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ICRU REPORT 96, DOSIMETRY-GUIDED RADIOPHARMACEUTICAL THERAPY

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Dosimetry-Guided Radiopharmaceutical Therapy

Preface

Radiopharmaceutical therapy is undergoing a renaissance. This is being driven by the clinical successes, federal approvals, and growing implementation of several radiopharmaceuticals for treating cancer, including Xofigo ($^{223}RaCl_2$), LUTATHERA (^{177}Lu DOTATATE), TheraSphere (^{90}Y glass microspheres), and SIR-Spheres (^{90}Y resin microspheres). These recent successes are supported by the proven therapeutic efficacy of Zevalin (^{90}Y ibritumomab tiuxetan) and the mainstay of radiopharmaceutical therapy, AZEDRA and HICON ($Na^{131}I$). These agents, and dozens of others under development (Sgouros *et al.*, 2020), comprise different classes of radionuclides and pharmaceuticals. To ensure that these radiopharmaceuticals are developed and implemented in a manner that maximizes tumor response while minimizing adverse toxicity to normal tissues, it is essential to adopt strategies analogous to external beam radiation therapy where dosimetry-based treatment planning plays a critical role. In external beam therapy, this entails planning and verifying the absorbed doses received by both tumor and normal tissues to assure optimal treatment for each patient. A record of the absorbed dose information also plays a key role in planning retreatments. The ICRU recognizes that treatment plans can only be formulated in a manner commensurate with the technology available at the treatment center. Therefore, the ICRU has established Reporting levels for prescribing, recording, and reporting of treatments with external beams of radiation and brachytherapy with correspondingly increasing levels of sophistication (Level 1, Level 2, Level 3) (ICRU, 1993b; 1999; 2010; 2013; 2014; 2016). Treatment centers are encouraged to elevate their standards to the highest level possible, and patients can benefit from seeking treatment at the highest level accessible to them.

Radiopharmaceutical therapy can realize similar benefits by embracing dosimetry in the practice of prescribing, recording, and reporting radiopharmaceutical therapies. However, it has been 18 years since the ICRU issued guidance on dosimetry for nuclear medicine, namely ICRU Report 67—Absorbed Dose Specification in Nuclear Medicine (ICRU, 2002), and more than 40 years since the ICRU first addressed this topic (ICRU, 1979a). The field has mushroomed since then, along with a proliferation of terms, quantities, units, and techniques. The present report establishes standardized terminology and nomenclature for radiopharmaceutical therapy, an important step to facilitate the common ground that is needed for communication and maturation of the field. The report also reviews advances in radiopharmaceutical therapy and provides recommendations regarding best practices for its clinical implementation, including levels for prescribing, reporting, and recording treatments with a variety of radiopharmaceuticals. Due to the unique properties of each radiopharmaceutical, the requirements to achieve a given level are specific to the radiopharmaceutical and will likely evolve as new technology develops.

