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Original Article

Outcomes and level of evidence in radiation therapy research and different categories of radiotherapy innovations: an ESTRO-VBRO bibliometrics analysis of the literature

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ABSTRACT

Aim: The ESTRO-Value-Based Radiation Oncology project aims to enhance patient access to high-value radiotherapy innovations, by identifying interventions delivering meaningful benefit. To understand the role of the quality of evidence in implementation decisions, this paper analyses the study designs and endpoints used to appraise selected types of radiotherapy innovations in the literature.
Methods: This review used a quantitative bibliometric approach to analyse a representative set of 23 radiotherapy innovations, identified within the radiation therapy research published between 2012 and 2022 in the Web of Science database. Abstracts were searched manually to extract information about study designs and endpoints. Interventions were allocated into one of four defined radiotherapy categories, based on a decision algorithm developed in a parallel project.
Results: 3,721 abstracts were identified and categorised using the decision algorithm into four categories: Drug-centred, Radiation-centred, Radiation-enabling or Operational radiotherapy interventions. The study designs were highly variable across these categories: in Drug-centred innovations, 20.3% were clinical trials compared to 6.8% for Radiation-centred. The predominant design across all categories was Prospective observational studies, ranging from 53.9% in Radiation-enabling to 23.0% in Drug-centred innovations. Regarding endpoints, the main focus for Drug-centred innovations was on Clinical endpoints and Overall survival. For Radiation-centred and Radiation-enabling innovations, Toxicity endpoints were more frequently reported.
Conclusion: This analysis demonstrates the differences in radiotherapy research output for various categories of radiotherapy interventions. This supports the development of a tailored appraisal strategy for each category, based on the required level of evidence and meaningful endpoints to support reimbursement and clinical implementation.

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Introduction

Despite its crucial role in cancer care, funding for radiation oncology treatment and research is less prioritised by governments and industry compared with other cancer treatment modalities such as pharmaceuticals [1–5]. The variation in research funding, is likely to have contributed to the disparity in the quantity and quality of cancer research outputs which in turn may limit the implementation of innovation into clinical practice [5–8]. Additionally, there are unique specificities of radiotherapy which make trial development and participation challenging. For instance, the need for a specialist workforce and high-cost equipment and infrastructure (e.g. bunkers) to deliver new techniques [5,9].

This deficiency in the quality of evidence to support practice change in radiation oncology is further exacerbated due to the variable requirements for evidence in regulatory decisions. While authorisations for medicinal products usually require randomised clinical trials to demonstrate clinical safety and efficacy, there are less stringent requirements or specifications for evidence on medical devices or other innovative technologies with regard to design, duration or endpoints of the studies [10,11]. This is made even more complicated by the large array of innovation types, which can encompass everything from complex technologies and devices (e.g. new types of linear accelerators), radiation beams with different biological properties (e.g. proton therapy), novel methods of treatment delivery (e.g. stereotactic body radiotherapy – SBRT) or immobilisation and positioning strategies (e.g. deep inspiration breath hold).

Clinicians and policy makers therefore need to make decisions on the available evidence, which is highly variable in design and quality, and without consensus on which level of evidence or meaningful benefit is acceptable to support uptake of different types of innovations [7,12,13]. The disparity in evidence generation, combined with the room for interpretation in regulations, can impede the clinical implementation and reimbursement approval of radiotherapy innovations, delaying or hindering access to care for patients, whilst potentially encouraging adoption of low value treatments of limited clinical benefit.

To inform future policy we sought to understand the current landscape of radiotherapy research output, characterising evidence in terms of study design and endpoints. By investigating the available evidence for radiotherapy in general and identifying differences in appraisal methods for various types of interventions, gaps and opportunities can be identified in view of developing an evidence-based appraisal framework for radiotherapy innovations. To this end, this paper presents a bibliometric analysis of radiotherapy literature from 2012 to 2022, examining study designs and endpoints that have been published for a range of representative radiotherapy interventions.

