Radiotherapy and Oncology xxx (xxxx) xxx

Contents lists available at ScienceDirect

Radiotherapy and Oncology

journal homepage: www.thegreenjournal.com

Review Article

Essential requirements for reporting radiation therapy in breast cancer clinical trials: An international multi-disciplinary consensus endorsed by the European Society for Radiotherapy and Oncology (ESTRO)

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ARTICLE INFO

Keywords:
Breast cancer
Radiation therapy
Systemic therapy
Quality assurance in radiotherapy
Clinical trial

ABSTRACT

The European Society for Radiotherapy and Oncology (ESTRO) has advocated the establishment of guidelines to optimise precision radiotherapy (RT) in conjunction with contemporary therapeutics for cancer care. Quality assurance in RT (QART) plays a pivotal role in influencing treatment outcomes. Clinical trials incorporating QART protocols have demonstrated improved survival rates with minimal associated toxicity. Nonetheless, in routine clinical practice, there can be variability in the indications for RT, dosage, fractionation, and treatment planning, leading to uncertainty. In pivotal trials reporting outcomes of systemic therapy for breast cancer, there

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https://doi.org/10.1016/j.radonc.2023.110060
Received 7 October 2023; Received in revised form 12 December 2023; Accepted 14 December 2023
Available online 19 December 2023

is limited information available regarding RT, and the potential interaction between modern systemic therapy and RT remains largely uncharted. This article is grounded in a consensus recommendation endorsed by ESTRO, formulated by international breast cancer experts. The consensus was reached through a modified Delphi process and was presented at an international meeting convened in Florence, Italy, in June 2023.

These recommendations are regarded as both optimal and essential standards, with the latter aiming to define the minimum requirements. A template for a case report form (CRF) has been devised, which can be utilised by all clinical breast cancer trials involving RT. Optimal requirements include adherence to predefined RT planning protocols and centralised QART. Essential requirements aim to reduce variations and deviations from the guidelines in RT, even when RT is not the primary focus of the trial. These recommendations underscore the significance of implementing these practices in both clinical trials and daily clinical routines to generate high-quality data.

Introduction

The European Society for Radiotherapy and Oncology (ESTRO) eagerly looks forward to further advancements in each discipline and calls for a concerted effort to provide guidance and establish guidelines for clinical practice [1]. Valentini et al. [2], acknowledged the challenges of radiation therapy (RT) in modern times and defined the ESTRO vision as the optimization of precision RT, alongside novel therapeutics and innovations in cancer care. This vision underscores the society's commitment to promoting tumour control and enhancing patient care.

Quality assurance in RT (QART) represents an essential component of daily practice and clinical trials, consistently proving paramount for treatment outcomes [3,4]. QART has been advocated for decades by various professional societies and national/international organizations, including ESTRO [5–7]. Its importance extends beyond RT-related toxicity, impacting disease outcomes, including breast cancer [8,9].

The close proximity of the breast/chest wall and regional nodes, especially the internal mammary nodes, to critical organs at risk (OARs) like the heart and lungs, requires meticulous planning and precise RT delivery. In certain breast RT scenarios, the therapeutic margin is narrow, making errors in planning or delivery consequential and potentially negating the benefits of RT [10]. Trials that incorporated protocols for QART were trailblazers, showcasing improvements in breast cancer survival with minimal long-term toxicity [11,12]. The Early Breast Cancer Trialists Collaborative Group (EBCTCG) conducted a meticulous evaluation of trials involving regional RT, focusing on RT techniques—an issue of controversy among professionals due to concerns about potential toxicity [10,13]. The EBCTCG reported that regional node RT significantly reduced breast cancer mortality and all-cause mortality in trials utilizing modern RT techniques (after the 1980 s), but not in older trials [13]. Over the years, the culture of quality assurance for breast cancer RT has evolved, with leading groups providing additional insights into the relationship between dose/fractionation, dose/volume, dose inhomogeneity, and planning techniques concerning outcomes, including acute and late toxicity [14–16].