Roger W. Howell
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Glossary

	Acronym or symbol	Definition
American Association of Physicists in Medicine	AAPM	The American Association of Physicists in Medicine is a scientific, educational, and professional organization of Medical Physicists.
Absorbed Dose	D	The mean value of the energy imparted per mass, $d\bar{\varepsilon}/dm$, by ionizing radiation. The unit of absorbed dose is joule per kilogram, with the special name gray (Gy) when applied to ionizing radiation.
Absorbed Fraction	ϕ_i	The fraction of the energy of type-i radiation emitted from a source region that is absorbed in a target region.
Activity	A	The activity, A, of an amount of a radionuclide in a particular energy state at a given time is the quotient $-dN/dt$, where dN is the mean change in the number of nuclei in that energy state due to spontaneous nuclear transformations in the time interval dt.
Administered Activity	A_o	The amount of activity administered to the subject. The typical routes are intravenous, intra-arterial, oral, inhalation, and intracavitary.
Alkaline Phosphatase	ALP	Alkaline phosphatase, or basic phosphatase, is a homodimeric protein enzyme of 86 kilodaltons. Each monomer contains five cysteine residues, two zinc atoms, and one magnesium atom crucial to its catalytic function, and it is optimally active at alkaline pH environments.
Auger Electron		Atomic electron emitted during the atomic transitions that follow creation of a vacancy by electron capture decays, internal conversion transitions, photoelectric effect, and Compton interactions.
Becquerel	Bq	The unit of activity (1 nuclear transition per second) in the International System of Units (SI).
Biologically Effective Dose	BED (or EQD0)	The absorbed dose that is required to cause a given biological effect if the absorbed dose is delivered in infinitely small doses per fraction or, equivalently, at very low absorbed dose rates such as in low-dose-rate brachytherapy. It is equal to EQD0 (see below).
Biological Half-time	T_b	The mean time for one half of the initial number of atoms or molecules of a specific type to be eliminated via biological processes.
Brachytherapy	BT	A cancer treatment in which radioactive material sealed inside a seed, pellet, wire, or capsule is introduced into the body using a needle, catheter, or applicator, either permanently (implant) or temporarily. The radiation given off by this source irradiates nearby cancer cells.
Bystander Effect	BE	A biological effect imparted by an irradiated cell to an adjacent cell or neighbor cell that may be as far away as 1 mm or more.
Collimator Detector Response	CDR	Point spread function associated with collimator in planar and SPECT imaging.
Computational Human Phantoms	CHP	Mathematical representations of the human anatomy needed for radiation transport simulations of external or internal radiation sources.
Computed Tomography	CT	A computerized X-ray imaging procedure in which a beam of X-rays is aimed at a patient and quickly rotated around the body, The transmitted fraction of photons that pass through the patient are measured and used to generate cross-sectional images (“slices”) of the body.

	Acronym or symbol	Definition
Continuously Slowing Down Approximation	CSDA	An approximation used to arrive very close to the average path length traveled by a charged particle as it slows down to rest.
Clinical Treatment Region	CTR	Region(s) to treat, including macroscopic disease and microscopic disease, ie, the total disease burden with margins for delineation uncertainty (applicable in RPT).
Clinical Target Volume	CTV	The tissue volume that contains the gross tumor volume (GTV) and putative adjacent subclinical microscopic malignant lesions (applicable in EBRT).
Delineable Source Region	SR_D	Source region that is measurable by macroscopic imaging such as SPECT/CT or PET/CT and for which the activity content, or activity concentration can be quantified by delineation of VOIs in these images
Delineable Region at Risk	RAR_D	A region at risk that can be measured by macroscopic imaging and that can be adequately delineated in these images (image segmentation) to estimate its mass and absorbed dose.
Delta Ray	δ-ray	A secondary electron, set in motion along a charged-particle trajectory, with enough energy to form a discernible track of its own.
Dose Point Kernel	DPK	Distribution of absorbed dose around an isotropic point source in an infinite homogeneous medium.
Dose Volume Histogram	DVH	A cumulative histogram that relates absorbed dose to tissue volume in radiation therapy planning.
Dosimetric Treatment Region	DTR	Region(s) of disease for which the mass and absorbed dose are estimated. The DTR is a subcategory of the CTR. The DTR is categorized into the delineable dosimetric treatment region(s) (DTR_D) and the nondelineable dosimetric treatment region(s) (DTR_{ND}), depending on the possibility to perform patient-specific estimation of the tissue mass from images, and the level of uncertainty in the absorbed dose estimate. A region of disease included as an SR is generally also included among the DTRs.
Double Strand Break	DSB	Damage consisting of breaks in each strand of a DNA double helix within a few base pairs, resulting in loss of continuity of the molecule.
Effective Half-time	T_e	The time for the activity in a region to decrease to one half of its value, through the combined effects of radioactive decay and biological uptake/clearance of the radiopharmaceutical.
Electron Capture	EC	Type of nuclear decay wherein an atomic electron is captured in a quantum mechanical process by the nucleus.
Equieffective Dose	EQDX	The total absorbed dose delivered by the reference treatment plan (fraction size X) that leads to the same biological effect as a test treatment plan that is conducted with absorbed dose per fraction d and total absorbed dose D. $\mathrm{EQD}X_{\alpha/\beta} = D \cdot \frac{\alpha/\beta + d}{\alpha/\beta + X}$ where α/β is an endpoint- and radiation quality-specific parameter that describes the effect of changes in dose per fraction. EQD0 is equal to BED (see definition in "Glossary").
European Association of Nuclear Medicine	EANM	A medical and scientific society that promulgates nuclear medicine.
European Medicines Agency	EMA	The European Medicines Agency is an agency of the European Union in charge of the evaluation and supervision of medicinal products.
Expectation Maximization	EM	Algorithm to find maximum-likelihood estimates for model parameters when your data are incomplete, has missing data points, or has unobserved (hidden) latent variables. It is an iterative way to approximate the maximum likelihood function.
External Beam Radiation Therapy	EBRT	The most common approach to delivering radiation for cancer therapy that uses high-energy photons, electrons or protons directed by machine sources outside the body.

