Reirradiation Collaborative Group (ReCOG) consensus on standards for dose evaluation and reporting in patients with multiple courses of radiation therapy: an AAPM/ACRO/ASTRO/CARO/COMP/CADRA/CPQR/ESTRO/NRG-endorsed consensus statement

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As cancer survivors live longer, technologies improve, and reirradiation (reRT) becomes more common, standardised methods for the assessment and reporting of cumulative radiation doses are needed to allow treatment optimisation and integration with other medical specialties managing these complex patients. This consensus statement, developed by an international collaboration of radiation oncologists, physicists, and other experts in the Reirradiation Collaborative Group, proposes a framework for consistent evaluation, documentation, reporting, and clinical decision making in reRT. This paper outlines practical strategies for dose accumulation from multiple courses of radiation therapy with the use of both image registration-based and point dose-based methods, accounting for uncertainties in data availability, physiological organ recovery, and anatomical changes. The emphasis of the consensus statement is on institutional workflows, improved software tools, and better capture of longitudinal patient outcomes. We also highlight the need for improved biological models, data infrastructure, and cross-specialty collaboration. Ultimately, reRT is framed as a transformative challenge for oncology, demanding interdisciplinary innovation across science, clinical care, and health systems. Widespread adoption of these recommendations could accelerate progress toward improved outcomes for patients receiving reRT worldwide.

Introduction

Advances in screening techniques, earlier cancer diagnosis, and improvements in local and systemic therapies have increased the life expectancy of cancer survivors worldwide.[1] Similarly, technical advances in radiation therapy, such as intensity modulation, image guidance, and stereotactic techniques, have revolutionised the ability to safely deliver reirradiation (reRT), even at relatively short intervals after a previous course. As a result of these advances, the likelihood that cancer survivors might receive one or more additional courses of radiation therapy, either alone or combined with other treatments for recurrence or subsequent cancer, is increasing. Although reRT is one of the most important evolving topics in radiation oncology today,[2] there is a dearth of prospective clinical evidence with which to optimise reRT outcomes. This issue is clear from the wide variation in clinical practice.[3,4] Data from a small number of prospective randomised studies,[5,6] as well as single-centre retrospective case series and consensus guidance for clinical management,[2,7] form the bulk of the evidence informing contemporary reRT practice. Individual patient treatment evaluation and reporting are highly varied. This variation affects not only clinical patient management but also cohort reporting and hampers pooling of data across multiple institutions and studies. Together, these issues confound the development of evidence-based reRT clinical practice guidelines.[8–13]

Despite efforts to standardise dose reporting for reRT,[3,7,8,14–16] no single comprehensive guideline for dose analysis and reporting in various clinical scenarios has been widely adopted. Standardisation is needed to improve the consistency of data aggregated from routine practice, which will facilitate the ability to summarise and model data linking exposure and outcome in reRT. Standardisation will support the development of guidelines to aid in the safe and effective administration of reRT.

To address this unmet need, the Reirradiation Collaborative Group (ReCOG),[17,18] an international multidisciplinary collaboration of experts, has developed this guidance document in collaboration with professional societies worldwide. This document was reviewed and approved for dissemination by the US National Cancer Institute (NCI) and has been endorsed by the European Society for Radiotherapy and Oncology (ESTRO), the American Society for Radiation Oncology (ASTRO), the American Association of Physicists in Medicine (AAPM), the American College of Radiation Oncology (ACRO), NRG Oncology (formed by the National Surgical Adjuvant Breast and Bowel Project [NSABP], Radiation Therapy Oncology Group [RTOG], and Gynecologic Oncology Group [GOG]), the Canadian Association of Radiation Oncology (CARO), the Canadian Organization of Medical Physicists (COMP), the Canadian Artificial Intelligence & Big Data in Radiotherapy Alliance (CADRA), and the Canadian Partnership for Quality Radiotherapy (CPQR).

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For more on the **Reirradiation Collaborative Group** see https://recog.care

Scope

This consensus guidance document is primarily focused on external beam radiation therapy (EBRT). Other important modalities, including brachytherapy and radiopharmaceutical therapies, and their potential combination with EBRT, are considered in the future directions section.

This work focuses on the dose analysis and reporting of reRT both in clinical practice and in the clinical research domains. The ESTRO–European Organisation for Research and Treatment of Cancer (EORTC) consensus on reirradiation defined reRT as: "a new course of radiotherapy, either to a previously irradiated volume (irrespective of concerns of toxicity) or where the cumulative dose raises concerns of toxicity."[7] Evaluation and documentation needs differ depending on the reRT indication, and whether there is a concern for toxicity (for which the expression "concern for side-effects" is used in this paper). The expected therapeutic benefit and the acceptable risk-severity threshold for adverse effects after reRT both affect the prioritisation between target coverage and organ-at-risk (OAR) sparing. This prioritisation has been considered by stratifying guidance for dosimetric evaluation into two categories based on whether there is a concern (or potential concern requiring further evaluation) for side-effects from cumulative doses or not.[7]

The 2022 ESTRO–EORTC consensus provided an essential foundation for reRT practice.[7] The current recommendations are intended to complement and operationalise these principles by providing pragmatic, workflow-oriented guidance, specifically addressing challenges related to varying data quality, workflow adaptation for real-world clinics, and documentation for future registry and outcomes research. This work builds on the established consensus by proposing pathways for harmonisation across diverse international practice environments, forming a bridge to future collaborative, global data collection and research efforts.