Indications for RT, as well as dose and fractionation, radiation planning, and delivery, vary among centres for both metastatic and non-metastatic breast cancer. Pivotal prospective randomised breast cancer trials evaluating postoperative systemic and locoregional therapies have contributed to continued uncertainty in current practice. This is partly due to issues such as lack of adherence to the RT protocol, the absence of a dedicated RT trial methods paragraph, or the uncontrolled allowance of heterogeneous RT schemes and indications [17–22]. This situation may lead to unnecessary interruptions in systemic treatment as a precautionary measure to avoid toxicity. Alternatively, when given concomitantly, it could result in increased or unaccounted for toxicity. Furthermore, the potential benefit of combining these modalities remains undetermined [23]. Unfortunately, trials involving RT often do not report quality assurance procedures, leading to uncertainty in the implementation of the trial's procedures or indications for RT [7].

The ESTRO breast course faculty, in collaboration with international leaders in breast cancer care, worked together to establish an international modified Delphi consensus recommendation for combining new systemic therapies with RT for breast cancer in both metastatic and non-metastatic settings [24]. Part of our task force's mission was to identify knowledge gaps in the combination of breast RT with modern systemic therapies routinely employed in breast cancer treatment [21,22]. This paper summarises the work of the task force on RT quality assurance. It provides requirements for collecting and reporting essential RT data, applicable to all clinical studies in breast cancer, including those in medical oncology, locoregional surgical and radiation oncology, prospective as well as retrospective studies.

Materials and methods

The task forces comprise a multidisciplinary group of experts in breast cancer, including clinical and preclinical scientists (**see** appendix 1). Time frame of this project was March 2022 – August 2023. This team includes individuals actively involved in pivotal prospective clinical trials of systemic therapies, consultants specializing in early-phase trials of targeted therapy, and professionals with expertise in clinical trials in radiation oncology, QART, and the development of clinical practice guidelines. The collaboration unfolded through teleconferences coordinated by consensus leaders and via email correspondence. Taskforce 4, responsible for QART and the development of clinical practice guidelines, submitted their recommendations for consideration by the entire group. Ultimately, consensus was achieved through a modified Delphi voting process and presented at an international meeting in Florence, Italy, in June 2023 [24]. A survey using Google Form collected statements anonymously, employing a 5-point Likert scale for participant agreement. Consensus was determined by a $\geq$ 75 % agreement threshold, with categories ranging from unanimous to strong support. Statements with initial consensus were excluded, and the remaining items underwent a second round of voting. Unresolved statements were excluded, and the final consensus was based on statements with consistent support across the survey. These recommendations are deemed as both "best requirements" and "essential requirements," with the latter aimed at defining minimum standards. Our recommendations are adaptable for application in other cancer types where radiation therapy is integral to the treatment modality.

Results

Best requirements

For optimal patient care and outcomes, we strongly recommend that trial sites strictly adhere to a predefined RT-planning pack for both personnel and RT delivery [25–27]. This predetermined RT-planning pack should include specifications for RT indications, dose/fractionation, guidelines for delineating targets and organs at risk (OARs), calculation algorithms used for treatment planning, defined dosimetry objectives, planning methodologies, and detailed instructions on data collection. Before initiating the trial, it is crucial to ensure that site personnel are adequately trained and credentialed in accordance with the trial's procedures and RT protocol. All clinical studies should adhere to Good Clinical Practice (GCP) recommendations, and all personnel

Table 1
Impact of QART protocol on trial outcomes in selected locoregional trials.