	Acronym or symbol	Definition
Food and Drug Administration	FDA	The United States Food and Drug Administration is a federal agency of the Department of Health and Human Services.
Fraction (treatment fraction)		Radiopharmaceutical therapy can be delivered in multiple administrations (eg, $^{223}RaCl_2$). Analogous to external beam radiation therapy, each administration is referred to as a fraction.
Full Width at Half Maximum	FWHM	Width of peak at half the maximum value.
Gray	Gy	SI unit of absorbed dose.
Gross Tumor Volume	GTV	A tumor volume that can be seen, palpated, or imaged.
High Dose Rate	HDR	High dose rate of radiation is delivered to the tumor in a short burst, lasting up to only a few minutes.
Homologous Recombination	HR	DNA repair mechanism which uses the undamaged sister chromatid as a template for base-pair sequence homology to guide the restoration of the damaged region of the DNA.
Homologous Recombination Deficient	HRD	Patients with deficient HR DNA repair mechanism.
Hypoxia Inducible Factor	HIF	A transcription factor that responds to decreased oxygen in the cellular environment.
International Commission on Radiological Protection	ICRP	The International Commission on Radiological Protection is an independent, international, nongovernmental organization, with the mission to protect people, animals, and the environment from the harmful effects of ionizing radiation.
Intensity Modulated Radiation Therapy	IMRT	A type of three-dimensional radiation therapy (EBRT) that uses computer-generated images to match radiation delivery to the size and shape of a tumor. In IMRT, thousands of tiny radiation beamlets enter the body from many angles and intersect the tumor. As the intensity of each beamlet can be controlled, the spatial distribution of absorbed dose can be shaped to conform to the tumor. The aim is to deliver a higher radiation dose to a tumor with less damage to nearby healthy tissue.
Linear Energy Transfer	LET	The linear energy transfer of charged particles in a medium is the quotient of dE by dl, where dl is the distance traversed by the particle and dE is the mean energy loss due to collisions with energy transfers less than some specified value.
Low Dose Rate	LDR	Low dose rate of radiation that is delivered to the tumor over extended periods of time (hours to days).
Line of Response	LOR	The annihilation photon pairs associated with positron decay are emitted simultaneously at approximately 180° apart, hence the point of origin of the pair occurs along a line between the two opposing detectors when they are detected in coincidence, known as the line of response.
Linear No-Threshold	LNT	The linear no-threshold model is a dose-response model used in radiation protection to estimate stochastic health effects such as radiation-induced cancer, genetic mutations, and teratogenic effects on the human body due to exposure to ionizing radiation.
Linear-Quadratic Model	LQ	Cell survival curves can be characterized mathematically by a linear-quadratic (LQ) dose-response model (Lea, 1946): $SF = e^{-(\alpha D + \beta D^2)}$ where SF is the surviving fraction, D is the absorbed dose (in Gy), α is the linear sensitivity coefficient (in Gy^{-1}), and β is the quadratic sensitivity coefficient (in Gy^{-2}).
Localization Region	LR	The organs, tissues, or cells to which the radioactive compound localizes.
Medical Internal Radiation Dose Committee	MIRD	Dosimetry committee of SNMMI. Publishes recommendations on performing dosimetry for radiopharmaceuticals.

