine-76
- Properties, 51

Bystander effects
- Definition, 452, 507
- Drug induced inhibition or enhancement, 520
- History, 510
- In Intensity Modulated Radiotherapy (IMRT), 517
- In targeted and conventional radiotherapy, 515

Mechanisms, 518
- Techniques for studying bystander effects, 514, 518
Caspases. See Radiation: Induced apoptosis
CD20
Rationale for targeting in non-Hodgkin’s lymphoma, 175
CD22. See Epratuzumab
CD33. See Acute myeloid leukemia (AML): Targets for radioimmunotherapy
CD45. See Acute myeloid leukemia: Targets for radioimmunotherapy
CD66c. See Acute myeloid leukemia: Targets for radioimmunotherapy
CD74. See Non-Hodgkin’s lymphoma: Auger electron radiotherapy with LL1 antibodies
Characterization of radiolabeled antibodies and peptides, 75
DTPA substitution level, 75
Evaluation of homogeneity, 75
Measurement of immunoreactivity, 78
Measurement of radiochemical purity, 77
Preclinical biodistribution, tumor imaging and dosimetry studies, 81
Preclinical studies of anti-tumor effects and normal tissue toxicity, 81
Stability testing, 80
Chimeric monoclonal antibodies, 5
ch17-1A, 5
ch81C6, 152
chB72.3, 5
Percent murine sequences, 6
Rituximab, 6
Chlorotoxin
Use for targeted radiotherapy of brain tumors, 157
Clinical Trial Application (CTA), 573
Common Technical Document (CTD), 574
Investigational Medicinal Product (IMP) dossier (EU), 574
Pre-CTA meetings, 573
Regulatory organizational structure in Canada, 573
Regulatory organizational structure in the EU, 574
Clinical trials
Immunogenicity testing, 606
Phase 1 to Phase 3, 605
Pre-Phase I and exploratory, 602
Clusterin. See Radiation: Adaptive response Co-ligands. See Radiometal labeling: HYNIC for 99mTc labeling
Copper radionuclides
Properties, 72
Copper-61. See Copper radionuclides: Properties
Copper-64. See Copper radionuclides: Properties
Comparison with 18F, 72
Copper-67. See Copper radionuclides: Properties
Cross-fire effect, 324, 451
Enhancement of combination gene therapy and radiotherapy, 368
Desferrioxamine (DFO)
Use for 68Ga labeling, 71
Diabodies. See Fv fragments - Multimeric forms
Diethylenetriaminepentaacetic acid (DTPA)
Cross-linking of proteins, 65
Dianhydride form, 64
Instability of dianhydride form, 65
Measurement of substitution level, 72
p-benzylisothiocyanate form, 64, 66
Radioiodinated DTPA-containing peptides, 49
Site-specific conjugation to the Fc domain of antibodies, 66
DNA strand breaks
ATM protein, 422
Base excision repair (BER), 426
Cellular DNA damage surveillance response networks, 422
Cellular threshold for DNA damage response, 435, 438
Double strand break repair pathways, 427
From 111In-NLS-trastuzumab in breast cancer cells, 319
γ-H2AX foci, 424
Homology directed recombination repair (HRR), 428
Induced by radiation, 421
Mammalian DNA repair pathways, 425
Non-homologous end-joining (NHEJ) repair pathway, 427
p21WAF-1 response, 421
p53 response, 424
DNA strand breaks (Continued)
Role of adaptive response, 453
Threshold for activating cell cycle
checkpoints, 443
Threshold for activating cell death
mechanisms, 443
Domain-deleted monoclonal antibodies, 12
ch18.14ΔCH2, 12
chB72.3ΔCH2, 12
chCC49ΔCH2, 12
Isoforms, 13
Pharmacokinetics in humans, 13
Dopamine receptor (DR)
Viral gene delivery, 380
DOTA
Immunogenicity, 70