Trial	Trial's question	RT details	Impact
RT/QART protocol unspecified			
ACOSOG Z0011 [41,42]	cT1-2 N0, 1–2 positive nodes, SLNB or ALND	RT was defined in the trial protocol. Noncompliance with trial recommendation: 51 % "high tangents", 19 % third regional nodal irradiation field.	The impact of RT on disease outcomes is unknown.
Sinodar One [43]	cT1-2 N0, 1–2 positive nodes, SLNB or ALND	RT was not defined and not reported.	The impact of RT on disease outcomes is unknown.
Sound trial [44]	cT1N0 Omission of SLNB	RT was not defined and not reported.	The impact of RT on disease outcomes is unknown. Early publication by the trial PI suggest that incidental dose of the tangential fields are important regional control
NSABP B-40 NSABP B-41 [30]	Stage T1c-3, and cN0, cN1, or cN2a. Sequencing of different systemic therapies and its effect on pCR	No RT protocol and quality assurance Regional node RT allowed at physician's discretion	The true impact of RT on disease outcomes is unknown. Disparity of care of Hispanic population was suggested.
RT protocol package and centralised QART			
EORTC 22922/ 10925 [8,45,46]	Stage I-III, the role of IMN-MS irradiation	RT protocol was only for IMN-MS RT, variation in RT to primary, including boost, chest wall, breast. RT was subjected to central quality assurance.	Central quality assurance for data collection and RT allowed for subsequent unplanned analysis. Unplanned analyses and limited event rates restrict in providing firm recommendations.
FAST-Forward [17]	pT1–3, pN0 [a] Two 5 fractions regimens were compared to standard of care	RT protocol and additional RT planning pack was predefined. RT was subjected to central quality assurance. Tumour bed boost was at the discretion of the treating physician, two dose/fractionation schemes were allowed.	Trial tested whole breast RT effectiveness.

Abbreviations. QART, quality assurance in radiotherapy; pCR, pathological complete response; RT, radiation therapy; IMN-MS, internal mammary nodes and medial supraclavicular nodes; ALND, axillary lymph node dissection; SLNB, sentinel lymph node biopsy.
[a] pN1 was allowed in FAST-Forward nodal trial.

involved should be certified in GCP. Central quality assurance is essential, encompassing the evaluation of machine output, institutional credentials, and quality control procedures [6,28]. Monitoring methods may include on-site dosimetry reviews, remote audit tools, and should incorporate a benchmark case, a dummy run before recruitment, and the planning of the first trial case [29]. Trials must include reporting on quality assurance protocols, audits, and any deviations [7].

Essential requirements

This section is tailored to trials where RT is administered as a standard of care without being the primary focus of the trial, and there is no established central quality assurance process. The recommended essential requirements may not necessarily represent the best possible practice but are intended to prevent instances of RT being administered at the discretion of the physician without reporting crucial information [30]. Assuming that physician preferences are based on institutional or national guidelines, we recommend establishing these guidelines beforehand, and any deviations from them should be reported. The essential requirements can serve as a guide for studies aiming to evaluate RT in centres already implementing quality assurance procedures and capable of documenting and reporting the outcomes of these procedures. As an illustration, the Dutch RAPCHEM study was designed in a cost-effective manner following a national RT approach [31]. In the Netherlands, national quality assurance procedures and audits are mandatory. This study provided essential insights into deviations from guidelines and their impact on disease outcomes [31].

The following steps are outlined to assist clinicians and researchers in establishing a RT planning procedure conducive to retrieving valuable data. This protocol can be integrated as a departmental procedure or implemented in a clinical trial with the aim of fulfilling essential, albeit minimal, requirements for RT data collection and reporting. When designing clinical trials, it is recommended to contemplate the inclusion of essential RT requirements in the main trial protocol. However, it is also wise to develop a separate RT planning pack, functioning much like a flexible Standard Operating Procedure (SOP). This RT planning pack can be regularly updated with version control to accommodate necessary wording adjustments and incorporate valuable additions as needed. By adopting this approach, trial designers can streamline the process of implementing RT-related changes, thereby avoiding potential delays and complexities associated with formal protocol amendments through ethics committees. It is suggested that trial documentation clearly distinguishes between the 'protocol' as the primary trial protocol and the 'RT planning pack' as its supporting documentation.

Discussion

Step 1: Establish guidelines for target volume delineation

It is imperative to delineate target volumes and OARs according to predefined guidelines, emphasizing volume-based RT planning for all RT treatments. OAR delineation may exhibit variations across clinical trials, potentially influencing toxicity outcomes significantly [32]. Several delineation protocols for different indications are accessible online, and it is recommended to adopt a delineation guideline endorsed by well-established international societies [33–36]. Adhering to these guidelines can mitigate dose variations to specific OARs [37]. Target volume delineation not only facilitates the analysis of incidental doses, such as those to the lower axillary levels resulting from breast/chest wall RT, but also enables the examination of their potential contribution to disease control [38].