	Acronym or symbol	Definition
Metaiodobenzylguanidine	MIBG	Iobenguane, or MIBG, is an aralkylguanidine analog of the adrenergic neurotransmitter norepinephrine. It acts as a blocking agent for adrenergic neurons. When radiolabeled, it can be used in nuclear medicinal diagnostic techniques as well as in neuroendocrine antineoplastic treatments.
Mismatch Repair	MMR	Corrects misrepaired nucleotides (eg, C with T).
Magnetic Resonance	MR	Magnetic resonance is a quantum mechanical resonant effect that can appear when a magnetic dipole is exposed to a static magnetic field and perturbed with another, oscillating electromagnetic field.
Maximum Tolerated Dose	MTD	The dose at which none or a small fraction of tumor-free subjects experience observable adverse effects (eg, body weight loss).
Maximum Tolerated Equieffective Dose	MTEQD*X*	Maximum tolerated dose in terms of equieffective dose (EQD*X*). The EQD*X* at which none or a small fraction of tumor-free subjects experience observable adverse effects (eg, body weight loss).
National Council on Radiation Protection and Measurements	NCRP	The United States National Council on Radiation Protection and Measurements (NCRP) seeks to formulate and widely disseminate information, guidance, and recommendations on radiation protection and measurements which represent the consensus of leading scientific thinking.
Nondelineable	ND	Activity content or activity concentration that is not measurable by delineation of VOIs in macroscopic imaging such as SPECT/CT or PET/CT.
Nondelineable Source Region	SR_{ND}	Designates a source region for which the activity content or activity concentration is not measurable by delineation of VOIs in macroscopic imaging such as SPECT/CT or PET/CT.
Nondelineable Region at Risk	RAR_{ND}	Normal tissue regions that cannot be readily delineated for the individual patient by conventional imaging, and whose mass cannot be easily measured, but for which dosimetric estimates are needed.
Nonuniform Rational Basis-Spline	NURBS	Nonuniform rational basis spline is a mathematical model commonly used in computer graphics for generating and representing curves and surfaces. It offers great flexibility and precision for handling both analytic shapes and modeled shapes.
Nucleotide Excision Repair	NER	Nucleotide excision repair (NER) is a DNA repair mechanism. The process removes a short segment of single-stranded DNA that contains the lesion. The undamaged single-stranded DNA serves as a template to synthesize a short complementary sequence. The replacement sequence is ligated to complete the repair.
Nonhomologous End-Joining	NHEJ	DNA repair mechanism wherein enzymes recognize the broken ends of the two damaged DNA strands and reattach them.
Normal Tissue Complication Probability	NTCP	The probability that a given absorbed dose of radiation will cause an organ or tissue structure to experience complications considering the specific biological cells of the organ or tissue structure. The NTCP is used in treatment planning as a tool to differentiate among treatment plans.
Oxygen Enhancement Ratio	OER	Ratio of absorbed dose needed to yield a given biological effect under hypoxic conditions to the absorbed dose to yield that same effect but under aerated conditions.
Physical Half-Life	T_p or $T_{1/2}$	The mean time required for the number of radioactive nuclei in a particular energy state to decay to one half of their initial number.
Positron Emission Tomography	PET	Nuclear medicine three-dimensional imaging technique that uses annihilation photons.
Paraneoplastic Limbic Encephalitis	PLE	Paraneoplastic limbic encephalitis is a subset of a larger group of autoimmune encephalitides characterized by the predominant involvement of the limbic system. Patients present with subacute onset of confusion, behavior changes, short-term memory loss, and seizures.

