Review

From Semantic Modeling to Precision Radiotherapy: An AI Framework Linking Radiobiology, Oncology, and Public Health Integration

Fernando Gomes de Souza Jr. * , José Maria Aliaga Jr. , Paulo C Duarte Jr. , Shirley Crispilho , Carolina Delfino , Daniele Silvéria Brandão e Silva , Fernando Zamprogno e Silva

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Review

From Semantic Modeling to Precision Radiotherapy: An AI Framework Linking Radiobiology, Oncology, and Public Health Integration

Fernando Gomes Souza, Jr. [1,2,3,*], José Maria Aliaga, Jr. [4,5], Paulo C. Duarte, Jr. [6,7], Shirley Crispilho [6], Carolina Delfino [2], Daniele Brandão [2] and Fernando Zamprogno e Silva [8]

[1] Instituto de Macromoléculas Professora Eloisa Mano, Universidade Federal do Rio de Janeiro (UFRJ), Centro de Tecnologia, Cidade Universitária, Rio de Janeiro 21941-598, Brazil. fernando_gomes@ima.ufrj.br

[2] Programa de Engenharia da Nanotecnologia – COPPE, Universidade Federal do Rio de Janeiro (UFRJ), Centro de Tecnologia, Cidade Universitária, Rio de Janeiro 21941-972, Brazil

[3] Department of Electrical and Computer Engineering, Florida International University (FIU), 10555 West Flagler Street, EC3900, Miami, FL 33174, USA; https://orcid.org/0000-0002-8332-4953

[4] Departamento de Oncologia, Hospital Paulistano, São Paulo, Brazil.

[5] Departamento de Oncologia, Prevent Senior, São Paulo, Brazil.

[6] Bioengineering Department, Institute Dante Pazzanese of Cardiology, Paulo, Brazil

[7] Department of Civil Construction, State University of Londrina, Londrina, Parana, Brazil

[8] Department of Oncology, Hospital Meridional S.A., Vila Velha, Espírito Santo, Brazil

* Corresponding author: fgsj@ufrj.br or fgomes@pent.coppe.ufrj.br or fgomesde@fiu.edu

Abstract

Background/Objectives: Radiotherapy, radiobiology, and oncology have evolved rapidly over the past six decades, generating vast and fragmented bodies of scientific evidence. This study aimed to systematically map and interpret their conceptual and temporal development using artificial intelligence (AI)–based methods, highlighting the integration between molecular mechanisms, clinical applications, and technological innovation toward a precision radiotherapy framework. **Methods:** A corpus of 3,343 unique documents (1964–2025) was retrieved from Scopus, PubMed, and Web of Science. Records were harmonized through deduplication, lemmatization, and metadata normalization. Topic modeling using Latent Dirichlet Allocation (LDA) and co-occurrence network analysis were applied to identify dominant research axes. Semantic and temporal analyses were conducted to reveal patterns, emerging trends, and translational connections across decades. **Results:** Three historical phases were identified: an initial period of limited production (1964–1990), moderate growth (1991–2010), and exponential expansion (2011–2024), with peaks in 2020 and 2023. LDA revealed two principal axes: a clinical–anatomical axis focused on cancer sites, treatment modalities, and prognosis, and a mechanistic–molecular axis centered on DNA repair, radiosensitivity, and biomarkers. The co-occurrence supergraph showed high density (0.5) and low modularity (0.02), indicating strong thematic integration. Case synthesis from 2014–2025 defined five operational classes: DNA repair and molecular response, precision oncology and genomic modeling, individual radiosensitivity, mechanisms of radioresistance, and advanced technologies such as FLASH radiotherapy and optimized brachytherapy. **Conclusions:** AI-driven semantic and temporal analyses revealed that radiotherapy has matured into an interconnected, interdisciplinary domain. The derived Precision Radiotherapy Implementation Plan translates molecular and computational insights into clinically actionable strategies that can enhance survival, reduce toxicity, and inform equitable health policies for advanced cancer care.

Keywords: AI-based semantic and temporal analysis; co-occurrence supergraph; clinical-anatomical axis; mechanistic-molecular axis; DNA repair and molecular response; advanced radiotherapy technologies (FLASH-RT; hadron therapy; voxel-level analytics)

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1. Introduction

In the past decades, the number of scientific research studies has grown exponentially, creating vast reservoirs of knowledge in many fields [1–4]. However, a significant fraction of that knowledge remains underutilized because it is scattered in databases and challenging to access or interpret, especially in very specialized areas [5–9].

This study is based on a straightforward premise: the combination of literature mining and artificial intelligence (AI) can revolutionize the mapping of the thematic evolution and conceptual foundations of radiotherapy [10–28], radiobiology [29–52] and oncology [53–72], because by enabling automated, scalable and interpretable analyses, this approach overcomes the limitations of traditional searches and manual curation, providing a broader, more current and more interdisciplinary vision of the state of the art [7,73–75].

Traditional bibliometric tools are often unable to capture the subtle patterns that matter in specialized areas, thus highlighting the value of AI-based approaches that exploit metadata, semantic models and co-occurrence networks; therefore, the use of unsupervised machine learning and text mining in our previous work revealed emerging trends and knowledge gaps in areas such as nanocomposites, controlled drug delivery, photovoltaics, catalysis, biosynthesis and spectroscopy, showing that computational approaches can accelerate the synthesis and application of scientific knowledge [76–93].

In this work, we apply this strategy to an interdisciplinary corpus of thousands of articles indexed in Scopus, PubMed and Web of Science, intending to rigorously structure, validate and interpreting how radiotherapy, radiobiology and oncology have consolidated as an interconnected domain from 1964 to 2025, because to our knowledge, this is the first comprehensive effort to apply AI-based semantic and temporal analysis to the literature of these disciplines at this scale and depth.

None of these studies has considered both the semantic and temporal dimensions of the literature by a unified analysis pipeline, and in particular, there is a gap in the methodological literature between bibliometric/quantitative approaches and clinically oriented predictive models. The rest of the literature is organized around four main strands, each one focused on a particular aspect of the problem, including bibliometric and visualization studies, which have been conducted by using tools such as VOSviewer and CiteSpace for analyzing the evolution of keywords and co-authorship networks. For instance, Wang *et al.* (2024) [94] reports a keyword co-occurrence network, which shows the main trends in the field from 2014 to 2025, however, these studies are essentially descriptive, and in general, they do not include topic modeling, deep semantic analysis, or time series methods.