Use for labeling with 111In, 68
Use for labeling with 212Pb or 225Ac, 75
Use for labeling with 90Y, 69
DOTATATE
Amifostine to reduce toxic effects labeled
with 177Lu, 130
Combined with capecitabine labeled with
177Lu, 132
Comparison with chemotherapy labeled
with 177Lu, 129
Labeled with 177Lu for radiotherapy, 124
Labeled with 90Y for radiotherapy, 129
Radiation dosimetry labeled with 177Lu,
126
Side effects labeled with 177Lu, 127
Therapeutic outcome labeled with 177Lu,
127
DOTATOC
Comparison of renal toxicity with 111In-
pentetreotide when labeled with
90Y, 308
Comparison with 111In-pentetreotide
labeled with 90Y, 304
Conjugation with nuclear localization
sequences (NLS), 308
Differences in binding affinity of
radiometal labeled analogues, 72
Labeled with 90Y for radiotherapy, 123
Labeled with 90Y for treatment of brain
tumors, 156
Labeling with 68Ga, 71
Labeling with 99mTc, 59
Radiation absorbed dose to the kidneys,
124, 491
Uptake in cells infected with adenovirus
harbouring somatostatin receptor
gene labeled with 111In, 359
Epidermal growth factor (EGF)
Conjugation to human serum albumin for
labeling with 111In, 67, 313
Conjugation to metal chelating peptide for
111In-labeling, 67
Kit for labeling with 111In, 316
Labeling with 111In, 311
Labeling with 99mTc, 59
Nuclear importation, 310
Epidermal growth factor receptors (EGFR)
111In or 125I-labeled monoclonal
antibodies for radiotherapy, 316
Biology and expression, 310
Epratuzumab, 187
Response in non-Hodgkin’s lymphoma
labeled with 90Y, 188
Estrogen receptors (ER)
Targeted Auger electron radiotherapy, 320
F(ab’)_2 fragments, 3
Imaging properties, 41
Monoclonal antibody 425 labeled with
125I for radiotherapy, 316
Fab fragments, 3
Imaging properties, 41
FDG. See Positron emission tomography
(PET): 18F-2-fluorodeoxyglucose
(18F-FDG)
FLT. See Positron emission tomography
(PET): 18F-fluoro-3’-deoxy-3’-
L-fluorothymidine (FLT)
FLT3-L (FMS-related tyrosine kinase 3
ligand)
Use for predicting myelotoxicity from
targeted radiotherapy, 491
Fv fragments, 14
Dimeric CC49 scFv, 18
Disulfide sFv (dsFv), 16
Fv dimers (diabodies), 17
Imaging properties, 41
Linker, 14
Multimeric Fv forms, 16
Radiotherapy, 17
scFv, 14
Triabodies and tetrabodies, 17

Gallium radionuclides
Properties, 71
Gallium-67. See Gallium radionuclides: Properties
Gallium-68. See Gallium radionuclides: Properties
Gamma (γ)-H2AX
Accumulation at sites of DNA double-strand breaks, 424
Gastrin releasing peptide receptor (GRPr)
Biography and expression, 375
Viral gene delivery, 376
Gene therapy. See Viral gene delivery
GEP tumors. See Neuroendocrine malignancies
Glioblastoma multiforme (GBM). See Brain tumors
Glucagon-like peptide-1 receptors (GLP-1R). See Auger electrons: 111In-labeled exendin-4
Good Clinical Practices (GCP), 601
Good Manufacturing Practices (GMP), 576
Bi-functional chelators for binding radiometals, 583
Cell banks for recombinant protein production, 577
Kit formulation, 587
Manufacturing process controls, 588
Purification of recombinant proteins, 578
Quality of radionuclides, 585
Quality of recombinant proteins, 580
Quality of synthetic peptides, 581, 583
Stability testing, 593
Validation of virus inactivation and removal, 579
GPCR. See Peptides: Molecular targets
Health economics