	Acronym or symbol	Definition
Pretargeted Radioimmunotherapy	PRIT	Pretargeting involves the separation of the localization of tumor with an anti-cancer antibody from the subsequent delivery of the imaging or therapeutic radionuclide. This has shown improvements in both imaging and therapy by overcoming the limitations of conventional, or one-step, radioimmunodetection or radioimmunotherapy.
Planning Organ at Risk Volume	PRV	Organs at risk are normal tissues whose radiation sensitivity may significantly influence treatment planning and/or prescribed dose (eg, spinal cord). The dose-volume response of normal tissues is a complex process, which changes progressively. Used in EBRT planning.
Planning Target Volume	PTV	Planning target volume (PTV) is defined as the CTV surrounded by adequate margin to account for variation in patient position, organ motion, and other movement. Used in EBRT planning.
Point Spread Function	PSF	The point spread function describes the response of an imaging system to a point source or point object. A more general term for the PSF is a system's impulse response, the PSF being the impulse response of a focused optical system.
Prostate-Specific Membrane Antigen	PSMA	Prostate-specific membrane antigen (PSMA) is a type II membrane protein originally characterized by the murine monoclonal antibody (mAb) 7E11-C5.3 and is expressed in prostate tissue, including carcinoma.
Quantitative Analysis of Normal Tissue Effects in the Clinic	QUANTEC	The QUANTEC reports provide a summary of knowledge of normal tissue reactions following radiation exposure in terms of clinical outcomes as a function of absorbed dose and organ volume irradiated during EBRT. The effort, funded by ASTRO and AAPM, culminated in a series of articles in a special issue of the *Red Journal*.
Radiopharmaceutical Therapy	RPT	Therapy which uses pharmaceuticals that have radioactive atoms that emit ionizing radiation.
Range	–	A general term used to indicate any of several measures of the average distance traveled by charged particles of a specified type and energy. The CSDA range assumes the particle travels along a straight path, while the mean penetration range is the average distance between the origin and end of the particle trajectory.
Region at Risk	RAR	Critical tissues that if irradiated could suffer significant morbidity or functional loss, and for which the mass and absorbed dose are estimated. The RAR is categorized into the Delineable Region(s) at Risk (RAR_D), the Nondelineable Region(s) at Risk (RAR_{ND}), and the Region at Risk for Secondary Effects (RAR_{SE}). The categorization into RAR_D or RAR_{ND} is determined by the possibility to perform patient-specific estimation of the tissue mass from images, and the level of uncertainty in the absorbed dose estimate. The RAR_{SE} refers to irradiated body regions for which absorbed dose estimates may be useful for estimating the long-term risk of stochastic effects. A normal tissue included as an SR is generally also included among the RARs.
Relative Biological Effectiveness (conventional definition)	RBE	An empirically determined dimensionless quantity defined as (ICRU, 1979b): $\mathrm{RBE} \equiv \frac{D_R}{D_T}$ where the reference radiation *(R)* is a sparsely ionizing, low-LET radiation and the test radiation (*T*) is the radiation for which the RBE for effect *Y* is being determined. The effect *Y* is a quantitatively defined biological effect and the absorbed doses of the reference and test radiations to induce that effect should be delivered under identical conditions.