Methodology

Bibliometrics analysis of radiation therapy research output

Using a previously validated bibliometric algorithm with prespecified title words and journal types, all radiotherapy articles were identified from the Web of Science database between 2012–2022 inclusive [6]. For the purpose of this analysis, the algorithm was further developed between two co-authors with a clinical background and the bibliometrics expert (AA, GL, MV) to identify research papers, evaluating a list of 23 defined radiotherapy interventions in a clinical setting or measuring clinical endpoints (such as mortality and morbidity). (See Addendum Table 1 for the bibliometrics filters developed for each intervention.) The selected 23 interventions aimed to represent the heterogeneity of innovations in the field of radiation oncology. The list was compiled based on literature review and experience of the involved multidisciplinary steering group (AA, JB, MA, ML, MV, PB, YL), including backgrounds in clinical radiation oncology, medical physics, radiation therapy (RTT), epidemiology, health services research and policy. Different radiotherapy-specific characteristics were considered for the interventions, for example radiobiological properties, different modes of delivery, different technology aspects and applications thereof.

Table 1
Endpoints grouped in twelve types with four main groups.

Main group of endpoints	Type of endpoint	Examples
Group I: Clinical endpoints	Local or loco-regional endpoints	*Local control; Local response rate; Local progression-free survival*
	Systemic progression endpoints	*Distant metastasis; Progression-free survival; Treatment-free interval*
	Overall survival	*Overall survival*
Group II: Toxicity and quality of life endpoints	Toxicity endpoints	*Complication rate; Acute or late toxicity (e.g. PROMs)*
	Functional endpoints	*Organ preservation; Symptom control (e.g. PROMs)*
	Quality of life endpoints	*HR-QOL changes*
Group III:Operational, structural or time-related endpoints	Time-related endpoints	*Planning time; Treatment delivery time; Waiting time*
	Operational and structure endpoints	*Bunker specificities (floorspace, instalment of shielding); Number or type of treatment units; Training level*
	Resources and costs	*Number of personnel (RTT, Physicists, Radiation Oncologists, …) required for treatment; Direct costs; Calculated indirect costs*
Group IV: Technical, quality and safety endpoints	Physics and planning endpoints	*Monitor units; Beam parameters; Air kerma*
	Accuracy endpoints	*DVH; dose distribution; V20; D50*
	Quality of care parameters	*Quality assessment; Robustness; Error rate; Positioning accuracy;*

Then, the interventions were grouped into four categories, defined through a multi-stakeholder mixed-method approach (See accompanying paper for full details of the categories and categorisation algorithm) [14]. Each category represents a group of interventions requiring a specific level of evidence and specific endpoints to support their clinical adoption or policy decisions such as reimbursement.

Four distinct categories of radiotherapy interventions are defined, based on their primary aim at either the patient or the operational level (see Table 2 for the categories with illustrative examples).

There are three patient-centred categories, aiming to improve outcomes or patient experience. Firstly, Drug-centred innovations, which combine drug therapies with radiation (e.g. radio-immunotherapy or radiosensitisers). Secondly, Radiation-centred innovations (e.g. hypofractionation or stereotactic radiotherapy), which aim to optimise therapeutic ratio of the radiation delivered, typically resulting in better local control or reduced toxicity. Thirdly, Radiation-enabling innovations (e.g., rectal spacers or surface-guided radiotherapy), aiming to improve outcomes and experience by improving patient positioning or reducing dose to normal tissues.

The fourth category of Operational interventions are not directly aimed to impact the patient, but instead aim to make a change at the organisational level or the operational workflow (e.g. AI-based autocontouring).

Table 2
Four categories of radiotherapy interventions with representative interventions and related number of abstracts, published in the literature 2012–2022.