Challenges and concerns, 554
Constrained optimization problems, 545
Evaluation of cost-effectiveness of Zevalin, 559
Funding the most effective treatments, 546
Funding treatments with the highest effectiveness/cost (E/C) ratios, 546
ICER (Incremental cost-effectiveness ratio), 548
ICER estimates for Zevalin vs. Rituxan, 561
Principles, 543
QUALY (Quality adjusted life year), 545
Using economic analysis to make healthcare decisions, 552
WTP (Willing to pay) vs ICER, 552
Heavy chain antibodies (HCAbs). See Nanobodies
HER2
Biography and expression, 318
Internalization and nuclear localization, 318
Transgenic mouse tumor models, 407
HRS-IRR response. See Radiation: Low dose hyper-radiosensitivity-increased radioresistance response (HRS-IRR)
Human anti-human antibodies (HAHA), 7
Human anti-mouse antibodies (HAMA), 2
Bexxar, 183, 185
Chimeric antibodies, 6
From bispecific antibodies, 270
Zevalin, 191
Human monoclonal antibodies, 9
Adalimumab, 10
Panitumumab, 10
Humanized monoclonal antibodies, 6
Abbreviated CDR grafting, 8
Alemtuzumab (Campath-1H), 7
Bevacizumab (Avastin), 7
CDR grafting, 6
Gemtuzumab ozogamicin (Mylotarg), 7
huCC49, 7
HuM195, 7
Immune response, 7
MN-14, 7
Percent murine sequences, 6
Pharmacokinetics, 7
SDR grafting, 8
Trastuzumab (Herceptin), 6
HYNIC. See Radiometal labeling: HYNIC for 99mTc labeling
Hypervariable domain region peptides, 13
Hypoxia. See Radiation: Role of hypoxia and fractionation effects
Ibritumomab tiuxetan. See Zevalin
Image of the year, xvii
Immunoreactivity. See Characterization of radiolabeled antibodies and peptides:
Measurement of immunoreactivity
Immunoreactive fraction (IRF), 78
Measurement of K and Bmax, 78
Indium radionuclides
Properties, 63
Indium-111
Kidney uptake, 68
Liver uptake, 68
Indium-111 EGF
Clinical pharmacokinetics, 316
Comparison of cytotoxicity with chemotherapeutic agents, 311
Cytotoxicity against breast cancer cells, 311
Effect of Iressa™ on nuclear uptake and cytotoxicity, 313
Internalization and nuclear importation, 311
Preclinical biodistribution and pharmacokinetic studies, 313
Preclinical dosimetry studies, 314
Preclinical toxicology studies, 315
Response to treatment in breast cancer, 316
Side-effects when used for therapy, 316
Indium-111 pentetreotide
Comparison of renal toxicity with 90Y-DOTATOC, 308
Comparison with 131I-mIBG for radiotherapy, 306
Comparison with 90Y-DOTATOC for radiotherapy, 304
Internalization and nuclear importation, 301
Radiotherapy, 122, 303, 305
Side effects when used for therapy, 123, 303, 306
Indium-111 Trastuzumab
Cytotoxicity towards breast cancer cells, 318
Radiosensitization by methotrexate, 319
Indium-114m. See Indium radionuclides: Properties
Investigational New Drug Application (IND), 793
Documentation components, 575
Pre-IND meetings, 573
Regulatory organizational structure in the USA, 574
Iodine-131
Use for treatment of brain tumors, 141
Iodine-125 Iododeoxyuridine (125I-IUdR).
See Auger electrons: 125I/123I-IUdR
Iso-Link kit. See Radiometal labeling: 99mTc (I)-tricarbonyl complex
Lanreotide
Labeled with 90Y, 128
Lindmo assay. See Immunoreactivity:
Immunoreactive fraction (IRF)
Linear energy transfer (LET)
Auger electrons compared to beta radiation, 289
Linear-quadratic model. See Radiation: Cell survival models.