Step 2: Engage in target volume delineation practice

Consistent and accurate delineation of target volumes necessitates regular practice and peer review to minimize inter-observer variability [35]. Accessible online or on-site courses can effectively mitigate this variability [39]. For ESTRO members, an educational video on breast and nodal target volume delineation is available via the ESTRO library (video credits: Birgitte Offersen and Peter Schultz, Denmark) [https://www.estro.org/library/item/9879/estro-consensus-for-target-volume-delineation–breast-and-regional-nodes–guided-tour]. A profound understanding of breast cancer anatomy, dissemination, delineation practice, and peer review is crucial for reducing variation, which can significantly impact disease outcomes and toxicity [35]. To ensure trial consistency, the protocol may incorporate a delineation review of three cases before enrolling the first patient to assess the quality of target volume delineation.

Table 2
Minimal RT details requirements for a trial case report form (CRF) for locoregional RT (adapted from [24]).

Locoregional RT			
Date of RT start	DD/MM/YYY		
Date of last RT fraction	DD/MM/YYY		
Laterality breast/chest wall RT treated			
Left	No		Yes
Right	No		Yes
Bilateral	No		Yes
Breast Reconstruction present prior to RT			
Was breast reconstruction present prior to RT?	No		Yes
if Yes, implant-based reconstruction	No		Yes
if Yes, autologous tissue reconstruction	No		Yes
if Yes, tissue expander	No		Yes
Prescribed Dose and Fractionation			
Target volume	Total prescribed dose (Gy)		Number of fractions
Breast/chest wall			
Tumour bed boost/partial breast			
Axilla level 1			
Axilla level 2			
Axilla interpectoral nodes (Rotter)			
Axilla level 3			
Axilla level 4			
Internal mammary nodes (parasternal)			
Use of bolus			
Did you use the bolus?	No		Yes
if Yes, daily	No		Yes
if Yes, alternating days	No		Yes
if Yes, until skin reaction (specify number of fractions with bolus)	No		Yes
if Yes, specify bolus thickness (mm)	No		Yes
RT course completion			
Did the patient complete RT course?	No		Yes
if no, total dose received (Gy)			
if no, specify the reason (comment):			
RT given during systemic therapy [a,b]			
Was RT given during systemic therapy?	No		Yes
if Yes, CDK4/6 inhibitors (specify)	No		Yes
if Yes, trastuzumab	No		Yes
if Yes, pertuzumab	No		Yes
if Yes, PARP inhibitors	No		Yes
if Yes, ADC TDM1	No		Yes
if Yes, other ADC (specify)	No		Yes
if Yes, capecitabine	No		Yes
if Yes, immunotherapy (specify)	No		Yes
if Yes, other (specify)	No		Yes
Timing [b]			
Systemic treatment interrupted $\leq$ 1 week before RT	No		Yes
Systemic treatment (re)started $\leq$ 1 week after last RT fraction	No		Yes
Systemic therapy interrupted 5-half lives of the drug before RT	No		Yes
Systemic therapy continued during RT	No		Yes
Toxicity			
Did any adverse events occur after the last visit	No		Yes
If yes, was the adverse event assumed to be associated with RT?	No		Yes
If yes, date of adverse event started	DD/MM/YYY		
Did the adverse event resolved?	No		Yes
If yes, date of adverse event resolved	DD/MM/YYYY		
If yes, specify type of adverse event (e.g., dermatitis, pneumonitis)			
Maximal grade of toxicity CTCAE v.05			
Has the patients had any other RT related conditions events since the last visit?	No	Yes	Not assessed
if Yes, please complete the following section *			
* CTCAE v.5.0 grade			
Describe 0 1 2 3 4 5			Present, not graded
Other, specify			
Other, specify			
Other, specify			
Other, specify			
Planning parameters [c]			
Lung			
Mean lung dose (both lungs) (Gy)			
V_{5Gy} – (both lungs) (%)			
Mean lung dose (ipsilateral lung) (Gy)			
V_{5Gy} – (ipsilateral lung) (%)			
V_{20Gy} – (ipsilateral lung) (%)			
Heart			
Mean heart dose (Gy)			
Heart D_{1cc} (Gy)			
Plan total			
D_{max} (Gy)			
$V_{90\%}$ of PTV breast/chest wall (%)			
$V_{95\%}$ of PTV breast/chest wall (%)			
$V_{105\%}$ of PTV breast/chest wall (cc)			
$V_{105\%}$ of body (cc)			
$V_{90\%}$ of PTV lymph node regions (combined, %)			
$V_{95\%}$ of PTV lymph node regions (combined, %)			