Category of radiation interventions (n abstracts)	Interventions (n abstracts)
Drug-centred radiation interventions (74)	Radiosensitiser (19) Radio-immunotherapy (55)
Radiation-centred radiation interventions (3096)	LATTICE radiotherapy (7) FLASH radiotherapy (9) MRI-Linac (13)Online adaptive radiotherapy (17) Cyberknife (53) Stereotactic radiosurgery (121) Volumetric modulated arc therapy (263) High-dose-rate brachytherapy (305) Tomotherapy (424)Hypofractionation (593) Stereotactic body radiotherapy (614) Proton radiotherapy (677)
Radiation-enabling radiation interventions (534)	Surface-guided radiotherapy (21) 4D CT simulation (24) Prone breast board (25) Fiducial markers (34)Rectal spacer (36) Deep inspiration breathhold (62) Image-guided radiotherapy (332)
Operational radiation interventions (17)	AI-based autocontouring (8) AI-based planning (9)

Data extraction

Abstracts of the identified papers were searched manually to extract relevant information about study design, study characteristics and endpoints, no full texts were reviewed.

Study designs were grouped in eight different types: phase 4 trial; phase 3 trial; phase 2 trial; phase 1 trial; prospective observational design (e.g. prospective cohort studies); retrospective observational design (e.g. retrospective cohorts), pre-clinical design (e.g. in vitro or in silico studies, veterinary studies, phantom studies); and alternative designs (e.g. trial emulation methods). Endpoints were divided into four main groups within which there are 12 types of endpoints (see Table 1 for more details).

Appraisal of interrater variability and statistical analysis

A standardised extraction form to support data extraction was developed in iterative rounds including two test rounds of data-extraction, using a random selection of 500 abstracts. In this way, relevant items of study design, study quality and endpoints were identified. To ensure consistency and quality of data extraction, two authors (HM, MV) independently reviewed a random sample of 100 abstracts. A Cohen's kappa (κ) measurement of interrater reliability for the study designs and grouped endpoints (13 items in total) was used to assess consistency for data extraction. The Bonferroni method was used to adjust p-values to correct for multiple testing, by dividing the critical level of significance by the number of tests [15].

To determine significant differences in distribution of study designs and endpoints across categories, a Fisher-Exact test was performed. All statistical analyses of the extracted data were performed using R statistical software (version 4.3.1).

Results

Bibliometric analysis

The bibliometrics algorithm identified 12,095 radiotherapy papers for the 23 defined interventions, of which 4,327 were identified as clinical studies through the algorithm and included for manual review of the abstracts. Of these, 606 were excluded after manual analysis for being a *meta*-analysis, review, conference abstracts, or case report, or if the imported abstract did not contain any text or processable information, resulting ultimately in 3,721 papers for analysis. (See Fig. 1).

Interrater reliability

Level of agreement in data extraction between two independent reviewers was substantial or almost perfect for most of the data extraction using a Cohen's kappa (κ) measurement, with 5 of 13 assessed items having a κ value > 0.9; 4 having a κ value between 0.80–0.90 and 4 having a κ value between 0.60–0.79 [16]. Reported p-values for all tests were below the Bonferroni corrected p-value for multiple tests ($p < 0.004$). Full overview of Cohen's kappa and corrected p-value per item can be found in the Addendum.

Different categories of radiotherapy interventions

The 3,721 included abstracts were grouped into one of the four categories, by categorising the 23 interventions using the developed algorithm (see Table 2). For each of the four categories, study designs and endpoints were analysed as shown in Tables 3-4 and Fig. 2.

Of all included abstracts, 6.7 % presented a clinical trial (with no phase 4 trials, 1.0 % phase 3, 4.8 % phase 2, 0.9 % phase 1). Prospective observational studies were represented in 48.1 %, retrospective observational studies in 37.8 %, pre-clinical studies in 7.3 % and alternative study designs in 0.1 % (See Fig. 2).

Across the four categories, the proportion of abstracts reporting clinical trials ranged from 0 %-20.3 %, with a range of 0 %-1.1 % for phase 3 trials, 0 %-14.9 % for phase 2 trials and 0 %-5.4 % for phase 1 trials. (See Fig. 2 and Table 3). There were no clinical trials reported in Operational interventions, while the highest representation was seen in Drug-centred interventions. Reporting of prospective observational designs ranged from 23.0 %-53.9 %, with the lowest proportion in Drug-centred interventions, the highest in Radiation-enabling interventions.