Analysis and reporting methods are subject to inherent limitations such as uncertainties in appropriate dose–volume metrics, normal-tissue recovery factors (TRFs), dose mapping, and the availability of complete information from previous treatments. Older radiation treatment summary files might be stored on paper, providing only basic information, or in a digital storage format that is not compatible with current technology (eg, floppy disks or non-compatible DICOM [digital imaging and communications in medicine] versions). Additionally, not all clinics have access to the same technology or clinical resources.

Based on these considerations and limitations, the strength of each recommendation has been indicated. Recommended standards focus on essential analyses or reporting elements that clinics should strive to evaluate, record, and report as a minimum standard of care. Optional standards might add valuable information in specific situations and should be considered on a per-patient basis.

This consensus statement is not intended to be prescriptive regarding how dose accumulation should be performed or to provide specific dose evaluation metrics or guide clinical decision making. Instead, these recommendations should be used in combination with existing guidance on nomenclature,[15,19,20] reRT data elements,[15] and cumulative dose evaluation methodology.[21] The aims are to help standardise cumulative dose assessment and reporting to enhance the field's ability to pool data across institutions with the use of methods that can be implemented in busy clinics, ultimately improving patient care.

Methodology

The Reirradiation Collaborative Group (ReCOG) is a multi-professional, international group supporting clinical practice, research, and policy development in reRT. ReCOG strongly supports collaboration and communication among professional societies, vendors, granting agencies, and clinical practices to develop detailed multi-institutional, multi-national evidence to address data gaps and provide guidance in reRT. The current project developed out of a pre-meeting survey and subsequent discussion regarding important dose-related reporting elements in reRT among attendees of the May 16 to 18, 2024, in-person ReCOG meeting. Varied perspectives and a desire for specific, collaboratively generated guidance led to the distillation of a task force (the manuscript authorship) from ReCOG membership to draft initial recommendations via multiple rounds of discussion. The task force members were chosen to ensure variation in geographical region and practice setting and wide-ranging expertise. Many members had extensive experience creating guidance documents and consensus statements as well as designing and managing clinical trials. The task force included experts in radiation oncology, medical physics, and radiobiology, from six different countries. The initial draft of recommendations was then circulated to the ReCOG Steering Committee and professional societies in the USA, Canada, and Europe for review and incorporation of feedback.

Terminology and background

To support a common understanding of this guidance document, we provide a brief overview of applicable terminology with background information as it relates to reRT. The terminology is presented in a logical sequence such that each concept builds upon the preceding definitions.

Absorbed dose

Absorbed dose, sometimes referred to as physical dose, is radiation dose reported in the SI unit gray (Gy), defined as 1 joule of energy absorbed in 1 kg of matter.

Equieffective dose

Two radiation treatment regimens are equieffective if they both have the same probability of achieving a specific clinical endpoint.[22] In the context of reRT, equieffective dose is often calculated more generally without pinpointing such endpoints or differentiating between them for different organs.

For megavoltage photon beam treatments, the linear quadratic model of equieffective dose for a voxel is calculated via: $EQDXGy(\alpha/\beta)=D*(d+\alpha/\beta)/(X+\alpha/\beta)$, where EQDXGy is the equivalent dose in X-Gy fractions (X is the reference fractional dose), D is the total voxel dose, assumed to be delivered in n equal fractions, and α/β is a parameter describing how the biological effect of the dose changes with $d=D/n$.[15,19,20] If the course consists of multiple non-concurrent plans/phases, the equieffective voxel dose must be calculated for each plan/phase separately and then summed to determine the total equieffective voxel dose. In case multiple plans contribute to the daily dose received by the patient, a sum of the concurrent fractions should be created and calculated separately from the remaining non-concurrent fractions of each plan.

The most common reference fractional doses used are the limit as $X \rightarrow 0$ Gy (which corresponds to the biologically effective dose) and X=2 Gy (EQD2Gy). Treatment planning systems and associated auxiliary software have varying abilities to calculate and display equieffective doses, which is important in the context of reRT.

Equieffective dose conversion

Conversion between physical and equieffective dose is done with the use of either point doses (eg, near-maximum doses) or voxel-by-voxel across an entire 3D dose distribution.

Dose mapping

Dose mapping describes the transfer of local radiation dose estimates from one imaging dataset to another based on an alignment of voxels (ie, via a registration) between the datasets.[23] The registration might be rigid (with the use of only translation and rotation) or deformable (accounting for complex, non-rigid deformations). The registration might focus on a specific region of interest if acceptable accuracy can only be achieved regionally. Multiple image registrations (and thus mapped doses) might then be created if needed, each focusing on a different region of interest.