Methodological proposals, such as the one by Andrei and Arandjelovic (2016) [95], use hierarchical Dirichlet processes and temporal similarity graphs to model the evolution of topics over time, but this framework has not been used in the biomedical context nor in radiotherapy. Meanwhile, AI for radiotherapy literature, including studies by Tabibi *et al.* (2025) [96] and Lastrucci *et al.* (2024) [97], use deep learning to predict clinical outcomes and refine treatment strategies in radiotherapy, consequently, precision and efficacy of the treatment have increased significantly, although these studies predict clinical endpoints, whereas the mining or semantic representation of the scientific literature itself has not been addressed.

Reviews, such as Momin *et al.* (2020) [98] and Trifiletti and Showalter (2015) [99], discuss the integration of clinical and genomic data in radiotherapy, but do not perform a semantic and temporal analysis of the scientific output, therefore, to summarize, these literature strands suggest a methodological gap between purely bibliometric studies and clinically oriented predictive models. To the best of our knowledge, there is no published study that performs an integrated analysis of combining semantic modeling (e.g., topic modeling, co-occurrence networks) with structured temporal analysis (e.g., historical time series, change point detection) in a unified framework for the radiotherapy, radiobiology, and oncology literature, which justifies the novelty of the present study,

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that aims at synthesizing bibliometric indicators, semantic modeling, and temporal dynamics in a single framework providing both analytical insight and predictive perspective on the scientific evolution of the field.

By integrating major databases and processing more than three thousand unique documents with advanced computational modeling, the study goes beyond traditional bibliometrics, providing a dynamic and interpretable view of how these fields have evolved over six decades, and linking molecular mechanisms, clinical practice, and technological development within a single analytical framework. In so doing, the study demonstrates a new approach to scientific progress: artificial intelligence as a tool for synthesis and interpretation, rather than allowing valuable findings to remain scattered and fragmented. AI can facilitate their transformation into cohesive insights that can inform translational advances and support more precise, efficient, and equitable healthcare.

2. Methods

The search strategies applied to Scopus, PubMed, and Web of Science were carefully harmonized to identify publications addressing the intersection of radiotherapy, radiobiology, and oncology, with the guiding question: “What are the key connections and advances at the interface of radiotherapy, radiobiology, and oncology as reflected in the recent scientific literature?” The query used in Scopus was TITLE-ABS-KEY ((radiotherapy) AND (radiobiology OR "radiation biology") AND (oncology)); in PubMed, a combination of MeSH terms and free-text fields was applied—("Radiotherapy"[MeSH Terms] OR "Radiotherapy"[All Fields]) AND ("Radiobiology"[All Fields] OR "Radiation Biology"[All Fields]) AND ("Oncology"[MeSH Terms] OR "Oncology"[All Fields]); and in Web of Science, the direct key (Radiotherapy AND Radiobiology AND Oncology) was used. These strategies initially retrieved 2,507 records from PubMed, 741 from Scopus, and 714 from Web of Science, yielding a total of 3,962 documents.

3. Results

The structured computational pipeline began with the automated ingestion of files from Scopus, PubMed, and Web of Science. We standardized and normalized the core data fields, and we retained additional metadata for each data source. We merged the data, and when the same publication was included twice, we selected the record with the most complete data, therefore we removed 594 duplicate publications based on ID numbers and 25 based on titles. This resulted in a total of 3,343 publications, and thus the final dataset was composed of a large number of unique publications. The majority of the publications were retrieved from PubMed (66.23%), followed by Scopus (21.96%) and Web of Science (11.82%), and so the distribution of publications across these databases was not uniform.

Figure 1 provides a graphical synthesis of the results, and in the upper part of the figure, the number of publications per year is presented, which shows three phases: low publication rate from 1964 to 1990, moderate growth from 1991 to 2010, and rapid growth from 2011 onward, because this coincides with the rise of stereotactic body radiotherapy, protons, and prediction models. The years 2020 and 2023 had the highest number of publications (~240), but the decrease in 2025 is probably due to incomplete indexing of the literature, and thus this decrease may not reflect the actual number of publications. The word cloud at the bottom of the figure was generated based on titles and abstracts, and common terms such as *radiat*, *cell*, *treatment*, *cancer*, *dose*, *patient*, *tumor*, *radiotherapi*, *fraction*, *therap*, and *radiobiolog*, are highlighted.

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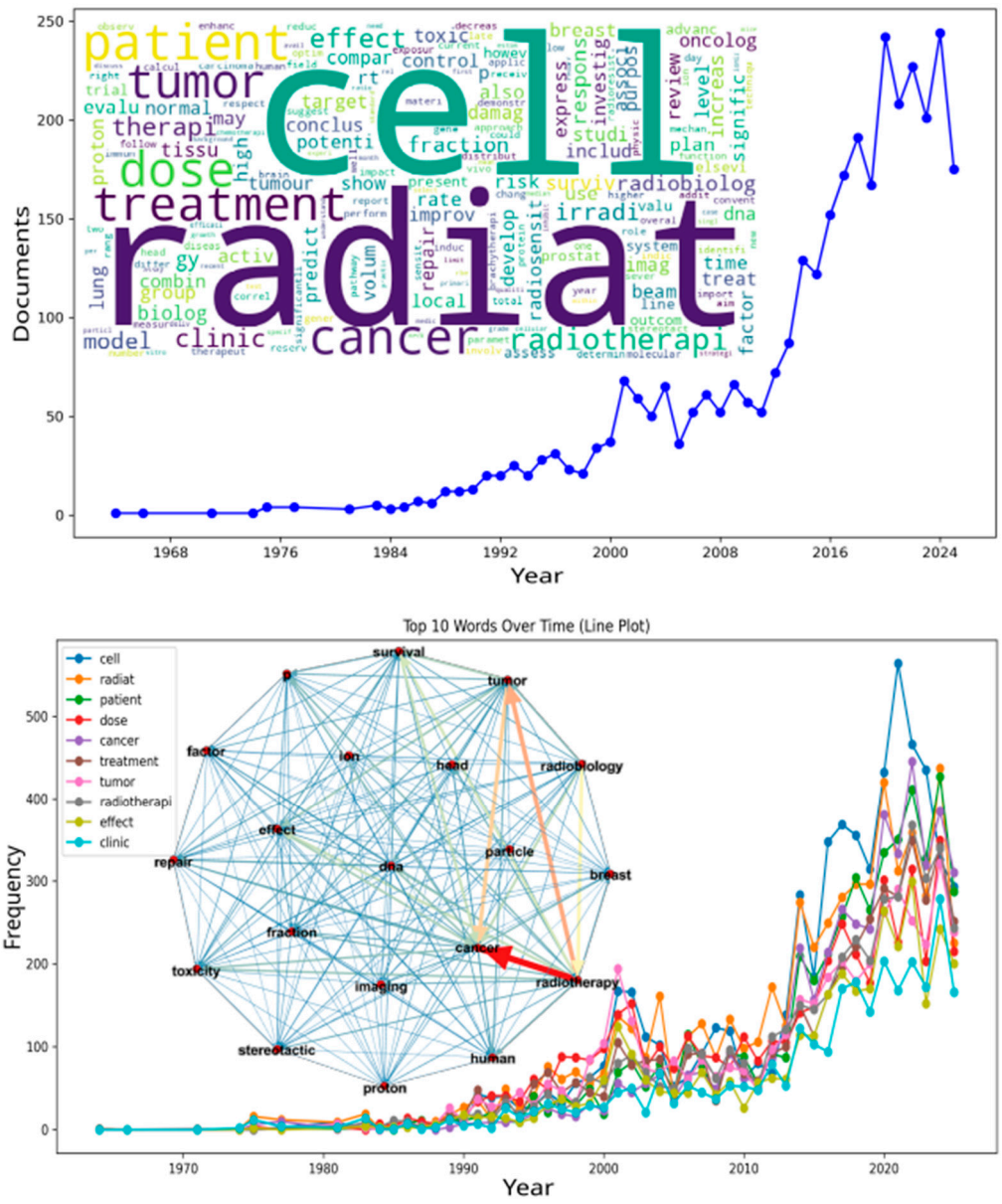