23.5 %-38.8 % of the studies were retrospective in design with the lowest proportion in Operational interventions and highest in Radiation-centred interventions (See Fig. 2 and Table 3). Pre-clinical studies ranged from 6.6 %-52.9 %, with the lowest proportion in Radiation-centred interventions and the highest in Operational interventions. Alternative designs are only reported in two categories: Drug-centred interventions and Radiation-centred interventions, representing 2.7 % (2 abstracts) and 0.03 % (1 abstract) respectively.

A Fisher-Exact test showed that the distribution of all study designs was significantly different across the four categories (p-values < 0.001).

Across the three patient-centred categories (Drug-centred, Radiation-centred and Radiation-enabling interventions) (see Table 4), the highest reporting of Clinical endpoints and OS specifically, is seen in studies of Drug-centred interventions (77.0 % and 55.4 % respectively), followed by studies of Radiation-centred interventions (56.2 % and 35.1 % respectively) and then Radiation-enabling (37.3 % and 21.7 % respectively). The highest proportion of papers reporting Toxicity and quality of life endpoints as well as QoL is found in studies of Radiation-centred interventions (61.0 % and 4.5 %), followed by studies of Radiation-enabling interventions (51.5 % and 3.7 %) and Drug-centred interventions (40.5 % and 2.7 %). For Operational intervention studies, there were no reports of Clinical endpoints, OS, Toxicity and quality of life endpoints or QoL.

Representation of Operational and economic endpoints and Technical, quality and safety endpoints is highest in Operational interventions (29.4 % and 94.1 % respectively) (see Table 4). For the three patient-centred categories, reporting of Operational and economic endpoints and Technical, quality and safety endpoints is highest in studies of Radiation-enabling interventions (5.1 % and 51.7 %

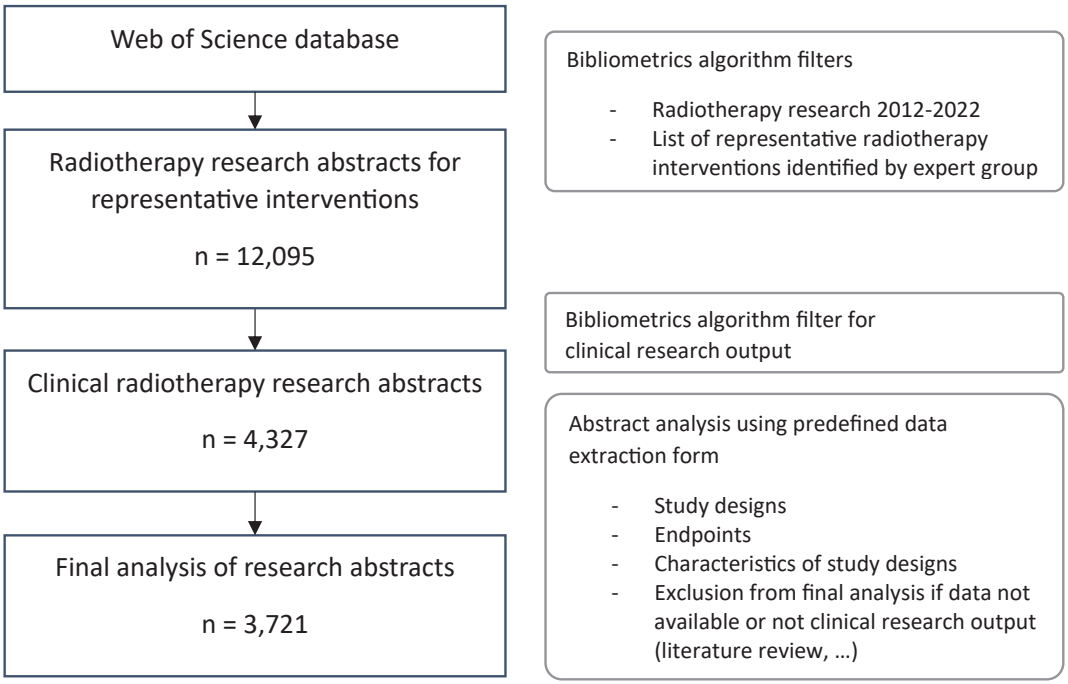

Fig. 1. Overview of data selection and inclusion using bibliometrics approach in Web of Science database (Aggarwal et al. 2018).