Tissue recovery factor

TRFs are used to estimate recovery from previous radiation dose effects.[20] In the simplest form, they are scalars between 0 and 1 that estimate the fraction of the equieffective dose to an OAR from previous radiation therapy that is recovered in the interval between courses. The potential for the recovery of normal tissues depends on many factors and is not yet well understood for most tissues. Factors affecting recovery include: clinical endpoint; organ in question and its ability to regenerate or compensate local loss of function; time interval between treatment courses, irradiated volume, total dose, and fraction size; treatment technique (ie, modality, particle type or radiation quality, dose rate, and dose homogeneity); other interventions and treatments (such as surgery or systemic therapy); and other patient-related factors. Similarly, the dose scaling factor is the fractional amount the previously delivered equieffective dose is scaled by, before dose accumulation, to account for the TRF (ie, dose scaling factor=1−TRF).[20] Throughout the document, the phrase "applying the TRF" in dose accumulations means scaling with the dose scaling factor.

Dose accumulation

Dose accumulation is the process of combining dose from multiple radiation treatment plans, whether performed volumetrically or by adding doses to the same region from individual treatment plans. Dose accumulation results in a cumulative dose estimation.

Cumulative dose estimation

A cumulative dose estimation is the sum of two or more dose distributions. This estimation might be voxel-based and displayed on an imaging and contouring dataset or point dose-based and displayed in a tabular format. A voxel-based sum requires a valid image registration between the involved datasets in the region of interest. Cumulative dose might be calculated and displayed in either physical or equieffective dose. The conversion from physical to equieffective dose is done as described in the equieffective dose conversion section. In a cumulative dose estimation, it is important to state explicitly whether the previously delivered dose has been adjusted for TRFs.

Cumulative dose evaluation

Cumulative dose evaluation is the assessment of the biological and clinical effects of the cumulative dose estimation. This evaluation might be done quantitatively or qualitatively. Clinical decisions in reRT are typically guided by cumulative dose evaluations. Calculated dose metrics are used as surrogates for predicting the risk of side-effects or probability of disease control.

Cumulative dose evaluation and bioeffect uncertainty

Many sources of uncertainty might affect the estimation of biological effects from multiple courses of radiation. These sources can broadly be categorised as dosimetric uncertainty and bioeffect uncertainty.

Dosimetric uncertainty includes treatment documentation limitations, delivered dose uncertainties, and registration uncertainties.

Treatment documentation limitations, such as the lack of adequate documentation of the dose delivered in the

prior course(s) of radiation therapy, might result in best guess estimates of dose to normal tissue. The resulting uncertainty in cumulative dose evaluation might be difficult to quantify.

Delivered dose uncertainties arise from several factors, including differences between the calculated and delivered dose (for example, inter and intrafraction motion, set up and positioning errors, deformation of organs), OAR delineation uncertainties due to inconsistency in how structures are segmented (for example, spinal cord versus spinal canal) that can affect many dose–volume metrics, deposited dose calculation uncertainties, such as the lack of accounting for tissue inhomogeneities and dose calculation grid resolution, and additional spatial uncertainties due to interpolation between dose grids, as illustrated in Radiation Oncology Incident Learning System Case Study 14.[24] These uncertainties affect both the initial and subsequent courses of radiation therapy.

Registration uncertainties and their associated dose mapping uncertainties are due to organ deformation and the registration methods used (for example, rigid, deformable, region of interest based point doses). These factors can be very difficult to quantify in clinical cases.[25]

Bioeffect uncertainty refers to the additional uncertainty, even if the cumulative delivered absorbed dose were accurately known, encountered when estimating the clinical risk–benefit of a course of reRT. One source of bioeffect uncertainty arises from bioeffect model uncertainties, due to model misspecification and statistical uncertainty in model parameters, for example α/β ratios, dose–volume parameters, and TRFs. Another source of bioeffect uncertainty comes from uncertainty in patient and organ level response modifiers, such as other treatment modalities, ageing, underlying organ dysfunction, comorbidity, and comedication.

Uncertainty in estimating the anti cancer effect of reRT reduces the ability to optimise the risk and benefit estimations of reRT. Estimated cumulative doses are approximate, and clinical teams must consider the clinical significance of these uncertainties when defining treatment planning goals and dose prescriptions. Roughly speaking, the dosimetric uncertainties are tool limited and process limited, while the bioeffect uncertainties are knowledge limited. There is interplay between these categories, and the ability to quantify these uncertainties and their combined impact on risk estimates used to guide decisions by radiation oncologists in reRT will evolve as the field develops.