Figure 1. Word cloud, temporal evolution of publication output, term frequency, and co-occurrence supergraph. The figure, which presents different layers of lexical evidence from the radiobiology and radiation oncology literature, to give an overview of how the field has grown and organized over time. The top panel is a line plot of the number of publications per year from the 1960s to the present, showing a prolonged period of gradual growth followed by a rapid increase over the last decade, and the word cloud to the right shows all terms scaled by frequency, with cell, radiation, patient, dose, treatment, and cancer being the most prominent, reflecting the sustained interplay of mechanistic biology, dosimetry, clinical application, and outcomes. The bottom panel shows the longitudinal trends of the top 10 terms to the right, with a steep increase in the 2000s, supporting the hypothesis of conceptual consolidation, and the co-occurrence supergraph is shown in the center, illustrating the relationships between these terms, where each node corresponds to a term, and the size of the node is proportional to its centrality, while the edges represent the relationships between these terms, with the color bar ranging from blue (weak) to red (strong), and with line thickness increasing with the co-occurrence of the corresponding terms. Together, these layers of analysis describe not only the surge of scientific output but the semantic structure underlying the evolution of contemporary precision radiotherapy, where cellular mechanisms, clinical end-points, and technological parameters are integrated to translate into progress.

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Additional terms, such as *proton, irradi, brachytherapy, repair, dna, toxicity,* and *response*, refer to molecular mechanisms and emerging techniques, while *surviv, risk, model,* and *outcome* emphasize prognosis, and *clinic, trial, meta,* and *evalu* indicate the prevalence of translational trials.

The lower panel depicts the top ten most frequent terms across years, and cell is the most frequent term, with >550 occurrences in 2020, which reflects the high number of cellular/molecular investigations, and terms such as radiat, patient, dose, cancer, treatment, tumor, and radiotherapi increased in parallel between 2015 and 2023, because they are closely related to the main topics of the field. Effect and clinic increased gradually, reflecting increasing efforts on therapeutic effects and clinics, and thus they are important for the development of the field.

Collectively, this indicates limited vocabulary use until the early 1990s, followed by gradual increase, and a sharp increase after 2010, which correlates with the development and consolidation of the field, and so the field has undergone significant changes over the years. Following text preprocessing, Latent Dirichlet Allocation (LDA) was performed using $k = 10$ *topics*, with lemmatization, biomedical stopword filtering, and frequency trimming (no_below=2–5, no_above=0.5) to ensure vocabulary stability. Models were trained separately for titles and abstracts (passes = 10, random_state = 42), and validated through inspection of word distributions and stability across runs. The top 20 LDA-derived keywords were subsequently used to construct the co-occurrence supergraph, providing a quantitative foundation for thematic mapping. Titles included head and neck, breast, and prostate cancer; adverse effects; image-guided planning; and highly conformal treatment, while abstracts included DNA damage and repair; dose-response modeling; clinical trials; immunoradiotherapy; and normal tissue adverse effects, therefore the topics covered a wide range of subjects. For each topic cluster, word association maps were created using the 20 most probable words, and these maps were integrated into a single large map, which thus provided a comprehensive overview of the field. Main nodes were radiotherapy, tumor, DNA repair, and adverse effects, and all files (CSV, SVG, PNG) were generated for visualization in Gephi and topological analysis, therefore the results can be easily visualized and analyzed. Yearly word counts and smoothed frequency curves indicated sustained growth in the most prominent biology and technology concepts, which is a significant finding.

This has led to an increasingly interdisciplinary field linking radiotherapy, radiobiology and oncology, with reciprocal interactions between technological developments, cellular processes and clinical practice, and so the field has become more complex and multidisciplinary. The approach emphasizes repeatability, transparency and reproducibility of methods to ensure the interpretability and verifiability of findings, therefore it is essential for the development of the field. Briefly, LDA was applied to the titles and abstracts of the 3,343 non-duplicate publications, identifying 10 topics for each corpus, reflecting the broad scope of a literature that encompasses radiotherapy, radiobiology and oncology, and full counts and model parameters are presented in Equations 1-20 of the Supplementary Information, which thus provides a detailed description of the methodology and results.

In the titles, topics ranged from clinical and anatomical foci to molecular mechanisms and technical approaches. **Topic_0t**, dominated by *cancer, radiotherapy, patient, head, neck, breast,* and *prostate*, underscores the concentration on specific tumor types treated with radiotherapy, including advanced cases and toxicity. **Topic_1t** highlights *radiobiology, clinical,* and *oncology*, indicating the integration of biological foundations with clinical practice. **Topic_2t** clusters *cancer, breast, carcinoma, prostate,* and *esophageal*, characterizing comparative studies. **Topic_3t** emphasizes *radiation, oncology, biology,* and *molecular*, reflecting interest in the mechanisms of radiation action. **Topic_4t**, centered on *stereotactic, body, radiosurgery,* and *lung*, captures the SBRT literature in pulmonary neoplasms. **Topic_5t** addresses *radiation, beam, ion,* and *proton*, underscoring dose delivery physics and tissue protection. **Topic_6t**, with *tumor, brain, model,* and *imaging*, points to modeling and preclinical studies of brain tumors. **Topic_7t** organizes *tumor, cell, DNA, repair,* and *pathway*, reflecting the molecular biology of DNA damage. **Topic_8t**, dominated by *cell, human, expression,* and *gene*, refers to in vitro

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experimentation. Finally, **Topic_9t**, with *dose, brachytherapy, model,* and *radiobiological*, is associated with dose modeling and brachytherapy.