	Acronym or symbol	Definition
Standardized Relative Biological Effectiveness (in the EQD*X* formalism)	sRBE*X*	Within the ICRU framework of EQD*X*, the nomenclature of the standardized relative biological effectiveness sRBE*X* is: $\mathrm{sRBE}X_{\alpha/\beta} = \frac{\kappa}{(\alpha + \beta X)}$, where κ is the coefficient in the log-linear cell survival response of cells to high LET radiation ($\mathrm{SF_H} = e^{-\kappa D_H}$), and α and β are the LQ parameters for the low-LET reference radiation. *X* is the fraction size (absorbed dose) of the low-LET reference radiation fractionation schedule.
Response Evaluation Criteria in Solid Tumors	RECIST	Methodology to evaluate the activity and efficacy of new cancer therapeutics in solid tumors, using validated and consistent criteria to assess changes in tumor burden.
Region of Interest	ROI	Region drawn in a two-dimensional image defining the image coordinates over which counts (or other quantity represented by image values) are integrated.
S-coefficient (S value)	*S*	The radionuclide-specific *S*-coefficient (also called the S value), $S(r_T \leftarrow r_S, t)$, is the mean absorbed dose to target tissue r_T per decay in source tissue r_S at time *t*.
Single-Photon Emission Computed Tomography	SPECT	Nuclear medicine imaging technique that uses gamma rays and/or characteristic X-rays to produce three-dimensional images using an image reconstruction method.
Society of Nuclear Medicine and Molecular Imaging	SNMMI	A medical and scientific society that promulgates nuclear medicine.
Single-Strand Break	SSB	Single-strand break in DNA.
Source Region	SR	The organs and tissues for which the activity content as a function of time and the time-integrated activity are estimated. The SR is a subcategory of the Localization Region. The SR is categorized into the Delineable Source Region(s) ($\mathrm{SR_D}$) and the Nondelineable Source Region(s) ($\mathrm{SR_{ND}}$), depending on the possibility to perform patient-specific image-based estimation of the time-integrated activity, and the level of uncertainty in the absorbed dose estimate.
Specific Absorbed Fraction	SAF	Specific absorbed fraction (Φ) is the ratio of the absorbed fraction for a specified region and the mass of that region.
Stochastic	–	Governed by random chance.
Surviving fraction	SF	Fraction of cell population that survives exposure to a toxic agent such as ionizing radiation.
Tumor Endothelial Marker	TEM	Tumor endothelial markers (TEM) are antigens enriched in tumor versus nonmalignant endothelia.
Target Region	r_T	Region of tissue irradiated by the source region, for which the absorbed dose is calculated.
Time Integrated Activity	$\tilde{A}$	The time integral of the activity [$\int A(t)\,\mathrm{d}t$], which is the sum of all the nuclear transitions during a given time interval (ie, the period of integration).
Triple Energy Window	TEW	Widely used SPECT scatter estimation method in the clinic.
Tumor Control Probability	TCP	The tumor control probability (TCP) is a formalism derived to compare various treatment regimens of radiation therapy, defined as the probability that for a given prescribed dose of radiation, a tumor has been eradicated or controlled.
Uncertainty Tolerance Limit	*U*	Tolerance limit of combined relative uncertainty. For absorbed dose, *D*, the value of $U(D)$ is expected to be specific for each kind of RPT.
Volume of Interest	VOI	Region drawn defining the image coordinates over which counts (or other quantity represented by image values) are integrated.

List of Symbols

A	activity
A_0	administered activity
$\tilde{A}$	time-integrated activity
a	fraction of the administered activity in source region
$\tilde{a}$	time-integrated activity coefficient
D	absorbed dose
D_{10}	absorbed dose required to achieve a surviving fraction equal to 10%
D_{37}	absorbed dose required to achieve a surviving fraction equal to 37%
D_{50}	absorbed dose required to achieve a surviving fraction equal to 50%
$\dot{D}$	absorbed dose rate
C	activity concentration
d	absorbed dose coefficient
Δ	mean energy emitted per decay
E_i	initial energy of the ith radiation
ε_i	energy deposit (in a single interaction i)
ε	energy imparted
f_{r_s}	fraction of administered activity taken up by a single identified source region r_S
G	Lea-Catcheside time factor
L	the unrestricted linear energy transfer
λ	rate constant
λ_e	effective rate constant
λ_{ec}	effective clearance rate constant
λ_{eu}	effective uptake rate constant
λ_p	physical decay constant
M	mass
μ	linear attenuation coefficient; also used for DNA repair rate assuming exponential repair
ϕ	absorbed fraction
Φ	specific absorbed fraction
Q	change in rest energies of the nucleus and elementary particles involved in the interaction
R	radiant energy
r_S	source region
r_T	target region
S	mean absorbed dose per decay
T_b	biological half-time
T_{bc}	biological clearance half-time
T_{bu}	biological uptake half-time
T_e	effective half-time
T_{ec}	effective clearance half-time
T_{eu}	effective uptake half-time
T_p	physical half-life (also $T_{1/2}$)
T_μ	repair half-time
τ	dose-integration period
u	atomic mass unit
u	uncertainty
U	uncertainty tolerance limit
y	lineal energy
Y_i	yield (mean number of ith radiation emitted per nuclear transformation)
Z	charge number of an atomic nucleus
Z1	the specific energy for a single energy-deposition event