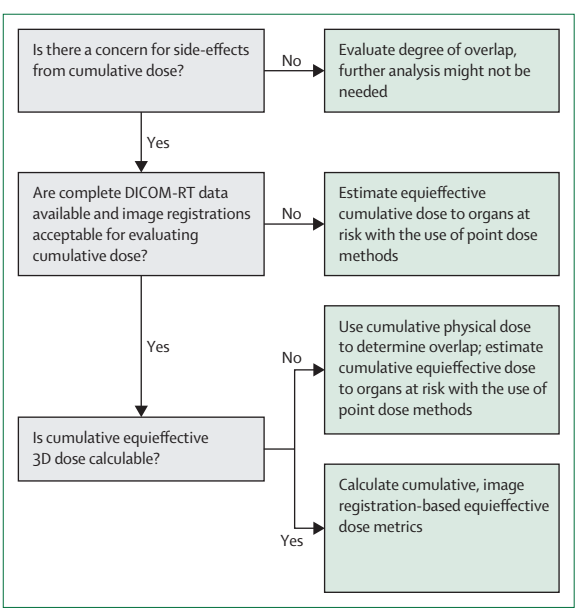

Figure 1: **Decision tree to guide reirradiation dose assessments for individual patients**
Point dose-based and image registration-based methods are described in the main text. Cumulative dose estimation might be performed with or without the use of tissue recovery factors. DICOM-RT=digital imaging and communications in medicine for radiotherapy. 3D=three dimensional.

Recommendations for reRT dose assessment in the setting of clinical decision making for individual patient care

Figure 1 depicts a decision tree for reRT dose assessment based on the concern for side-effects, data availability, image registration accuracy, and ability to calculate equieffective dose distributions. The table describes the recommended assessment standards stratified by whether there is a concern for side-effects from cumulative dose.

In the reRT workflow, the radiation oncologist integrates the relevant available clinical and dosimetric information. They determine (with support as needed from other team members) the relevant OARs in case there are concerns for potential side-effects due to cumulative doses, relative priorities of target coverage and OAR sparing, and whether enough information about previous treatments and estimated cumulative doses is available to safely re-treat. Although performing the reRT dose analysis before initiation of radiation therapy is preferred, it might not always be possible given time constraints and resource availability. This decision should be made with a focus on patient safety. The decision-making process is discussed with a patient-centred focus and within the broader clinical context by Marks and colleagues.[18] The medical physicist, radiation oncologist, or other trained team members should review the available imaging and treatment data, document estimated cumulative doses for the OARs and quantify the associated uncertainties in these estimates.

As with de novo radiation therapy, it is recommended that for reRT, each clinic have a written internal document describing its workflow, personnel roles and responsibilities, analysis and documentation requirements, institutional dose objectives and planning priorities, and the values of any biological parameters to be applied (eg, tissue-specific α/β ratios, TRFs). This

internal guideline should include when and how image registration is applied, dose accumulation methods used, how uncertainties in these processes are evaluated, and quality assurance tasks to ensure each workflow step is performed correctly. The standard application of this guideline within a clinic or institution should be prioritised whenever possible.

Dose accumulation methods for multiple radiation therapy plans

Dose accumulation methods can be stratified into two categories: image registration-based and point dose-based. General workflows are not intended to be rigidly prescriptive as to how dose accumulation should be performed. These methods will likely evolve as the associated technologies and radiobiological understanding improve. The ESTRO Physics Working Group on Reirradiation has published a consensus-based overview of radiation dose accumulation methodologies and techniques, as well as recommendations for their use.[21]

Unless the purpose of dose accumulation is only to determine potential overlap, it is recommended that cumulative doses for OARs be evaluated in equieffective dose, and (optionally) accounting for organ-specific recovery as appropriate. Conversion to equieffective dose is needed even when treatment plan prescription doses are delivered with the use of conventional fractionation (ie, 2 Gy per fraction) or with the same fractionation schedule across multiple courses, as the absorbed dose per fraction varies across organs and tissues at risk.

Regardless of the type of dose accumulation used, the cumulative dose evaluation focuses on the high-risk regions of interest. These are areas where the irradiated volumes overlap (ie, overlap regions) to produce a dose that is clinically significant compared with normal tissue tolerance.[7]

Image registration-based dose accumulation is usually the preferred method for determining cumulative dose. Although the exact strategy will be department-dependent, this method generally involves registering each previous imaging dataset to the reRT dataset, mapping dose between the imaging datasets based on the registrations, converting dose distributions to equieffective dose, applying TRFs (if used) to previously delivered doses, adding the dose distributions together, and then determining cumulative dose metrics using the cumulative dose distribution. This method requires complete DICOM-RT (digital imaging and communications in medicine for radiotherapy) records, commissioned software to convert three dimensional (3D) dose distributions to equieffective dose, and acceptable image registrations (in overlap regions) between datasets. Whether the registration is acceptable depends on the type of registration method available (rigid *vs* deformable), the degree of anatomical change between datasets, and the dose gradients in the regions of interest.[23] Importantly, in the case of interval surgery where previously irradiated tissue is no longer anatomically or biologically the same (eg, after mastectomy, flap reconstruction, or bowel interposition), standard dose constraints might not apply. These are patient-specific factors and, therefore, must be evaluated on a case-by-case basis.