Lintuzumab. See Acute myeloid leukemia (AML)
Lutetium-177
Properties, 74
DOTATATE, 124
Maximum tolerated dose (MTD)
111In- or 67Ga-LL1 antibodies, 236
125I-A33, 321
125I-CO17-1A, 322
131I-ch81C6, 153
131I-labeled 81C6 for treatment of brain tumors, 148
Bexxar, 183
No Observable Adverse Effect Level (NOAEL), 598
Pre-clinical studies for determination, 598
Pre-targeted radioimmunotherapy of brain tumors, 156, 264
Pre-targeted radioimmunotherapy of small cell lung cancer, 267
Zevalin, 186
Metaiodobenzylguanidine (mIBG)
Bystander effects labeled with 131I, 211At or 123I, 517
Uptake in virally-infected cells and tumors expressing NET labeled with 131I/123I, 378
Microdosing. See Clinical trials: Pre-Phase 1 and exploratory
Minibodies, 19
  Flex minibody, 19
Molecular imaging
  Definition, 527
  Evaluating radiation dosimetry, 481
  Evaluating viral gene delivery, 371
Molecular recognition units (MRUs). See Hypervariable domain region peptides
Monoclonal antibodies
  1C6. See Tenascin-C: Monoclonal antibody 81C6
  4D5 Labeled with 111In, 421
  528 Labeled with 111In, 316
  Anti-CEA-anti-EDTA bispecific antibody, 249
  Anti-EDTA antibodies, 248
  Anti-tenasin monoclonal antibody 81C6
    Labeling with 211At, 56
Good Manufacturing Practices (GMP), 580
HuM195. See Acute myeloid leukemia (AML): lintuzumab
  Kit formulation, 82, 587
Nomenclature, 7
NR-LU-10 - Toxicity to GI tract from pre-targeted radioimmunotherapy, 261
Pharmacokinetics - effect on tumor targeting, 242
  Tenascin-C, 144
  Tumor and normal tissue uptake, 40, 400, 596
  Type 1 vs. type 2 CD20 antibodies, 171
Monoclonal antibody C225
  Labeling with 111In, 67
Murine monoclonal antibodies, 2
  90Y-ibritumomab tiuxetan (Zevalin), 2
Myelodysplastic syndrome (MDS)
  From treatment with 111In-pentetreotide, 124, 305
  From treatment with 177Lu-DOTATATE, 127
  From treatment with Bexxar, 183, 193
  From treatment with Zevalin, 194
  Possible role of bystander effects, 520
Nanobodies, 10
Neonatal Fc receptors (FcRn), 23
  Anti-CD20 scFv-Fc, 24
  Anti-CEA scFv-Fc, 23
Neuradiab J. See Tenascin-C: Monoclonal antibody 81C6
Neuroblastoma
  Auger electron radiotherapy with 123I/125I-mIBG, 330
Neuroendocrine malignancies, 121
Non-Hodgkin’s lymphoma
  131I-tositumomab (Bexxar), xvii
  90Y-ibritumomab tiuxetan (Zevalin), xvii
  Auger electron radiotherapy using 1F5 (anti-CD20) antibodies, 326
  Auger electron radiotherapy with LL1 (anti-CD74) antibodies, 324
Economic analysis of cost-effectiveness of Zevalin, 559
  Long-term outcome following radioimmunotherapy, 193
  Molecular imaging, xvii, 535, 536
  Pre-targeted radioimmunotherapy, 262
  Response to Bexxar or Zevalin, 180
Norepinephrine transporter (NET)
  Biology and expression, 377
  Viral gene delivery, 378
Nuclear localization sequences (NLS)
  Conjugated to HuM195 (lintuzumab), 328
  Conjugated to trastuzumab (Herceptin), 318
  Conjugation to 111In-DOTATOC, 308
  Conjugation to DNA intercalators, 332
  Present in the EGFR, 310
OBOC (One Bead One Compound). See Peptides: Combinatorial libraries
Octreotide. See Indium-111 pentetreotide

\[ p21^{\text{WAF1}} \]
  Response to DNA damage, 424
\[ p53 \]
  Response to DNA damage, 424
  Role in dose-dependency of DNA damage response, 442
PEGylation, 25
Effect on immunoreactivity, 25

Peptides
111In-DTPA-peptide for pre-targeting with bispecific antibodies, 256
111In-labeled exendin-4, 322
125I-labeled bombesin targeting of GRPr, 524
Advantages, 102
Altering their pharmacokinetic behaviour, 113
Combinatorial libraries, 106