Table 3
Proportion of abstracts reporting study designs, by category.

% of total abstracts (n abstracts)	All abstracts	All clinical trials (phase 3–1)	Phase 3	Phase 2	Phase 1	Prospective observational designs	Retrospective observational design	Pre-clinical design	Alternative designs
Drug-centred intervention	74	20.3 % (15)	0.0 % (0)	14.9 % (11)	5.4 % (4)	23.0 % (17)	35.1 % (26)	18.9 % (14)	2.7 % (2)
Radiation-centred intervention	3096	6.8 % (211)	1.1 % (33)	4.8 % (150)	0.9 % (28)	47.8 % (1481)	38.8 % (1200)	6.6 % (203)	0.0 % (1)
Radiation-enabling intervention	534	4.5 % (24)	0.7 % (4)	3.4 % (18)	0.4 % (2)	53.9 % (288)	33.1 % (177)	8.4 % (45)	0.0 % (0)
Operational intervention	17	0.0 % (0)	0.0 % (0)	0.0 % (0)	0.0 % (0)	23.5 % (4)	23.5 % (4)	52.9 % (9)	0.0 % (0)

Table 4a
Proportion of abstracts reporting main types of endpoints, by category.

% of total abstracts(n abstracts)	All abstracts	Clinical endpoints	Toxicity and quality of life endpoints	Operational, structural or time-related endpoints	Technical, quality and safety endpoints
Drug-centred intervention	74	77.0 % (57)	40.5 % (30)	0.0 % (0)	5.4 % (4)
Radiation-centred intervention	3096	56.2 % (1741)	61.0 % (1888)	2.4 % (75)	30.4 % (941)
Radiation-enabling intervention	534	37.3 % (199)	51.5 % (275)	5.1 % (27)	51.7 % (276)
Operational intervention	17	0.0 % (0)	0.0 % (0)	29.4 % (5)	94.1 % (16)

respectively), followed by studies of Radiation-centred interventions (2.4 % and 30.4 %) and Drug-centred interventions (0.0 % and 5.4 %).

A Fisher-Exact test showed significantly different distribution of the grouped endpoints for all categories (all p-values $p < 0.001$).

Discussion and conclusion

This analysis shows the differences in evidence generation and appraisal for different categories of radiotherapy interventions, suggesting that a 'one size fits all' approach cannot address implementation and policy-relevant questions for different types of innovations.

Despite randomised controlled trials (RCTs) being the gold standard to establish the efficacy of a clinical intervention, they represent only 1 % of the evidence in this analysis. This paucity of RCT research in radiotherapy has been observed before: radiotherapy-related RCTs represent less than 10 % of oncology RCTs, which predominantly focuses on drug or systemic therapies. This lack of RCTs in radiotherapy is due to a number of structural challenges, such as the high upfront investments or infrastructural requirements, rapidly evolving technologies, or the lack of support by funding agencies and industry for

Table 4b
Proportion of abstracts reporting specific endpoints, by category.

	Clinical endpoints			Toxicity and Quality of life endpoints		
Proportion of endpoints per category % (n)	**Local or loco-regional endpoints**	**Systemic progression endpoints**	**Overall survival**	**Toxicity endpoints**	**Functional endpoints**	**Quality of life endpoints**
Drug-centred intervention	36.5 % (27)	36.5 % (27)	55.4 % (41)	37.8 % (28)	1.4 % (1)	2.7 % (2)
Radiation-centred intervention	40.2 % (1246)	32.7 % (1012)	35.1 % (1086)	56.1 % (1737)	12.1 % (375)	4.5 % (138)
Radiation-enabling intervention	24.9 % (133)	23.8 % (127)	21.7 % (116)	47.6 % (254)	8.6 % (46)	3.7 % (20)
Operational intervention	0.0 % (0)	0.0 % (0)	0.0 % (0)	0.0 % (0)	0.0 % (0)	0.0 % (0)