	Concern for side-effects from cumulative doses	
	Yes	No
Evaluate the degree of overlap between irradiated volumes	Recommended	Recommended
Import images, plan, and dose distribution into treatment planning system*	Recommended	Optional
Register treatment planning datasets with the use of commissioned image registration workflow*	Recommended	Optional
Evaluate registration uncertainty as related to the ability to determine cumulative dose estimation*	Recommended	Optional
Evaluate contouring accuracy for OARs based on institutional standards on all applicable datasets*	Recommended	Optional
Evaluate cumulative dose with the use of at least one dose accumulation method	Recommended	Optional

Concern for side-effects means that, before cumulative dose evaluation, there is at least one organ for which the radiation oncologist believes cumulative doses could pose a clinically meaningful degree of risk. OAR=organ-at-risk. *If digital imaging and communications in medicine for radiation therapy data are unavailable, alternative workflow and dose accumulation methods can be used, as described in the main text.

Table: **Recommendations for reirradiation dose analysis for individual patient care**

Point dose-based accumulation is another method for determining cumulative dose. This method is used when DICOM-RT records are unavailable, conversion of dose distributions to equieffective dose is not possible, uncertainties in image registration are too high for estimated cumulative doses to be clinically useful, or when a conservative estimate of the cumulative dose provides sufficient information for the treating radiation oncologist to make a treatment decision. This approach will also vary across clinics and on a case-by-case basis. This method generally involves finding the near-maximum doses (eg, D0.1cc[Gy]) for each OAR in the overlap regions for each treatment plan, converting these doses to equieffective dose, applying TRFs to the previously delivered dose (if used), and then adding the equieffective doses together for each OAR. However, it can be difficult to determine the locations of overlap, for example if only paper records of previous treatment are available or if there is substantial deformation between the datasets. When identification of overlapping sub-volumes cannot be made but the treatments are known to overlap, the overall maximum dose for each OAR can be used when

Documentation standards for reRT when there is no concern for side-effects

Recommended standard

1 Previous and current radiation anatomical treatment sites (including laterality, where applicable), treatment dates, and the reason there was no concern (eg, low cumulative doses or non-overlapping)

Documentation standards for reRT when there is concern for side-effects

Recommended standards, as applicable and achievable†

1 Previous and current radiation anatomical treatment sites (including laterality, where applicable), target prescription doses, treatment techniques and modalities‡, and treatment dates
2 Any radiobiological parameters applied, if applicable (eg, α/β, radiobiological effectiveness, TRF)
3 Method(s) used to register imaging datasets
4 Method(s) used to calculate cumulative dose
5 Evaluation of uncertainties in the dose accumulation process§
6 OAR-specific, dose–volume histograms-based dose metric estimates, dose type as specified:

Previous relevant treatment(s)	Physical
Current treatment(s)	Physical
Cumulative dose	Equieffective
Cumulative dose with TRF (if applicable)	Equieffective

7 Patient informed consent for reRT risks, documentation of shared decision making, and discussion of alternative treatment strategies considered[26]

Optional standards, as applicable

1 Visual documentation of the degree of overlap between relevant treatment plans, such as with axial, coronal, and sagittal colour dose images centred on clinically relevant regions and normal tissues
2 Cumulative equieffective dose–volume histograms for relevant organs at risk

For research cohorts only

Recommended standard

1 Whenever possible, report patient-specific, per-plan, and cumulative 3D dose and/or cumulative dose–volume histogram data including uncertainties¶

Figure 2: **Recommendations for reRT dose and consent documentation***
*The term dose is used in a general manner and can refer to physical doses, near-maximum doses such as D0.1cc[Gy] or D0.03cc[Gy], mean, or volumetric dose metrics such as V20Gy[%], where Dx[Gy] is the minimum dose to the hottest sub-volume x specified in Gy, and Vx[%] is the percentage of the structure volume receiving ≥dose x.[19] †Might be limited by available technology; see figure 1 for guidance on dose accumulation strategies. ‡Treatment techniques and modalities (ie, photons, protons, and other particles, intensity-modulated radiation therapy, volumetric-modulated arc therapy, brachytherapy). §eg, uncertainties due to incomplete data, image registration, contouring, dose calculation algorithms used, or image guidance strategies employed; might be largely qualitative depending on quantity of data, analysis methods, and resources available. ¶Could be published as an appendix[27] or dataset article.[28] OAR=organ-at-risk. ReRT=reirradiation. TRF=tissue recovery factor. α/β=alpha/beta ratio. 3D=three dimensional.

there are no other options. Paradis and colleagues[2] showed how in some cases of high dose gradients or high deformation between imaging datasets, point dose-based methods can be more accurate than image registration-based methods in determining the cumulative dose to OARs.

When complete DICOM-RT files are unavailable, alternative strategies must be used to estimate OAR dose. These strategies depend on what data are available and could include reviewing printed records (eg, images of dose in the axial, coronal, and sagittal planes, dose–volume histograms, and printed OAR metrics), assuming OARs received either the prescribed dose or the (potentially estimated) maximum planned dose, or by recreating previous treatment plans on the current dataset as an estimate of the previous delivered dose.