Abbreviations. RT, radiation therapy; Gy, Gray; cc, cubic centimetre; CDK4/6, cyclin-dependent kinase 4 and 6; PARP, poly (ADP-ribose) polymerase; ADC, antibody-drug conjugates; T-DM1, ado-trastuzumab emtansine; CTCAE, Common Terminology Criteria for Adverse Events; PTV, planning target volume.

[a] Endocrine therapies excluded.

[b] More than one option possible.

[c] All doses should be reported as physical doses.

Step 3: Establish indications for RT, dose/fractionation, templates, planning objectives for target volumes, and constraints for organs at risk and techniques

The protocol should precisely define the indications for RT. In instances where a trial protocol lacks specific indications, it is crucial to adhere to national or institutional guidelines. For example, physician preferences regarding a tumour bed boost or nodal boost can introduce additional dose and potential toxicity, potentially hindering a comprehensive evaluation of treatment benefits (Table 1) [8,17,30,40–46]. Therefore, it is imperative to document which guidelines are being followed. Similarly, define the dose and fractionation to be employed, preferably in alignment with international guidelines [47]. For instance, moderate hypofractionation for breast cancer can be administered in 16 or 15 fractions, and the potential variation in toxicity between these regimens may go unnoticed if not predefined [18].

The inclusion of a boost dose may lead to significant differences in the risk of fibrosis [40] or potentially elevate complication rates, especially in cases of breast reconstruction [48]. The use of tissue bolus, particularly in postmastectomy RT, is associated with a higher rate and grade of toxicity and may result in treatment interruptions [49,50]. All these factors can introduce variations in outcomes that might influence the reported results of the study. If reaching an agreement between centres is unfeasible or entails substantial additional costs, an alternative approach is for each site to adhere to their respective written institutional or national guidelines regarding indications for RT and fractionation. This agreement should be documented and established in advance. This approach has been employed in a few prospective randomized clinical trials, allowing researchers to conduct subsequent analyses on the trial results [8,46,51].

An international nomenclature for naming targets and OARs has been proposed to improve interinstitutional data sharing and enhance the functionality of clinical trial repositories, integrated multi-institutional collaborative databases, and quality control centres [52]. Therefore, in routine practice and when reporting RT details in trials, it is advisable to consistently utilize a standardized template for target volumes and OARs, particularly within a single institute. This practice ensures the consistent delineation of relevant volumes for all patients

Table 3
Minimal RT details requirements for a trial case report form (CRF) for distant metastasis RT (adapted from [24]).