Design for multimodality imaging, 114
Good Manufacturing Practices (GMP), 581
Internalization of agonists and antagonists, 114
Inter-species differences in protein binding, 408
Isomers due to incorporation of radiometal complexes, 112
Molecular targets, 101
Phage display libraries, 108
Physiological response, 103
Radionuclide labeling, 108, See Radiohalogenation and Radiometal labeling
Rational vs. random approach to discovery for targeting cancer, 104
Single amino acid chelator (SAAC) for labeling with 99mTc, 110
Site-specific conjugation of metal chelators, 109
Strategies to diminish renal uptake, 113
Structural modifications to increase stability, 103
Use of antagonists for radiotherapy, 131
Phage display
Anti-Tenascin-C antibodies, 144
For establishing peptide libraries, 108
Positron emission tomography (PET), xvii
18F-2-fluorodeoxyglucose (18F-FDG), xvii, 529
18F-fluoro-3'-deoxy-3'-L-fluorothymidine (FLT), 530, 532, 536
Combination with computed tomography (CT), 530
Evaluation of viral gene delivery, 371
False positive and false negative studies, 532
Principles, 41, 528
Procedures and image analysis, 531
Standardized uptake value (SUV), 531
Use for evaluating radiation dosimetry, 487
Use for evaluating response in non-Hodgkin’s lymphoma, 535
Use for evaluating response to 90Y-epratuzumab in non-Hodgkin’s lymphoma, 537
Use for evaluation of response in solid tumors, 535
Use in evaluating response to Zevalin in non-Hodgkin’s lymphoma, 536
Pre-clinical studies
Genotoxicity, 599
Immunogenicity, 598
Pharmacokinetics and metabolism, 596
Safety pharmacology, 597
Toxicology, 598
Pre-clinical testing
Biodistribution studies, 596
Immunohistochemical assessment of normal tissue cross-reactivity, 595
Radiopharmacology studies, 595
Pre-formed chelator. See Radiometal labeling: N2S2 and N3S chelators for 99mTc labeling
Pre-targeted radioimmunotherapy
Anti-CEA x anti-(In)DTPA bispecific antibodies, 266
Anti-G250 x anti-(In)DTPA bispecific antibodies in renal cell carcinoma, 256
Avidin-biotin system, 250
Basic concepts, 252
Bispecific antibodies and radiolabeled haptons, 247
Combination with chemotherapy, 269
Galactosylated biotinylated albumin clearing agent, 260
Radiation absorbed doses to tumor and normal tissues, 261, 262, 264, 267
Radiolabeled morpholino oligomers (MORFs), 251
Streptavidin-conjugated HMFG1 antibodies, 250
Streptavidin-conjugated NR-LU-10 antibodies, 250, 260
Treatment of brain tumors, 155, 264, 269
Treatment of leukemias, 226
Treatment of medullary thyroid carcinoma, 267
Treatment of non-Hodgkin’s lymphoma, 262
Treatment of small cell lung cancer and medullary thyroid carcinoma, 267
Two and three-step targeting using the avidin-biotin system, 263
QUALY. See Health economics: QUALY (Quality adjusted life year)
RAD51. See DNA strand breaks: Homology directed recombination repair (HRR)
Radiation
Adaptive response, 453, 456
Bystander effect from targeted radiotherapy, 452, 456
Cell survival models, 431
Induced accelerated senescence, 430
Induced apoptosis, 428, 455
Induced autophagy, 430
Induced mitotic catastrophe, 430
Induced necrosis, 429
Inverse dose rate effects, 447
Linear non-threshold (LNT) model, 513
Low dose hyper-radiosensitivity-increased radioresistance response (HRS-IRR), 433
Role of hypoxia and fractionation effects, 457
Ultra-fractionation strategies, 445
Radiation dosimetry
131I-81C6 for treatment of brain tumors, 149, 150
211At-81C6 for treatment of brain tumors, 155
3D dose planning system for targeted radiotherapy, 485, 487
Å: Cumulated radioactivity and residence time, 650