In some instances, a combination of image registration-based and point dose-based methods will be used for a single patient—eg, if registration uncertainty is acceptable for some OARs but not for others.

Regardless of the method of dose accumulation used, the medical physicist should communicate the uncertainty in the cumulative dose estimates based on each of the steps in the process and the dose gradients in the regions of interest.

Recommendations for reRT dose documentation

Documentation recommendations after completion of the dose assessment for individual patient care are provided in figure 2. Except as noted, these recommendations apply to both clinical documentation and data obtained for research with the intention of presentation or publication (eg, clinical trials, registries, retrospective reports, and other research cohorts). The current recommendations align with those of the multiprofessional society endorsed Operational Ontology for Oncology (O3), including recommendations that focus specifically on aspects related to cumulative dose assessment in reRT.[15,16,19,20] The professional society-based O3 standard is comprehensive and in-depth, incorporating the broad range of concepts used in cancer care including chemotherapy, patient-reported outcomes, geographical factors, and more, along with radiation treatment details (eg, dose rate categorisations, particle therapy, brachytherapy, imaging, radionuclides, etc). O3 used a cohesive consensus-building methodology, providing a framework for standardising reporting and integrating details of treatments with a broad range of clinical cofactors to streamline multi-institutional learning from real-world, registry, and clinical trials data.

Given the risks and uncertainties associated with reRT, informed consent has special importance. The concept of organ tolerance, implicit in the usual clinical decision making in radiation oncology, is not well developed with reRT given uncertainties in cumulative dose estimations and understanding of resultant biological effects. Each clinic's policies on reRT should include processes for informed consent, dosimetric documentation, and enhanced peer review. Marks and colleagues discuss further clinical considerations for reRT in detail,

including the importance of goals of care, competing risks, underlying organ function, previous therapies, and concurrent medications.[18]

For research cohorts, it is recommended that patient-specific dose–volume histogram metrics calculated from 3D cumulative dose for relevant OARs are reported.[21] Ideally, these data would be recorded for each relevant treatment plan. Recording comprehensive dosimetric data on a per-plan basis would allow greater flexibility in modelling normal tissue and tumour response to reRT compared with reporting cumulative dose directly. Additionally, relevant clinical data (eg, patient age, time between treatment courses, receipt of systemic therapy or surgery, existing comorbidities, underlying OAR dysfunction, medications, etc) need to be reported in a way such that this information can be linked to dosimetric data on a per-patient or per-plan basis. In practice, this type of reporting implies the use of either appendices, referenced dataset articles, or data repositories. These recommendations are particularly important for prospective reRT trials to facilitate both evaluation of the primary and secondary trial outcomes as well as explorative analyses and secondary analyses of TRFs, dose-response, and dose–volume–response relationships.

Future directions

Areas for research opportunities include optimal integration of systemic therapies with reRT, considerations regarding OAR tolerance and optimal deployment of multimodality therapies and medical management in subsequent treatment courses, and models to help predict tumour control, normal tissue complications, and other treatment outcome parameters. Novel modalities, such as ultra-high dose rate (FLASH), microbeam radiation therapy, heavy particle therapy (including proton and carbon ion therapy), MR-guided radiation therapy, spatially fractionated techniques, and targeted radiopharmaceutical therapies are rapidly advancing the field and might further expand the therapeutic window for reRT. However, these modalities also present new challenges for accurate dose accumulation and require corresponding advancements in biological modelling. Given the increasing integration of radiopharmaceutical therapies in contemporary practice, improved dosimetry of this modality is needed, as well as the further examination of combinations of radiopharmaceutical therapies and EBRT.[29,30]

Serum-based and non-serum biomarkers are expected to have an increasingly important role in predicting both response to treatment as well as the risk of side-effects. The use of novel biomarkers, such as cytokines, circulating tumour DNA, exosomes, as well as other genomics and radiomics, promises to assist clinicians in navigating the delicate balance between response and side-effects, enabling a more robust informed consent. The array of biomarkers are yet to be standardised, but they offer the opportunity for incorporation in clinical trials, facilitating biologically adaptive radiation therapy. Key areas of scientific need to advance reRT science are summarised in the panel.

Discussion

ReRT is an increasingly adopted and important treatment approach that needs additional preclinical and clinical evidence generation.[17] ReCOG described the importance of integrating standardisations into clinical practice, delineating the connections and advantages to routine practice, registries, and clinical trials.[17] The adoption of the recommendations presented in this Policy Review will help clinical research by enabling pooled data analysis (eg, via registries or clinical trials) across multiple institutions and studies to generate evidence for improved models of tissue response to reRT, mitigation of radiation complications, and improved understanding of how radiation therapy effects accumulate over time. Establishing large, curated datasets with granular exposure (dosimetry) data and patient-level co-factors linked with graded normal-tissue adverse-event endpoints will allow refinement of bioeffect models. Critical testing of model specification and improved estimates of model parameters will allow better estimates of the risk of adverse events after a given course of reRT and will provide a base for prescription and optimisation of reRT plans. Although standardised retrospective registry data remain scarce, the guidance provided herein is an enabling prerequisite: wide adoption will allow pooling of properly harmonised data. International partners, especially in under-represented regions, can leverage this framework, ensuring future registry and network efforts are built on shared principles for maximum clinical and scientific yield.