	Operational. structural or time-related endpoints			Technical, quality and safety endpoints		
Proportion of endpoints per category % (n)	**Time-related endpoints**	**Operational and structure endpoints**	**Resources and costs endpoints**	**Physics and planning endpoints**	**Accuracy endpoints**	**Quality of care endpoints**
Drug-centred intervention	0.0 % (0)	0.0 % (0)	0.0 % (0)	0.0 % (0)	1.4 % (1)	4.1 % (3)
Radiation-centred intervention	1.7 % (52)	0.1 % (3)	0.7 % (23)	4.2 % (129)	19.4 % (601)	19.9 % (616)
Radiation-enabling intervention	4.3 % (23)	0.0 % (0)	0.9 % (5)	2.8 % (15)	27.9 % (149)	36.5 % (195)
Operational intervention	29.4 % (5)	0.0 % (0)	0.0 % (0)	17.6 % (3)	41.2 % (7)	82.4 % (14)

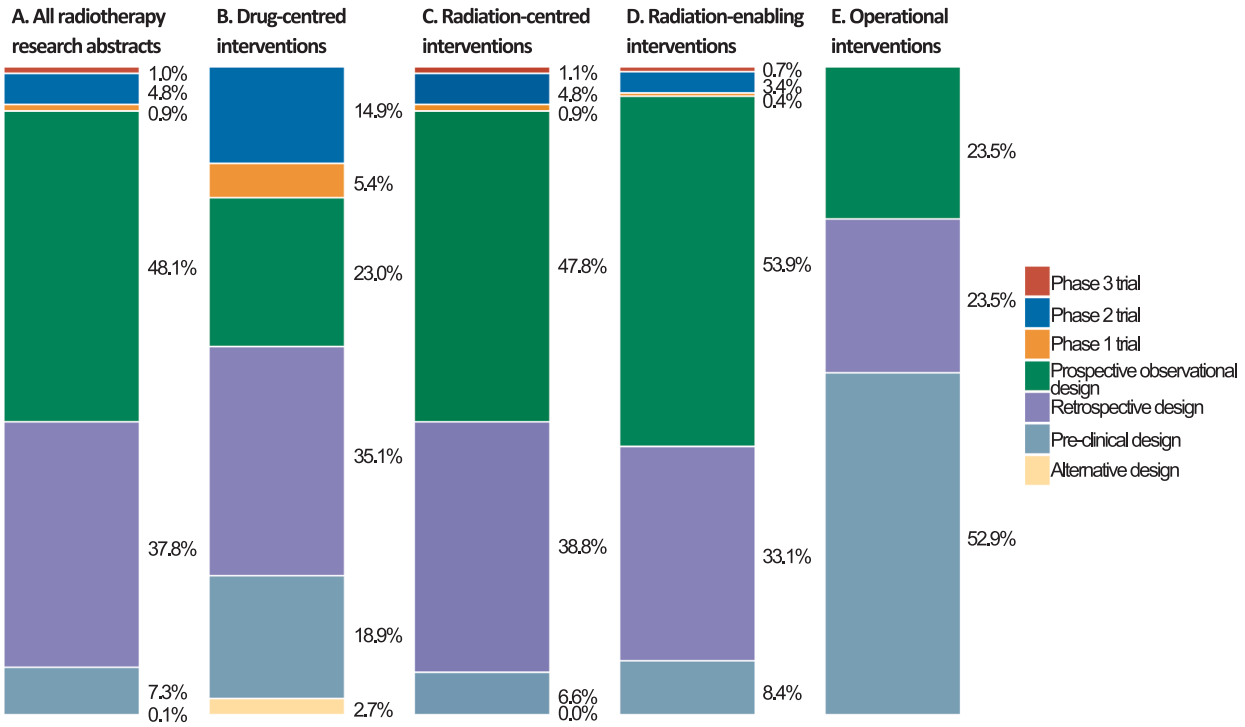

Fig. 2. Proportion of abstracts reporting study design for all analysed papers (A) and by category (B-E).

radiotherapy research [4–6,9,17–19].