In the abstracts, methodological granularity is greater. **Topic_0a**, with *model, dose, imaging,* and *flash*, suggests imaging-based modeling and planning for FLASH-RT. **Topic_1a**, centered on *cell, tumor, DNA, repair,* and *damage*, focuses on the biological mechanisms of radiation. **Topic_2a**, with *proton, ion, RBE,* and *particle*, delineates the literature on particle therapies. **Topic_3a**, clustering *patient, survival, RT,* and *surgery*, reflects prognostic clinical studies. **Topic_4a**, with *toxicity, breast, risk, Gy,* and *SBRT*, addresses toxicity in breast cancer patients treated with precision radiotherapy. **Topic_5a**, highlighting *trial, immunotherapy, preclinical,* and *targeted*, points to the rise of immunoradiotherapy and combination therapies. **Topic_6a**, with *expression, gene, protein,* and *blood*, characterizes research on molecular biomarkers. **Topic_7a**, with *dose, Gy, plan,* and *mouse*, refers to preclinical trials and validation in animal models. **Topic_8a**, dominated by generic terms such as *clinical, therapy, oncology,* and *development*, likely reflects institutional or editorial texts. Finally, **Topic_9a**, with *dose, fraction, tissue,* and *effect*, emphasizes studies on dose fractionation in normal tissues.

The thematic landscape emerging from our analyses is two-dimensional. It consists of interdependent clinical-anatomical and mechanistic-molecular axes, because the clinical-anatomical axis encompasses disease sites, therapeutic modalities, and patient-centered outcomes, including survival and toxicity. In contrast, the mechanistic-molecular axis encompasses cellular responses to ionizing radiation, DNA damage and repair pathways, gene expression programs, and biomarker development. The overlap of the axes is not coincidental; rather, it represents a truly translational ecosystem where conceptual and experimental advances are translated into clinical decision-making, and, reciprocally, clinical needs drive mechanistic inquiry. Consequently, several novel fronts have been gathering steam within this matrix, including ultrafast radiotherapy (FLASH-RT), immunoradiotherapy, individualized predictive modeling, and the routine inclusion of molecular biomarkers. Collectively, these fronts constitute a precise, forward-looking map of how the field is maturing and where it is headed; therefore, the co-occurrence supergraph (Fig. 1 inset) denotes the semantic backbone of the literature encompassing radiotherapy, radiobiology, and oncology.

In the graph, nodes represent keywords extracted from titles, abstracts, and descriptors, while edges encode the frequency of co-occurrence. Edges are visually weighted according to connection strength: thicker, reddish edges correspond to stronger semantic relations (as among cancer, radiotherapy, tumor, and particle), while thinner, bluish edges correspond to weaker associations. From a topological perspective, the network is dense and cohesive, displaying a density of 0.5, a diameter of 1, an average degree of 9.5, and an average weighted degree of 1962.2, reflecting intense co-occurrence relationships. A mean clustering coefficient of 0.5 with 1140 triangles reveals substantial local cohesion, while a low modularity of 0.02 and a single weakly connected component indicate a highly integrated thematic space.

All network metrics were computed in Gephi using a directed, weighted setup, which means the numeric ranges are shifted, and hence why diameter = 1 and density = 0.5 correspond to the directed adjacency definition and not a fully connected graph, because the weighted degree is a count of total co-occurrence, which is why these values are higher than unweighted degrees. Together with low modularity and high clustering, the metrics paint a picture of a tight but non-trivial lexical network, i.e. evidence of thematic convergence without the network collapsing into a single blob. However, when we re-ran the analysis on an undirected, thresholded version of the data, we found the relative ordering of important nodes and communities to be essentially unchanged, with a Pearson correlation coefficient greater than 0.9, which therefore supports the robustness of our interpretation.

From a practical point of view, the literature has converged into a single, integrated domain rather than a collection of disconnected subfields; thus, it is well positioned for efficient knowledge transfer. The primary node in this topology is cancer, closely connected to tumor, radiotherapy,

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particle, and breast, while technical subfields (proton, stereotactic, imaging) are peripherally located yet act as anchors for technological and methodological development.

When mapped onto term frequency curves over time, the topology confirms an increasing frequency of terms starting in the 2000s and accelerating after 2010, mirroring the overall surge in biomedical research. Key terms (*cell*, *cancer*, *dose*, *treatment*, *r*adiotherapy) have expanded sharply, confirming their central role. The consistency between temporal dynamics and network topology reinforces the centrality of cancer and radiotherapy, while highlighting the growing prominence of molecular response terms (DNA, repair), clinical outcome terms (survival, toxicity), and technical parameters (dose, fraction).

In aggregate, this literature is characterized by strong interdependencies among clinical, molecular, and technological concepts, without rigid semantic boundaries. Therefore, this consolidation implies efficient knowledge transfer across scales—from DNA repair pathways to dose planning and patient outcomes. Practically, the supergraph provides a decision-ready analytical tool to frame systematic reviews, identify underexplored clusters, and guide targeted literature mining strategies in oncological radiotherapy. Thus, the semantic cohesion of the field is not only descriptive but functional, furnishing a robust and verifiable backbone for a continuously learning, precision-oriented radiotherapy ecosystem capable of integrating emerging innovations such as FLASH-RT, immunoradiotherapy, and biomarker-driven personalization.

From this integration, four main hypotheses emerge: (1) cancer and radiotherapy function as structuring axes of recent scientific production; (2) the growth of terms such as cell, dose, effect, and treatment reflects the emphasis on therapeutic personalization, mechanisms of action, and clinical efficacy; (3) the co-occurrence of tumor, DNA, repair, and survival indicates intensified research in precision medicine and response biomarkers; and (4) the densely connected network confirms the transversal nature of the field, integrating molecular biology, medical physics, and clinical practice within a unified scientific ecology.

We iterated these hypotheses to inform the search strategies used to locate research at the interface of radiotherapy, radiobiology, and oncology. In Scopus, we searched titles, abstracts, and author keywords for records that are limited to biomedical subject areas, and from post-2014, which retrieved 25 records, and in PubMed, we combined MeSH with broad field searches and limited results to 2015-2024, and to clinical or translational publication types, which retrieved 10 records. Together, the refined search strategies maximised specificity and translational relevance to precision radiotherapy, and thus limited the resulting corpus to studies that are most likely to inform precision radiotherapy. In Web of Science, the query applied to the abstract field yielded 35 documents. After automated deduplication by DOI and title, the records were consolidated into a corpus of 61 articles, representing an analytical set centered on the molecular, therapeutic, and clinical trends of contemporary radiobiological oncology. This corpus serves to empirically validate the thematic and structural hypotheses identified through semantic analyses, providing a solid foundation for the investigation of high-impact case studies.