ReRT represents not just a technical challenge, but a transformative frontier for modern cancer medicine and will require new science, new tools, and new models of care. The implications are broad—reRT will give rise to a host of clinical and biological questions, and with them, a spectrum of discovery opportunities across medical disciplines. To meet this moment, collaboration must extend beyond radiation oncology. Patients might present with novel organ injury patterns, new forms of late complications, and complex survivorship trajectories. Many patients will live long enough to achieve long-term disease control if their side-effects can be effectively managed, making longitudinal, multispecialty care key to survival. Innovation in prevention, monitoring, and mitigation strategies must move in lockstep with therapeutic advances.

The scope of the challenge is large. Radiation therapy is used in more than half of all cancer cases, and if even 10% of those patients ultimately require reRT, the global burden will be substantial. Meeting this challenge will require not only scientific progress but also infrastructure development and workforce education, clinical

Panel: **Areas in need of resources and research to advance reirradiation (reRT) science—needs and benefits**

Software tools

The introduction of software tools in commercial systems to visualise and evaluate cumulative dose estimations in biologically equieffective doses has been slow to emerge.[31] This lack of technological support undermines reproducibility, standardisation, and the availability of quantitative data in clinical practice, clinical trials, and data registries.

Biological models

The development of empirical biological dose–response and tissue recovery models, including in association with systemic therapies, would add value across many aspects of medicine. Although trials in humans to test tissue recovery factors and risk thresholds present challenges for maintaining equipoise, experiments examining time, volume, and dose in a granular fashion are needed. These studies should be linked to pharmaceutical and mitigation research to treat and prevent side-effects from reRT, which in turn could be useful for de novo radiation therapy and other radiation event scenarios.

Normal tissue radiation injury

A better understanding of normal tissue radiation injury, including preclinical, translational, and clinical research on tissue injury, regeneration, and mitigation (eg, regenerative medicine and stem cell therapies) could lead to safer reRT. Additionally, as reRT is increasingly combined with systemic agents, the effect of these therapies on normal tissue tolerance and the appropriate timing of irradiation must be examined.

Patient molecular and imaging data before, during, and after treatment

More data are needed across cellular, tissue, organ, and host scales to better resolve optimal care both in de novo treatment and reRT. This type of data collection is the focus of the NCI ROBIN network and increasingly many other research projects. More focus on this will be needed to both inform reRT and address side-effects after any radiation. This includes the development of biomarkers (serum and non-serum) to broadly provide information regarding radiation biology. Functional imaging assessment of both neoplasia and healthy tissues, including via artificial intelligence methods, might enable patient-specific determination of optimal reRT doses in the future. Dosiomics, the extraction of quantitative features from dose distributions with the use of data mining and machine learning techniques, is an emerging field that might enhance cumulative dose analysis and risk modelling in reRT, especially when combined with imaging features at the time of reRT.

Data capture

Critical outcomes of side-effects and survival are not routinely captured in extractable formats in electronic records for integration with treatment data when patients do not return to the treatment centre for follow-up. Additional important data include patient-reported outcome measures, quality of life, decision regret, and recordings of shared decision making. These missing or incomplete data undermine the ability to develop models of outcomes from real-world data. Means to improve capture of endpoint data are needed.

Data sharing infrastructure

Sharing of data will be key for mathematical bioeffect modelling as well as other data science approaches (eg, digital twins and artificial intelligence). Standardisation will aid in data sharing and optimal use of automated data processing (eg, autosegmentation) and might reduce both effort and cost for analysis. Examples of such standardisations are the Operational Ontology for Oncology (O3) and TG-263 nomenclature.[15,16,19,20] The QUANTEC (Quantitative Analysis of Normal Tissue Effects in the Clinic), HyTEC ("Hy"-dose per fraction, Hypofractionated Treatment Effects in the Clinic), and PENTEC (Pediatric Normal Tissue Effects in the Clinic) efforts all provided reporting standards, many of which are relevant in the reRT setting.[32–36] Reirradiation Collaborative Group also previously highlighted pathways for incorporating registries to improve hypothesis generation and study design and validation.[17] Alignment of data capture and sharing to the professional society-based O3 standard provides a framework for routine practice integration of reRT with novel modalities of irradiation, such as ultra-high dose rate radiation therapy and microbeam radiation therapy, with other clinical cofactors such as chemotherapy, biomarkers, medications, etc.

Workforce development

Development of expertise in the areas described might help with optimal reRT hypothesis testing. The current institutional workforces might not be sufficient to apply for standard training grants, so virtual, national or international approaches might be needed in the reRT space.

For more on **NCI ROBIN network** see https://rrp.cancer.gov/programsResources/robin.htm

innovation, and new models of access to reduce burden on both patients and health systems. Early alignment with specialists across the medical continuum will be essential. The complexity, promise, and necessity of reRT call for a coordinated, forward-thinking strategy that integrates innovation from the beginning and spans disciplines, geographies, and care systems.