Distant metastasis RT								
Date of RT start	DD/MM/YYY							
Date of last RT fraction	DD/MM/YYY							
Prescribed Dose and Fractionation								
Target volume	Total prescribed dose (Gy)	Number of fractions						
Bone (non-spine). Specify:								
Bone (spine). Specify:								
Lung								
Liver								
Intrabdominal (non-liver)								
Brain								
CNS (Spinal Cord)								
Other (specify)								
Other (specify)								
RT course completion								
Did the patient complete RT course?	No	Yes						
if no, total dose received (Gy)								
if no, specify the reason (comment):								
RT given during systemic therapy [a,b]								
Was RT given during systemic therapy?	No	Yes						
if Yes, CDK4/6 inhibitors (specify)	No	Yes						
if Yes, trastuzumab	No	Yes						
if Yes, pertuzumab	No	Yes						
if Yes, PARP inhibitors	No	Yes						
if Yes, ADC TDM1	No	Yes						
if Yes, other ADC (specify)	No	Yes						
if Yes, capecitabine	No	Yes						
if Yes, immunotherapy (specify)	No	Yes						
if Yes, other (specify)	No	Yes						
Was RT given during systemic therapy?	No	Yes						
if Yes, CDK4/6 inhibitors (specify)	No	Yes						
Timing [b]								
Systemic treatment interrupted $\leq$ 1 week before RT	No	Yes						
Systemic treatment (re)started $\leq$ 1 week after last RT fraction	No	Yes						
Systemic therapy interrupted 5-half lives of the drug before RT	No	Yes						
Systemic therapy continued during RT	No	Yes						
Toxicity								
Did any adverse events occur after the last visit	No	Yes						
If yes, was the adverse event assumed to be associated with RT?	No	Yes						
If yes, date of adverse event started	DD/MM/YYY							
Did the adverse event resolved?	No	Yes						
If yes, date of adverse event resolved	DD/MM/YYY							
If yes, specify type of adverse event (e.g., dermatitis, pneumonitis)								
Maximal grade of toxicity CTCAE v.05								
Has the patients had any other RT related conditions events since the last visit?	No	Yes	Not assessed					
if Yes, please complete the following section *								
* CTCAE v.5.0 grade								
	Describe	0	1	2	3	4	5	Present, not graded
Other, specify								
Other, specify								
Other, specify								
Other, specify								
Other, specify								

Abbreviations. RT, radiation therapy; Gy, Gray; cc, cubic centimetre; CDK4/6, cyclin-dependent kinase 4 and 6; PARP, poly (ADP-ribose) polymerase; ADC, antibody-drug conjugates; T-DM1, ado-trastuzumab emtansine; CTCAE, Common Terminology Criteria for Adverse Events.
[a] Endocrine therapies excluded.
[b] More than one option possible.

and enhances pattern recognition through the consistent use of colours. Moreover, collecting information from treatment plans regarding volumes, dose homogeneities, and doses becomes more straightforward when all naming conventions are uniform. Adhering to the same nomenclature, colour codes, and delineation guidelines will also facilitate the implementation of automated treatment plan quality control processes.

The recommended planning objectives for various RT regimens should be defined, taking into account the site of RT and the fractionation used, and they should be consistent across multiple centres. Most RT facilities rely on planning objectives for RT planning and assessment. It is advisable that these planning objectives align with international recommendations and mirror those used in large prospective trials that have published outcomes related to specific dose and fractionation schemes. The choice of RT techniques should align with the established planning objectives and should be based on the centre's capabilities and expertise. However, it's essential to recognize that variations in RT techniques, even for curative breast RT, can pose challenges to centralized quality assurance, as dose distribution may impact toxicity and treatment outcomes [8,53–55].

Techniques to improve RT delivery, such as deep inspiration breath-hold and image-guided RT, should be employed and thoroughly

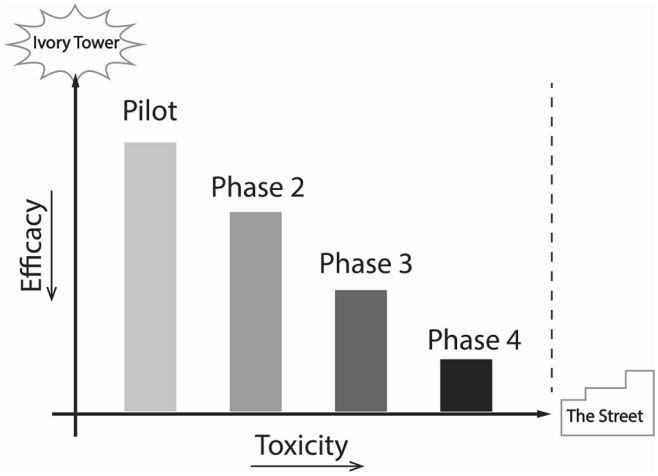

Fig. 1. This illustration depicts that early-phase trials are often not directly applicable to the general population. As a result, in routine clinical practice, efficacy may be compromised while toxicity increases. An example of this scenario is trials designed to assess a new systemic therapy for breast cancer, excluding RT in the trial design. In daily clinical practice, RT may need to be administered concurrently, but the lack of reporting on RT in the trial design can create challenges (Original illustration by Professor David Brizel, Duke, North Carolina, USA, 2016).