Semantic analysis of the corpus by Latent Dirichlet Allocation (LDA) reveals a three-part thematic structure, and when combined, topics extracted from titles collapse into three separate themes. The first theme is translational, with terms such as *radiotherapy, effect, cell, combination, metastatic,* and *clinical*, and corresponds to work that bridges combined therapeutic approaches in cellular systems with clinical trials. The second theme is biomarkers, with terms such as *cancer, patient, trial, biomarkers, hypoxia,* and *radiosensitivity*, and corresponds to work that bridges molecular signatures and microenvironmental factors with outcomes such as response and toxicity, while the third theme is mechanistic, with terms such as *model, tissue, flash, normal, genomics,* and *learning*, and corresponds to work that applies radiobiological modeling and machine learning to predict tissue responses, including under ultrafast dose-rate conditions, such as FLASH radiotherapy. Together, these three themes suggest a field that seamlessly bridges laboratory findings, molecular profiling, and clinical practice, while also developing data-driven approaches to predict and improve patient outcomes.

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The analysis of abstracts confirms this tripartite thematic segmentation while adding a more refined methodological layer. Terms such as response, damage, DNA, repair, radiosensitivity, and cellular reinforce the focus on molecular responses to radiation, whereas words like parameter, model, radiobiological, high, and biological indicate the development and calibration of quantitative models. At the same time, expressions such as dose, risk, volume, and fractionation point to the optimization of dosing schemes. The consistent presence of signature, hypoxia, biomarker, and median cohort reveals the adoption of genomic signatures and clinical cohort analyses as predictive tools.

Co-occurrence analysis of the top 20 seed terms with the highest probability, such as prediction, parameter, radiobiology, vitro, biology, personalized, protocol, effect, response, and cancer, revealed densely connected graphs, and terms like response, cancer, normal, and radiobiology were found to be high-centrality bridge terms that linked clinical themes, including patient outcomes, protocols, and therapeutic effects, and mechanistic themes, including cellular responses, radiobiological parameters, and in vitro evidence. In a practical sense, these nodes are semantic hinges that orient experimental modeling and biological insight towards clinical application, thereby weaving together disparate strands of the literature into a cohesive translational narrative.

To refine the selection of the most relevant articles for case studies, priority was given to expressions that simultaneously encompass molecular dimensions, clinical applications, and therapeutic innovation. Terms in titles and abstracts corresponding to the translational and mechanistic cores of the field (e.g. *biomarker signature, radiosensitivity, DNA repair, hypoxia-induced, FLASH radiotherapy, dose-response model, genomic classifier, precision oncology, radioresistance, therapeutic window, combined modality, clinical trial phase, translational framework, machine-learning prediction, brachytherapy dose escalation*) were combined, so as to reflect the temporal evolution of the frequency curves and the density of the semantic supergraph, thus ensuring that the extracted literature remains closely connected to the thematic axes generated by the computational analysis, and this strategy prevented the search from spreading away from the literature that bridges molecular mechanisms and clinical decision-making as well as technological implementation.

A total of 28 out of the 61 documents met the predefined criteria, namely those that mentioned in their titles or abstracts at least one of the fifteen recommended key expressions: *biomarker signature, radiosensitivity, DNA repair, hypoxia-induced, flash radiotherapy, dose–response model, genomic classifier, precision oncology, radioresistance, therapeutic window, combined modality, clinical trial phase, translational framework, machine-learning prediction,* or *brachytherapy dose escalation*. Documents lacking a DOI or equivalent identifier, as well as those outside the 2014–2025 timeframe, were excluded from the analysis. **Table 1** presents the selected documents, indicating year of publication, identified terms, and the corresponding numerical classes assigned according to the established thematic axes [37–62].

Screening was conducted using a Python script that loaded the consolidated records, removed duplicates, and systematically examined the title and abstract fields. The algorithm applied a lexical search function, converting texts to lowercase and checking, term by term, for the exact presence of expressions defined from LDA modeling and the most relevant co-occurrence patterns. For each record, lists of identified terms were generated and subsequently unified into a new column, enabling structured thematic analysis. The documents were then classified into one or more of the five main classes: DNA repair and molecular response, precision oncology and genomic models, individual radiosensitivity, tumor radioresistance, and emerging technologies in radiotherapy.

Each document group was analyzed individually using the *PaperProcessor* [100] script, which performs semantic extraction and summarization guided by large language models (LLMs). The process is directed by the *subject* parameter, which steers the thematic interpretation of each textual segment. To ensure analytical coherence and conceptual focus, the *subject* was adapted to the nature of each document class. In the first four classes, focused on molecular mechanisms, genomic stratification, clinical variability, and tumor resistance, open and interpretative prompts were used to generate explanatory syntheses, mechanistic articulations, and conceptual inferences. The fifth class, dedicated to technological innovation in areas such as FLASH radiotherapy, heavy charged

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particles, and voxel-level analytics, was conceived to clarify the underlying physical principles, the design of delivery systems, and the first steps toward clinical application. This structure enabled a balanced and interpretative reading of the literature supported by artificial intelligence.

Even though large language models (LLMs) are central to the semantic synthesis stage, their use within the PaperProcessor pipeline is carefully bounded by independent preprocessing, normalization, and statistical validation steps. This layered design ensures methodological transparency: all prompts are fixed and stored in the source code, allowing for external auditing and exact reproducibility of each run. Each model inference is time-stamped and logged to a CSV file to create a complete auditable record of all outputs, and at the same time, an independent unsupervised topic modeling check using Latent Dirichlet Allocation (LDA) is performed to provide confirmation that the themes are consistent across all the documents. Together, these steps help minimize interpretive bias and ensure that the AI synthesis is evidence-based, transparent, and reproducible.

Table 1. Selected studies based on key expressions and thematic classification.