Abstract

Radiopharmaceutical therapy (RPT) is a radiation delivery modality that uses radionuclides to irradiate tissues with various forms of ionizing radiation. In most forms of RPT, the radionuclide is targeted to the diseased tissue following systemic administration of the pharmaceutical that circulates throughout the body and delivers radiation to sites of radiopharmaceutical accumulation. Three major classes of radionuclides are used in RPT including beta-particle emitters, alpha-particle emitters, and Auger-electron emitters. Recent therapeutic successes and regulatory approval of some commercial radiopharmaceuticals have spurred development of new agents. Unfortunately, comparisons of clinical results and optimization of RPT are hindered by the absence of standardized practices for prescribing, reporting, and recording of dosimetric quantities related to RPT. The present report provides information necessary to standardize techniques and procedures and to harmonize the clinical prescription, recording, and reporting of dosimetry for RPT in a manner that facilitates the use of RPT alone or in combination with other modalities. The Report's introduction briefly outlines the rationale and historical development of RPT. Then fundamental concepts of radionuclides and radiation dosimetry are reviewed. This is followed by a description of the radiobiology of RPT as compared with external photon radiation, along with bioeffect models used to calculate relative biological effectiveness (RBE) and equieffective dose for treatment planning. The cornerstone of the report comprises key concepts and terminology needed to implement dosimetry and treatment planning for RPT. These definitions are used in the recommended absorbed dose prescriptions. Essential to this end are reproducible procedures for quantifying activity in the various source regions. Accordingly, an extensive set of recommendations for activity quantification are described within, along with how to acquire and use pharmacokinetic data to obtain the time integrated activity in source regions. This is followed by methods to calculate the absorbed dose to the dosimetric treatment regions and regions at risk (RARs). The implementation of absorbed dose in RPT treatment planning, and in combination therapies, is then addressed. Subsequent sections describe recommendations for prescribing, recording, and reporting treatments. The report ends with four clinical examples of RPT for different tumor entities to illustrate the application of the recommendations. Specific recommendations in this report include the use of the quantity equieffective dose (EQD*X*) in units of gray (Gy) which accounts for the dependence of radiobiological responses on absorbed dose rate, fractionation, and linear energy transfer (LET). To avoid confusion, both absorbed dose and equieffective dose should be specified. A new quantity, the standardized relative biological effectiveness (sRBE*X*), is defined to facilitate bioeffect modeling for high LET radiations such as alpha particles and Auger electrons. In addition, new ICRU definitions of regions and geometric concepts to be used in RPT include localization regions, source regions, clinical treatment regions, dosimetric treatment regions, and RARs; reflecting a unique aspect of RPT relative to radiotherapy, these regions may be delineable or nondelineable. Finally, analogous to external beam radiation therapy, specific recommendations for ICRU reporting levels for RPT are recommended which are specific to each radiopharmaceutical. The Report should be an important and useful reference for all practitioners in RPT and should facilitate comparisons of clinical results from different centers. The focus of dosimetry-guided RPT makes explicit the potential of RPT to target and control tumors while reducing normal tissue toxicity. For all new users and interested readers, the description of the basic concepts and background of RPT should enable them to understand the techniques involved in RPT.