documented when deemed necessary. The evaluation and execution of treatment plans should adhere to institutional quality assurance protocols and meet national and international standards. When primary results of clinical trials are initially published, the trial protocol is typically provided in supplementary files. This provision offers convenient access to detailed RT planning and constraints, as seen in initiatives like FAST-Forward [17], DBCG HYPO [14], and DBCG PBI [56]. Best practice trials to give an adequate example for both essential and best RT requirements are represented by the RT-package of the FAST-Forward trial [17] and the QART of the EORTC 22922/10925 study [8,45,46] (Table 1).

The harmonization of RT protocols can be accomplished without compromising the ability to tailor therapy to individual patient needs. It can serve as a valuable tool for facilitating the analysis of quality data and achieving high-quality treatment outcomes.

Step 4: Recording and reporting

In addition to offering comprehensive and accurate guidelines in the protocol for the delineation and treatment planning process, it is crucial to record and report the delivered doses within the target volumes and OARs. Tables proposed as case report forms (CRF) outlining essential requirements for recording and reporting data on RT during systemic therapy for breast cancer, both in the curative (Table 2) and metastatic (Table 3) settings, can be found in the appendix of the international consensus paper [24]. These CRFs enable researchers to capture essential data, facilitating the later reporting and analysis of RT-related outcomes.

In cases where advanced QART is planned, it is advisable to collect all DICOM files from radiation treatment planning into a central database. This should include the planning CT scan, all delineations, and the radiation plan. Such a practice ensures easier access to extract relevant dose levels and other critical information that may not have been initially considered at the start of the trial. Reporting in this manner is anticipated in trials such as DBCG Skagen 1 (NCT02384733) and HYPOG-01 (NCT03127995).

The Netherlands has a nationwide registry of RT data for breast cancer in the postoperative setting, known as the Breast Cancer Audit-Radiotherapy (NBCA-R) [57]. They have published recommendations that pave the way for future national collaboration. By adopting and implementing our recommendations, centres can establish the means to report and exchange valuable information, ultimately fostering the potential for collaboration in large multicentre studies [57]. Likewise, initiatives such as the CANTO-RT database provide valuable models for other countries to adopt [58,59].

In summary, these recommendations aim to provide valuable tools for all future studies where RT is a component of patients' treatment. This extends beyond the RT-systemic therapy combination in prospective trials focus on investigational medicinal products, which initially drew our attention to this general and widespread shortcoming in reports on breast (and other) cancer clinical research. Our group strongly advocates for QART procedures and the implementation of best requirements. However, we also provide practical tools in the essential requirements section.

Fig. 1 illustrates the potential risks or lack of benefit encountered in routine clinical use compared to controlled clinical trials. This discrepancy can arise because trials are often highly selective, and there may be a lack of transparency in reporting trial procedures, which can lead to inappropriate implementation in clinical practice [7]. It is important to note that QART procedures may be time-consuming for the first trial, but much of the credentialing exercise can be applied to subsequent trials or easily updated. Furthermore, centers participating in prospective trials typically possess the necessary infrastructure, personnel, and high-performance capabilities to support these trials. However, the literature indicates that major deviations may occur in up to one-third of cases in trials, and this can have significant implications for patient outcomes, including local control and overall survival [8,28,29,60].

Quality assurance and adherence to the treatment protocol have been demonstrated to enhance patient outcomes. Therefore, maintaining a high level of QART and adhering to treatment planning guidelines, along with the independent and transparent reporting of deviations and outcomes, as well as optimised education and specialisation of radiation oncologists, medical physicists, and radiotherapy technicians should be the standard for clinical trials. This applies whether the trial is evaluating a new RT protocol or if irradiation is administered as part of the standard of care in a trial focused on systemic therapy or surgery. Implementing our recommendations, even in routine clinical practice and not exclusively within the context of a clinical trial, will facilitate the future generation of high-quality data.