#	DOI	Title	Reference	Year	Terms Found	Classes *
1	10.1007/s12553-024-00895-y	Current trends and future perspectives in hadron therapy: radiobiology	[101]	2024	DNA repair	[1]
2	10.3389/fonc.2021.687672	The Time for Chronotherapy in Radiation Oncology	[102]	2021	DNA repair	[1]
3	10.1667/RADE-24-00037.1	What's changed in 75 years of RadRes? - An australian perspective on selected topics	[103]	2024	DNA repair	[1]
4	10.3389/fnano.2025.1603334	Radiobiological perspective on metrics for quantifying dose enhancement effects of High-Z nanoparticles	[104]	2025	DNA repair, precision oncology	[1, 2]
5	10.1016/j.clon.2021.09.003	Can Rational Combination of Ultra-high Dose Rate FLASH Radiotherapy with Immunotherapy Provide a Novel Approach to Cancer Treatment?	[105]	2021	flash radiotherapy	[5]
6	10.1016/j.canlet.2025.217895	Unraveling the dual nature of FLASH radiotherapy: From normal tissue sparing to tumor control	[15]	2025	flash radiotherapy, radiosensitivity	[5, 3]
7	10.18632/oncotarget.10996	Next generation multi-scale biophysical characterization of high precision cancer particle radiotherapy using clinical proton, helium-, carbon- and oxygen ion beams	[106]	2016	precision oncology	[2]
8	10.3390/ijms26136375	Radiation Therapy Personalization in Cancer Treatment: Strategies and Perspectives	[107]	2025	precision oncology	[2]
9	10.1080/14737140.2018.1458615	The effects of radiotherapy on the survival of patients with unresectable non-small cell lung cancer	[108]	2018	precision oncology	[2]
10	10.1016/j.hoc.2019.07.001	Toward a New Framework for Clinical Radiation Biology	[109]	2019	precision oncology	[2]
11	10.1016/S0007-4551(18)30383-7	Kidney cancer and radiotherapy: Radioresistance and beyond	[110]	2018	radioresistance	[4]
12	10.1093/jrr/rrz048	Carbon-ion irradiation overcomes HPV-integration/E2 gene-disruption induced radioresistance of cervical keratinocytes	[111]	2019	radioresistance, radiosensitivity	[4, 3]
13	10.1016/j.radonc.2022.08.001	Accurate prediction of long-term risk of biochemical failure after salvage radiotherapy including the impact of pelvic node irradiation	[112]	2022	radiosensitivity	[3]
14	10.1186/s13014-024-02566-8	Alpha/beta values in pediatric medulloblastoma: implications for tailored approaches in radiation oncology	[113]	2025	radiosensitivity	[3]

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15	10.32471/exp-oncology.2312-8852.vol-43-no-3.16554	Can SARS-CoV-2 change individual radiation sensitivity of the patients recovered from COVID-19? (experimental and theoretical background).	[114]	2021	radiosensitivity	[3]
16	10.3390/cells12030360	Comparison of Radiation Response between 2D and 3D Cell Culture Models of Different Human Cancer Cell Lines	[115]	2023	radiosensitivity	[3]
17	10.2298/SARH220131085N	Current aspects of radiobiology in modern radiotherapy – our clinical experience	[116]	2022	radiosensitivity	[3]
18	10.1002/mp.13751	Genomics models in radiotherapy: From mechanistic to machine learning	[117]	2020	radiosensitivity	[3]
19	10.1016/j.rpor.2014.11.006	Hypersensitivity to chemoradiation in FANCA carrier with cervical carcinoma-A case report and review of the literature.	[118]	2015	radiosensitivity	[3]
20	10.3390/cancers8030028	Paradigm Shift in Radiation Biology/Radiation Oncology Exploitation of the H2O2 Effect for Radiotherapy Using Low-LET (Linear Energy Transfer) Radiation such as X-rays and High-Energy Electrons	[119]	2016	radiosensitivity	[3]
21	10.1259/bjr.20170949	Radiation biology and oncology in the genomic era	[120]	2018	radiosensitivity	[3]
22	10.1088/1361-6560/aac814	Radiobiological parameters in a tumour control probability model for prostate cancer LDR brachytherapy	[121]	2018	radiosensitivity	[3]
23	10.1136/bmjopen-2021-059345	The COMPLETE trial: HolistiC early respOnse assessMent for oroPharyngeaL cancEr paTiEnts; Protocol for an observational study	[122]	2022	radiosensitivity	[3]
24	10.1016/j.radonc.2023.109868	Voxel-based analysis: Roadmap for clinical translation	[123]	2023	radiosensitivity	[3]
25	10.1002/cnr2.1126	Progressive breast fibrosis caused by extreme radiosensitivity: Oncocytogenetic diagnosis and treatment by reconstructive flap surgery.	[124]	2019	radiosensitivity, DNA repair	[3, 1]
26	10.1002/mp.15177	Radiobiological comparison between Cobalt-60 and Iridium-192 high-dose-rate brachytherapy sources: Part I—cervical cancer	[125]	2021	radiosensitivity, hypoxia-induced	[3, 5]
27	10.1016/j.ijrobp.2015.11.013	Influence of Nucleoshuttling of the ATM Protein in the Healthy Tissues Response to Radiation Therapy: Toward a Molecular Classification of Human Radiosensitivity	[126]	2016	radiosensitivity, radioresistance	[3, 4]
28	10.3390/proteomes13020025	Deciphering Radiotherapy Resistance: A Proteomic Perspective	[127]	2025	radiosensitivity, radioresistance, DNA repair, precision oncology	[3, 4, 1, 2]

* Classes: (1) DNA repair, (2) Precision oncology, (3) Radiosensitivity, (4) Radioresistance, and (5) Flash radiotherapy.

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By analyzing these elements together, the study made the physical foundations of the techniques more tangible through models and quantitative metrics, while the examination of device architectures and workflow constraints provided a realistic perspective on feasibility. Early clinical findings offered valuable reference points for assessing translational potential. In this way, the discussion remained coherent and comparative, reflecting the main thematic axes of oncological radiotherapy, both clinical and molecular, and showing how technological innovation acts as a connecting element that integrates these two dimensions within contemporary practice.

The questions used as *subject*, according to each thematic class, were as follows:

Classe 1 – DNA Repair and Molecular Response: *What are the key molecular responses to radiation discussed in the document, including DNA damage signaling, DNA repair pathways, and checkpoint activation mechanisms?*

Classe 2 – Precision Oncology and Genomic Modeling: *How does the document address precision oncology, including the use of genomic profiling, machine learning models, and patient stratification in radiation therapy?*

Classe 3 – Individual Radiosensitivity and Clinical Risk: *What evidence does the document present on interindividual radiosensitivity, clinical risk assessment, and predictive biomarkers for radiation response?*

Classe 4 – Radioresistance and Associated Mechanisms: *What mechanisms of radioresistance are described in the document, including tumor hypoxia, metabolic reprogramming, stem cells, and viral integration?*

Classe 5 – Advanced Technologies and Innovative Radiotherapy: *How does the document explore advanced radiotherapy strategies, including FLASH, hadron therapy, voxel-based analysis, and dose enhancement with high-Z nanoparticles?*

Cosine similarity is a measure of the extent to which two texts point in the same direction in feature space, and for non-negative representations (such as TF-IDF), it ranges from 0 (the texts share no terms and are therefore unrelated) to 1 (the texts have maximal lexical or semantic overlap). For the 37 text pairs compared here, cosine similarity scores ranged from 0.291 to 0.669 (span of ~0.378), with an overall mean of 0.5235 0.0271 (95% CI: 0.4964-0.5506), which indicates a moderate degree of similarity between the outputs of Llama3 (8B) and GPT-4o. This moderate degree of similarity is further broken down by class, where we find the following: Class 1 (n = 6): 0.4693 0.1542 (0.3151-0.6235), Class 2 (n = 6): 0.5387 0.0439 (0.4948-0.5826), Class 3 (n = 18): 0.5520 0.0289 (0.5231-0.5810), Class 4 (n = 4): 0.4592 0.0869 (0.3723-0.5460), and Class 5 (n = 3): 0.5167 0.2541 (0.2626-0.7708), and these classes show that Classes 2 and 3 have the highest means with the tightest confidence intervals, suggesting that Llama3 (8B) is able to reliably reproduce GPT-4o content in those domains, while Classes 1 and 4 have lower averages with wider intervals, indicating greater thematic or stylistic variability and sensitivity to domain-specific terminology, and Class 5 is inconclusive due to its very small sample size and wide uncertainty.