Absorbed doses and hepatic toxicity, 492
Absorbed doses and renal toxicity, 491
Absorbed doses to the bone marrow from targeted radiotherapy, 488
Absorbed fraction for penetrating and non-penetrating radiation, 477
Attenuation corrections in quantitative imaging, 482
Auger electrons, 296
Correlation with myelotoxicity from targeted radiotherapy, 490
Cross-dose effect, 298
Cross-fire effect, 324
Definition of Gray (Gy) and rad, 475
Dose rates to tumors from targeted radiotherapy, 431
Effects of radioactivity on viability of peripheral blood stem cell (PBSC) infusion, 489
Estimation of tumor doses using MIRD or OLINDA, 492
Evaluation in humans, 481
Evaluation using preclinical animal models, 401, 477
Medical Internal Radiation Dosimetry (MIRD), 475
Microdosimetry of Auger electrons and implications for renal toxicity, 308
Monte Carlo methods, 480, 486, 493
Mouse S-values, 480
Phase I trial estimates, 605
Planar conjugate view imaging, 481
Projection of human doses from preclinical animal studies, 479
Scatter corrections in quantitative imaging, 483
Tumor dose rates from targeted radiotherapy, 420
Tumor responses to targeted radiotherapy despite low absorbed doses, 455, 494, 517
Radiochemical purity. See Characterization of radiolabeled antibodies and peptides: Measurement of radiochemical purity
Radiofluorination
Prosthetic groups. See Radiohalogen labeling: fluorine radionuclides
Radiohalogen labeling, 47
18F-NPFP, 55
18F-SFB, 55
18F-SFBS, 54
211At-SAB, 56
211At-SAPC, 57
76Br-SPBrB, 52
Astatine radionuclides, 56
ATE, 48
Bromine radionuclides, 51
Chloramine-T, 47
Fluorine radionuclides, 53
In vivo instability, 47
Iodine radionuclides, 47
Iodine-124, 51
Iodogen, 47
Polyhedral boron clusters, 53
Radiiodinated tyramine cellobiose (TCB), 51
SGMIB, 49
SIPC, 49
Radiolysis
Due to 90Y labeling, 70
Radioprotectants, 70
Radiometal labeling
99mTc(I)-tricarbonyl complex, 61
Copper radionuclides, 72
DOTA for labeling with 90Y, 69
DTPA conjugation for 111In labeling, 64
Gallium radionuclides, 71
Good Manufacturing Practices (GMP), 583
HYNIC for 99mTc labeling, 59
Indium radionuclides, 63
Lead, bismuth and actinium radionuclides, 74
N2S2 chelators for 99mTc labeling, 61
N3S chelators for 99mTc labeling, 61
Reduction of thiols for 99mTc labeling, 57
Rhenium radionuclides, 62
Single amino acid chelator (SAAC) for 99mTc labeling, 61
Site-specific labeling with 111In, 66
Starburst dendrimers, 67
Technetium radionuclides, 57
Yttrium radionuclides, 69
Radionuclide
Good Manufacturing Practices (GMP), 585
Selection for targeted radiotherapy, 44, 295, 456
Selection for targeted radiotherapy of brain tumors, 141
Selection for tumor imaging, 41
Radiosensitivity
Phase of cell cycle, 443
Radiosensitizers
Combined with peptide directed radiotherapy, 131
Combined with radioimmunotherapy, 402
RECIST (Response Evaluation Criteria in Solid Tumors), 534
Renal cell carcinoma
Pre-targeted radioimmunotherapy, 256
Residualizing radioidination. See Radiohalogen labeling: ATE
Rhenium radionuclides
Properties, 62
Rituximab (Rituxan)
Labeling with 131I for treatment of non-Hodgkin’s lymphoma, 187
Labeling with 188Re, 63
Response in non-Hodgkin’s lymphoma, 170
Rituximab (Tituxan)
Economic analysis compared to Zevalin, 561
Scatchard assay. See Immunoreactivity: Measurement of Ka and Bmax
Schwartz method. See Radiometal labeling: Reduction of thiols for 99mTc-labeling
Selective high-affinity ligands (SHALS), 21
SIB. See Radiohalogen labeling - ATE
Single photon emission computed tomography (SPECT)