The procedures recommended herein can be labour-intensive, and it might not be realistic for them to be widely adopted in a short timeframe. Accordingly, these initiatives need to be prioritised with a focus on simplified, practical implementation of methods that can be adapted as the field evolves. Creation of software tools to help perform these tasks, automating where possible, is urgently needed.[31] Importantly, standardised workflows can ultimately reduce the burden on clinics by streamlining processes and minimising the need for ad-hoc management of complex cases.

The complexity of reRT workflows introduces resource implications for clinical practice globally. The

standardised steps described in this consensus require substantial time, specialised expertise, and close multidisciplinary coordination. Many reRT cases are inherently labour-intensive, often requiring advanced software tools, and their management can substantially affect departmental workload and operational costs. These challenges are not unique to high-resource centres; they are felt in community and academic hospitals worldwide, highlighting the need for guidance that is scalable across diverse settings. ReCOG is actively working on additional guidance documents illustrating practical implementation of the current recommendations and is collaborating with vendor partners to help ensure effective software tools are widely available.

As reRT becomes increasingly common, there is a pressing need for institutions to engage in proactive resource planning and re-assess health economic strategies. Adoption of streamlined, standardised processes and ongoing investment in automation and decision support software will be pivotal in maintaining quality and sustainability as practice patterns evolve. Recognising that care models must adapt to keep pace with these demands, these recommendations are intentionally designed to be flexible, enabling implementation both in settings with advanced technological infrastructure and in clinics with fewer resources.

Wide adoption of the standardisations and reporting guidelines recommended by ReCOG would facilitate a future ReTEC (Reirradiation Treatment Effects in the Clinic) effort, synthesising published data on dose, volume, and time-to-reRT similar to: the Quantitative Analysis of Normal Tissue Effects in the Clinic (QUANTEC); "Hy"-dose per fraction, Hypofractionated Treatment Effects in the Clinic (HyTEC); and Pediatric Normal Tissue Effects in the Clinic (PENTEC) projects.[32–36] This effort would provide useful evidence-based guidelines for reRT to clinicians and would spur further research, including guidance for future clinical trial design.

Developing improved methods to perform dose accumulation for two or more reRT courses will require creative thinking and collaboration. O3, the multi-professional society-based ontology, provides a practice-based framework assuring that precursor concepts, including plans and courses, are handled consistently and cohesively integrate reRT with other treatment factors.[15,16] Broad multi-professional society engagement in developing standardisations and infrastructure supporting reRT and standard practice is an example of the type of creative approach needed.

Conclusions

ReRT is a complex form of radiation therapy that has not yet been addressed systematically in a scientific, exploratory way. International collaborative groups are working to provide guidance across the spectrum of clinical disease entities. We need to increase our fundamental knowledge of the relationship between exposure and risk; how the effects of dose change over time across tissues, variable tumour micro-environments, and treatment combinations; how tissue recovers from previous radiation; and how to best address clinical situations in which dose likely needs to exceed classic tolerance limits. Data collected need to include all treatments received by the patient, with chronological rigor, including non-oncological and supportive medications, ideally including tissue data (omics) if available for tumour and normal tissues, and incorporating granular side-effect data. Standardised dose assessment and reporting is paramount to achieving these goals. This is a problem that will be best addressed by integration of innovation from the start and with global collaboration across specialities, from physicians, to physicists, data scientists, biologists, pharmaceutical and policy experts, and educators. This approach will support a fundamental shift in radiation therapy utilisation from a one-time only modality to a repeat treatment option that will help many more patients with cancer achieve palliation or long-term cancer control.

Search strategy and selection criteria

Comprehensive searches of PubMed were done on Jan 1, 2025, with the search strategy: (reirradiation OR re-irradiation [MeSH Major Topic]) for papers published from Jan 1, 2015, to Dec 31, 2024. All languages were included. After this date, published literature was reviewed periodically as the current manuscript was developed with new relevant papers being included as needed up until June 2025. Inclusion was based on discussion with the authorship team. Citations from the included publications were reviewed for any additional relevant references. The expertise of the authorship team was also leveraged as many had participated in previous relevant efforts.

Contributors

KCP, ALA, SMB, NC, DG, DEH, LH, LBM, CM, KES, CBS, YX, EY, PP, and JCB: conceptualisation. KCP and CM: funding acquisition. KCP, ALA, NC, ELC, LAD, DG, DEH, LH, LBM, CM, KES, CBS, YX, EY, PP, and JCB: methodology. KCP, LBM, and JCB: project administration. LBM and JCB: supervision. KCP, LBM, and JCB: visualisation. KCP, ALA, SMB, NC, DG, DEH, LH, LBM, CM, KES, CBS, YX, EY, PP, and JCB: writing of the original draft. KCP, ALA, NC, ELC, LAD, DG, DEH, LH, AJ, LBM, CM, KES, CBS, YX, EY, PP, and JCB: review and editing.

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