Cosine similarity was used as a robustness check only to compare lexical and semantic congruence between two LLMs, given the same prompts, because it measured congruence, but did not influence any bibliometric or clinical inferences. The mean similarity value of ~0.52 provides evidence for moderate cross-model reproducibility, and thereby, methodological robustness, and consequently, no hybrid inference or model fusion was performed; instead, the outputs were compared for completeness and terminological accuracy, prior to manual curation. The notation "Llama → GPT-4o" reflects only the editorial workflow (i.e., Llama3 generated the first draft and GPT-4o refined the language)without altering any analytic results, which improved clarity, consistency, and readability, while maintaining all quantitative and bibliometric content. While Llama3 remains a useful tool for fully offline analyses, which are important for data security and sovereignty, the comparison provided here demonstrates cross-model consistency, rather than hybrid modeling, and therefore serves to strengthen transparency and reproducibility in the pipeline, thus maintaining the integrity of the results.

3.1. CASE STUDIES

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Class 1 studies (DNA Repair and Molecular Response) focus on the molecular mechanisms of radiation response, including DNA repair, checkpoint regulation, and therapeutic modulation. Norbert Mészáros et al. (2019) [124] reported progressive breast fibrosis in patients with extreme radiosensitivity, associated with high rates of chromosomal aberrations, supporting the use of cytogenetic tests for risk stratification. Luis Bermúdez-Guzmán *et al.* (2021) [102] demonstrated that chronoradiotherapy, by aligning dose delivery with the circadian rhythms of genes such as *BMAL1, CLOCK, PER,* and *CRY*, accelerates DNA break resolution and reduces toxicity. Michael D. Story *et al.* (2024) [101] showed that high-LET radiation induces complex lesions and activates the cGAS–STING pathway, with radiosensitization enhanced by inhibitors of HR, NHEJ, ATM, and ATR. Olga A. Martin *et al.* (2024) [103] reviewed 75 years of radiobiology, highlighting the impact of radiation quality on γH2AX persistence and the tumor microenvironment. Davide Perico and Pierluigi Mauri (2025) [127] correlated the overexpression of *RAD51* and *BRCA1* and the hyperactivation of NHEJ with radioresistance, while Yan Luo (2025) [104] demonstrated that high-Z nanoparticles amplify damage and reactive species, proposing standardization of metrics such as NER and SER.

Class 2 (Precision Oncology and Genomic Modeling). Ivana Dokic *et al.* (2016) [106] used ion beams and the Cell-Fit-HD technology to demonstrate that the persistence of γH2AX foci after 72h is a stronger biomarker of radiosensitivity than the initial lesion count, suggesting the development of biodosimetric repositories. Paolo Tini *et al.* (2018) [108], analyzing 17,412 cases of lung carcinoma, showed that radiotherapy provides the greatest benefit in advanced stages and squamous histology, advocating for the integration of molecular data. Henning Willers *et al.* (2019) [109] proposed the use of RSI and GARD to guide personalized dosing. Perico and Mauri (2025) [127] identified proteins such as RAD51, PARP1, CHK1, and MAPK15 as associated with resistance, while Marco Calvaruso *et al.* (2025) [107] argued for multi-omic biomarkers and artificial intelligence to predict treatment response. Yan Luo (2025) [104] developed a multidimensional index for high-Z nanoparticles, incorporating biological variability and immune modulation.

Class 3 (Individual Radiosensitivity and Clinical Risk) gathered the largest number of studies. Igor Sirák *et al.* (2015) [118] reported *FANCA* mutations associated with severe toxicities, while Adeline Granzotto *et al.* (2016) [126] identified ATM nucleoshuttling kinetics as a functional marker. Yasuhiro Ogawa (2016) [119] introduced KORTUC II as a radiosensitizer based on H_2O_2. Sarah L. Kerns *et al.* (2018) [120] reviewed the use of RSI and GARD, and E.J. Her *et al.* (2018) [121] modeled TCP for prostate brachytherapy. Nathalie Arians *et al.* (2019) [111] demonstrated that carbon ions overcome HPV-induced resistance. Mészáros *et al.* (2019) [124] correlated cytogenetic profiles with severe fibrosis. John Kang *et al.* (2020) [117] reviewed genomic and machine learning models, while Chekhun and Domina (2021) [114] suggested that COVID-19 may increase radiosensitivity. Dayyani *et al.* (2021) [125] compared ^{60}Co and ^{192}Ir in cervical brachytherapy, and Cesare Cozzarini *et al.* (2022) [112] developed a TCP model validated in 795 post-prostatectomy patients. Nikitović and Stanojković (2022) [116] linked microRNAs and cytokines to prostate cancer toxicity. Verduijn *et al.* (2022) [122] developed the COMPLETE protocol, integrating multiparametric imaging, omics data, and machine learning. Raitanen *et al.* (2023) [115] showed greater radioresistance in 3D spheroids, while McWilliam *et al.* (2023) [123] highlighted voxel-based analysis to map critical regions. Jazmati *et al.* (2025) [113] assessed pediatric medulloblastoma, identifying homogeneous α/β values. Perico and Mauri (2025) [127] emphasized proteomics for identifying radioresistance profiles, and Guo *et al.* (2025) [15] reviewed mechanisms of FLASH-RT, including oxygen depletion and mitochondrial preservation, highlighting its integration with immunotherapy.

Class 4 (Radioresistance and Associated Mechanisms). Granzotto *et al.* (2016) [126] linked delayed ATM nucleoshuttling to radioresistance. Mery *et al.* (2018) [110] showed that *VHL* mutations induce pseudohypoxia in renal carcinoma through HIF activation, suggesting carbon ions and repair inhibitors as therapeutic options. Arians *et al.* (2019) [111] demonstrated that carbon ions restore checkpoint control in HPV-positive cervical tumors with disrupted *E2*, with RBE values ranging from 1.3 to 4.3. Perico and Mauri (2025) [127] integrated pathways of hypoxia, metabolism, stemness, viral

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integration, and apoptosis evasion into proteomic maps, advocating their use for biomarker discovery and selective therapies.