Moreover, the categories with patient-centred innovations (Drug-centred, Radiation-Centred and Radiation-Enabling) show a variable level of evidence: clinical trial-related evidence (Phases 1–3) represented 20.3 % in Drug-centred interventions, 6.8 % in Radiation-centred interventions and 4.5 % in Radiation-enabling interventions, and are mostly Phase 2 designs. About half of the evidence in Radiation-centred and Radiation-enabling interventions is a prospective observational design, but there are still a substantial number of retrospective designs (33–39 % of abstracts) in the patient-centred categories.

The use of retrospective non-comparative evidence, such as case series, to demonstrate potential benefits for patients or justify clinical use has been rightly questioned for a long time. [20,21]. Well-designed prospective observational research holds untapped potential for providing more high-quality evidence, especially when RCTs are not feasible [19,21]. Prospectively collected data can assist in early stages of hypothesis generation or feasibility assessment, but equally appraise an innovation against the standard treatment, or allow for long-term

follow-up of effectiveness on a large scale [21,22]. Furthermore, the use of clinical registry data or real-world evidence can be valuable in these prospective observational designs, especially if there is no agreement on the appropriate comparator arm, for rapidly changing technologies or for underrepresented patient groups [5,23,24].

Additionally, the use of blended and statistically novel approaches for evidence generation can be considered, such as trial emulation methodologies or pragmatic designs. Although these methodologies can address some of the practical challenges of clinical trials, fewer than 1 % of the abstracts in this analysis report such an alternative design. It is however essential to acknowledge that for each methodology, including prospective observational or alternative designs, quality and robustness is of paramount importance, requiring strong statistical input, high quality data and a clear understanding of how differences between populations can be adequately adjusted [5,23,25,26].

An important factor in the variability of the available evidence is the limited regulatory requirements for radiotherapy innovations [10,11,27]. After market approval, there is little incentive to generate additional evidence, nor is there is consensus within the radiotherapy community on which threshold of evidence is required for adoption into clinical routine. Consequently, wide-spread clinical implementation or regulatory authorisation often occur without robust evidence of patient benefit or healthcare system impact. This puts patients and healthcare systems at risk of exposure to low-value expensive care, and equally can delay access to high-value interventions, for example if there is insufficient data to justify reimbursement [19].

Certain strategies aim to justify early access to innovations, such as coverage with evidence development schemes. In these approaches access or reimbursement is limited in time or to an evidence-based selection of patients, and conditional on further data being collected for evaluation of benefit and reduction of existing clinical and economic uncertainty [28,29]. This is particularly useful for new treatment indications where alternatives do not exist, if evidence generation through RCT is infeasible or difficult to pursue, or for specific interventions where assessment in regular clinical use is preferable (such as technologies with an operator learning curve). These strategies have a clear merit, but should not be used for rationalising marginal benefits for new technologies, and a prolonged follow-up is essential to gain insight into real-world clinical and economic performance of innovations to justify continued use or reimbursement [5,29].

Another finding in this analysis is a predominance of well-established clinical endpoints in the patient-centred categories, such as overall survival or disease-progression outcomes. In contrast, Quality-of-life (QoL) is reported in less than 5 % of papers in these categories, despite its increasing importance in policy decision-making, driven by shared decision-making or longer life expectancies of patients. This neglect may be explained by challenges in collecting or interpreting patient-reported data, leading to reliance on alternative or surrogate endpoints which are easier to measure [5,30,31]. Demonstrating meaningful clinical benefit for radiotherapy innovations however may require a broader range of clinical endpoints and include local control, reduced toxicity or functional organ preservation [7,19,23]. Moreover, although Operational interventions are not directly aimed at the patient-level, including Clinical or Toxicity endpoints in their appraisal may demonstrate a clinical benefit but also can prove their safety, which is sometimes simply assumed.