CRediT authorship contribution statement

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Declaration of competing interest

IMe declares advisory boards supported by Eli Lilly, Novartis, Pfizer, Pierre Fabre, SeaGen, Daiichi Sankyo, Astra Zeneca. CB declares honoraria supported by declares advisory boards supported by Eli Lilly, Novartis, Pfizer, and Amgen. ML received honoraria and/or participated in advisory board from Roche, Novartis, Lilly, Pfizer, AstraZeneca, Daiichi Sankyo, Gilead, SeaGen, MSD, Exact Sciences, Takeda, Ipsen, Sandoz, Libbs & Knight, a travel grant from Gilead and research support to the Institution from Gilead. EdA disclosed honoraria and/or advisory board from Roche/GNE, Novartis, SeaGen, Zodiac, Libbs, Pierre Fabre, Lilly, AstraZeneca. JC disclosed consulting/advisor for Roche, Celgene, Cellestia, AstraZeneca, SeaGen, Daiichi Sankyo, Erytech, Athenex, Polyphor, Lilly, Merck Sharp & Dohme, GSK, Leuko, Bioasis, Clovis Oncology, Boehringer Ingelheim, Ellipses, Hibercell, BioInvent, Gemoab, Gilead, Menarini, Zymeworks, Reveal Genomics, Expres2ion Biotechnologies. NH disclosed honoraria for lectures and/or consulting from AstraZeneca, Daiichi-Sankyo, Gilead, Lilly, MSD, Novartis, Pierre-Fabre, Pfizer, Roche, Sanofi, Sandoz, SeaGen. HSR disclosed institutional research support by Astellas Pharma Inc., AstraZeneca, Daiichi Sankyo Inc., F. Hoffmann-La Roche AG/Genentech, Inc., Gilead Sciences Inc., GlaxoSmithKline, Lilly, Merck & Co. Inc., Novartis Pharmaceuticals Corporation, OBI Pharma, Pfizer, Pionyr Immunotherapeutics, Sermonix Pharmaceuticals Inc., Taiho Oncology Inc., and Veru Inc. GC reports personal fees for consulting, advisory role and speakers' bureau from Roche/Genentech, Novartis, Pfizer, Lilly, Foundation Medicine, Samsung and Daiichi Sankyo; honoraria from Ellipses Pharma and fees for travel and accommodations from Roche/Genentech and Pfizer. LV declares participation on advisory board from Daiichi Sankyo and Pfizer. ME declares advisory board supported by Pfizer and Novartis and lecture fees supported by AstraZeneca. GM declares consultancy honoraria from Roche, Novartis, AstraZeneca, Pfizer, Jensen, Lilly, and Sanofi. LDM declares consulting fees from Roche, Novartis, Eli Lilly, MSD, Daiichi Sankyo, SeaGen, Gilead, Eisai, Pierre Fabre, AstraZeneca, Stemline Menarini, Exact Sciences, Agendia, GSK, Pfizer. No other competing interests declared.

Acknowledgments

We want to express our appreciation to the international experts who dedicated months of collaborative effort leading up to the meeting to develop these recommendations for our community (listed in Appendix 1). Our sincere gratitude goes to Marco Banini, Marianna Valzano, and Pietro Garlatti from the University of Florence, Florence, Italy. We would also like to express our appreciation to Frank Vicini, Saverio Cinieri, Asal Rahimi, Maryam Garousi, Marta Perachino, Paola Francica, Chelain Goodman, Fatjona Kraja, and Alizee Camps Malea for their valuable contributions. CEC is funded by the National Institute of Health and Care Research (NIHR) and supported by the NIHR Cambridge Biomedical Research Centre. The views expressed are those of the author and not necessarily those of the NIHR or the Department of Health and Social Care.

We extend our thanks to Fondazione Radioterapia Oncologica (FRO) non-profit organization and all those who have provided essential support for scientific research. We also acknowledge the unconditional support of all the companies involved in the implementation of scientific research and studies, including IFCA Spa, Fondazione Cassa di Risparmio di Pistoia e Pescia, Conad Società Cooperativa, Fabiani Gioiellerie, Permira, Rinascente, Giorgio Tesi Group.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.radonc.2023.110060.

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