Attenuation corrections in quantitative imaging, 482
Evaluation of viral gene delivery, 371
Principles, 4
Scatter corrections in quantitative imaging, 483
Sodium iodide symporter (NIS). See Viral gene delivery: Sodium iodide symporter (NIS)
Somatostatin receptors
Adenoviral gene delivery, 358
Biology and subtypes, 300, 354
Radioligands, 300
Targets for combined viral gene therapy and targeted radiotherapy, 357
Streptavidin
Use in pre-targeting. See Pre-targeted radioimmunotherapy: Avidin-biotin system
Substance P
Use for targeted radiotherapy of brain tumors, 157
SUV. See Positron emission tomography (PET): Standardized uptake value (SUV)
Targeted radionuclide therapy
Prediction of myelotoxicity, 490
Radiobiological concepts, 420
Technetium labeling. See Radiometal labeling: Technetium radionuclides
Technetium-94m
Labeling methods, 62
Technetium-99m
Properties, 57
Tenascin-C
Aptamers, 144
BC-2 and BC-4 antibodies, 144
Monoclonal antibodies, 144
Monoclonal antibody 81C6, 146
Structure, 142
Target for radiotherapy of brain tumors, 142
TETA
Use for labeling with 67Cu, 73
TM-601. See Chlorotoxin: Use for targeted radiotherapy of brain tumors
Tositumomab, 131I-labeled. See Bexxar
Trastuzumab (Herceptin)
Labeling F(ab')\textsubscript{2} fragments with 99mTc, 59
Labeling with 111In, 318
Labeling with 212Pb or 225Ac, 75
Labeling with 76Br, 53
Tricine. See Radiometal labeling: HYNIC for labeling with 99mTc
Vascular endothelial growth factor (VEGF)
Transferrin fusion protein for labeling with 111In, 66
Viral gene delivery
Adenoviruses, 352, 353
CEA promotor for selective tumor expression, 367
Combined with chemotherapeutic agents, 369
Combined with targeted radiotherapy, 363, 381
Deleted Vesicular Stomatitis Virus (VSV) for selective tumor expression, 368
Dopamine receptor (DR), 380
Dopamine transporter (DAT), 380
Effect of radiation on viral replication, 371, 381
Evaluation using radiopharmaceutical probes, 359
Gastrin releasing peptide receptor (GRP), 376
Herpes simplex virus thymidine kinase (HSV-1 TK), 369, 380
Imaging of Sodium Iodide Symporter (NIS) expression, 371
Measles virus, 353
MUC1 promotor for selective tumor expression, 367
Norepinephrine transporter (NET), 378
Probasin promotor for selective tumor expression, 367
Radiopharmaceutical biodistribution and dosimetry, 374
Retroviruses, 352
Sodium iodide symporter (NIS), 363, 365
Vaccinia virus (VV), 354
Vesicular stomatitis virus (VSV), 353
Yttrium radionuclides
Properties, 69
Use for treatment of brain tumors, 141
Yttrium-86. See Yttrium radionuclides: Properties
Yttrium-90. See Yttrium radionuclides: Properties
Zevalin, 175
Administration procedure, 173, 176
Chemotherapy following radioimmunotherapy, 194
Comparison with rituximab in clinical trials, 188
Zevalin (Continued)

Economic analysis of cost-effectiveness, 559
Following stem cell transplantation, 199
High dose with stem cell support, 198
Phase 1 trials, 185
Phase 2 trial in patients with mild thrombocytopenia, 186
Radioimmunotherapy following chemotherapy, 195
Rationale for administration of unlabeled antibody pre-dose, 175
Rejection of funding by Scottish Medicines Consortium, 562

Response in Mantle Cell Lymphoma (MCL), 192
Response in non-Hodgkin’s lymphoma, 180
Response in relapsed large cell lymphoma, 191
Response in rituximab refractory patients, 189
Response to retreatment, 285
Side-effects, 187
Treatment in children with non-Hodgkin’s lymphoma, 201
Use in primary central nervous system lymphomas, 200
Use of 111In-labeled Zevalin for dosimetry, 175