In addition, technical treatment information can also be crucial to correctly interpret study results or assess the quality of a radiation treatment, even in novel drug-radiotherapy combinations. Physics and planning or Accuracy endpoints however are mentioned in only a minority of the patient-centred categories. Initiatives such as reporting guidelines or nationwide radiotherapy data registries can be valuable tools to improve access to these essential radiotherapy-specific data [26,32,33]. Additionally, technical treatment information and operational endpoints can be helpful for decision-making at an organisational level. These endpoints can help identify innovations which provide benefit not only for the patient but also at a hospital or healthcare system level and can provide value for money for both patients and society [34].

Study limitations

A limitation to consider in this study is that information was extracted from WoS through a bibliometrics algorithm: other sources (e.g. non-English language journals) are not included, potentially leaving out relevant articles. Additionally, as with any bibliometric evaluation, it is not possible to guarantee inclusion of all relevant articles, however the algorithm itself had previously been validated and co-designed with an experience bibliometrician [6]. In total 62,550 articles over a 10-year period across all radiation therapy articles were identified, of which 12,095 articles involved the 23 specific interventions we had identified.

Only papers identified as ‘clinical’ by the macrofilters of the algorithm are analysed, excluding earlier research stages (in-vitro studies) that might provide additional insights into the evolution of evidence for innovations but these studies were specifically intended to be excluded.

Data was extracted from abstracts only. We acknowledge therefore that some study characteristics may be under-reported, for example, only 27 % of clinical trials reported the number of recruiting centres in the abstract. To ensure a consistent and correct data extraction, the extraction form was refined through multiple iterations by multiple authors and an interrater reliability comparison was performed.

Additionally, only a ten-year study period (2012–2022) was reviewed across a selected number of radiotherapy interventions, and some interventions returned only a limited number of publications. This could potentially lead to an under- or misrepresentation of certain aspects, and for some interventions it can be expected that more mature data may still emerge. Of note, the list of 23 interventions, used to build the bibliometrics subfilters, only contained two examples in the Operational innovations, as opposed to seven for Radiation-enabling innovations for example. These different amount of examples included per category lead to a significantly larger number of papers to be analysed for Radiation-centred and Radiation-enabling innovations. One major consideration particularly with the Operational interventions, is that Operational innovations can include those that aim to improve efficiency of workflows and are in effect or often “updates” of existing software or represent changes in safety signalling procedures. These may be under-represented relatively in the clinical literature. However, due to the methodology and large overall dataset, the conclusions of this report adequately reflect the general trends and characteristics in radiotherapy research output.

In conclusion

This bibliometrics analysis provides a landscape overview of radiotherapy research output, highlighting the limitations in the evidence available to support clinical and policy decision-making of radiotherapy interventions. In addition, significant differences in evidence generation suggest that a tailored approach for various categories of radiotherapy innovations can enhance appraisal. The currently ongoing ESTRO-HERO Value-Based Radiation Oncology project is dedicated to determine the minimum acceptable level of evidence and key endpoints to demonstrate meaningful benefit for each category, to identify high-value innovations and support their dissemination through evidence-based policy decision-making [34].

CRediT authorship contribution statement

M. Vandemaele: Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology, Investigation, Formal analysis, Conceptualization. **G. Lewison:** Writing – review & editing, Validation, Software, Methodology, Investigation, Formal analysis. **H. Martinussen:** Writing – review & editing, Validation, Investigation,

Formal analysis. **J.M. Borràs:** Writing – review & editing, Investigation, Formal analysis, Conceptualization. **M. Leech:** Writing – review & editing, Investigation, Formal analysis, Conceptualization. **M. Aznar:** Writing – review & editing, Investigation, Formal analysis, Conceptualization. **P. Blanchard:** Writing – review & editing, Investigation, Formal analysis, Conceptualization. **Y. Lievens:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Investigation, Formal analysis, Conceptualization. **A. Aggarwal:** Writing – review & editing, Writing – original draft, Visualization, Validation, Supervision, Methodology, Investigation, Formal analysis, Conceptualization.

Declaration of competing interest

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.radonc.2025.111165.

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