Class 5 (Advanced Technologies and Innovative Radiotherapy) addresses the adoption of cutting-edge modalities. Zhang *et al.* (2021) [105] investigated FLASH-RT (≥40 Gy/s), showing comparable efficacy to conventional radiotherapy but with enhanced tissue preservation and immune modulation, including lymphocyte sparing and tumor remodeling with increased $CD8^+$ infiltration. Dayyani *et al.* (2021) [125] compared ^{60}Co and ^{192}Ir in cervical cancer, concluding that both can be used with dose adjustments, with physical advantages of ^{60}Co and higher RBE for ^{192}Ir. Guo *et al.* (2025) [15] further explored the mechanisms of FLASH-RT, such as free radical modulation, mitochondrial preservation, and vascular integrity, emphasizing the need for dosimetric standardization and voxel-based mapping. Collectively, these studies consolidate the integration of FLASH-RT and optimized brachytherapy into next-generation personalized protocols.

The synthesis of the case studies presented above provides the scientific foundation for structuring the **Integrated Implementation Plan in Precision Radiotherapy**. Each class analyzed—from DNA molecular response to the adoption of innovative technologies such as FLASH-RT—revealed mechanisms, biomarkers, models, and strategies directly translatable into personalized clinical protocols. By organizing these findings into five interdependent operational blocks, the plan transforms experimental and translational evidence into a continuous flow of investigation, validation, and clinical application, establishing a framework capable of supporting both individual therapeutic advances and the incorporation of objective indicators into public health policies.

3.2. IMPLEMENTATION PLAN IN PRECISION RADIOTHERAPY

The **Integrated Implementation Plan in Precision Radiotherapy (IIPPR)** is organized into five classes that structure a continuous flow of investigation, validation, and clinical application, with the potential for direct integration into public health policies. **Class 1 – DNA Repair and Molecular Response** constitutes the operational block responsible for establishing the molecular and functional foundation upon which all subsequent stages are built. Its objective is to identify DNA repair mechanisms, regulate checkpoints, and characterize signaling pathways that determine each patient's response to radiation. This step provides indispensable biomarkers and functional parameters for therapeutic personalization, enabling biologically precise decisions regarding technique, dose, fractionation, and adjuvant combinations from the outset of the workflow. Implementation requires functional assays, omics analyses, and molecular modeling at multiple levels of complexity.

Norbert Mészáros *et al.* (2019) [124] reported that patients with progressive radiation-induced breast fibrosis exhibited high frequencies of chromosomal aberrations even in non-irradiated cells, demonstrating that genomic instability and persistent checkpoint failures can be detected cytogenetically and used as predictive tools. Temporal modulation strategies, as shown by Luis Bermúdez-Guzmán *et al.* (2021) [102], revealed that synchronizing irradiation with circadian phases of maximal repair activity accelerates the resolution of double-strand breaks and enhances the efficiency of HR, NHEJ, NER, and BER, reducing toxicity and improving efficacy. Michael D. Story *et al.* (2024) [101] demonstrated that high-LET radiation, such as that used in hadron therapy, induces complex lesions and activates immune pathways via cGAS–STING, whose radiosensitizing potential can be amplified by pharmacological inhibition of HR, NHEJ, ATM, and ATR. The review by Olga A. Martin *et al.* (2024) [103] consolidated the relevance of radiation quality in the persistence of γH2AX, remodeling of the tumor microenvironment, and integration with immunotherapy. Davide Perico and Pierluigi Mauri (2025) [127] highlighted proteomic integration as a tool to identify functional profiles of key proteins associated with radioresistance, while Yan Luo (2025) [104] demonstrated that high-Z nanoparticles enhance radiosensitization by overloading repair pathways, with standardization in metrics such as NER and SER.

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The central action of this class is to integrate different levels of molecular and functional information into a validated panel of predictive biomarkers, delivering to subsequent phases a comprehensive map of tumor vulnerabilities and the repair limitations of normal tissues.

Class 2 – Precision Oncology and Genomic Modeling transforms molecular and radiobiological data into parameters guiding the choice of technique, dose, and fractionation, replacing empirical protocols with personalized prescriptions. Ivana Dokic *et al.* (2016) [106], using Cell-Fit-HD technology, showed that repair kinetics is a more robust marker than initial lesion count and proposed biodosimetric repositories to support biological prescriptions. In a population-based analysis, Paolo Tini *et al.* (2018) [108] examined 17,412 cases of non-small cell lung carcinoma and demonstrated the need to integrate genomic markers and predictive models to improve patient selection. Henning Willers *et al.* (2019) [109] proposed indices such as RSI and GARD to calibrate dose based on gene expression, dosimetry, and imaging, further integrating immunotherapy and real-time adjustments. Davide Perico and Pierluigi Mauri (2025) [127] added functional proteomic layers to stratification, identifying proteins such as RAD51, PARP1, CHK1, and MAPK15, thereby enhancing predictive power when combined with transcriptomic data. Marco Calvaruso *et al.* (2025) [107] demonstrated that multi-omic biomarkers, combined with FLASH-RT and predictive algorithms, enable fine-tuning of intensity and technique while minimizing toxicity. Yan Luo (2025) [104] developed a multidimensional index integrating biological variability, immune modulation, and DER, SER, and RBE metrics. Recent advances in endometrial cancer research highlight the role of genomic modeling in improving radiotherapy through molecular classification. The PORTEC-3 study showed that distinguishing *POLE*-mutated from *TP53*-mutated tumors predicts treatment response and prognosis, supporting adaptive dosing based on molecular phenotype. The PORTEC-4 trial is expanding this approach by integrating molecular data into therapeutic decision-making, aiming for biologically guided radiotherapy optimization. The TCGA classification defines four subtypes, *POLE*-mutated, *MMRd*, *p53abn*, and *NSMP*, each with distinct prognostic value. *POLE* and *MMRd* tumors show favorable outcomes, while *p53abn* tumors are linked to poor prognosis [128–137]. Incorporating these molecular markers into clinical workflows enables more precise, personalized radiotherapy, improving efficacy and patient outcomes. This class delivers a therapeutic plan calibrated to both tumor and patient, pre-tested in predictive simulations and ready for clinical application.

Class 3 – Individual Radiosensitivity and Clinical Risk is the block dedicated to identifying and integrating variables that define individual tolerance to radiation, adjusting therapeutic protocols according to genetic, functional, and clinical predispositions. Igor Sirák *et al.* (2015) [118] documented exacerbated toxicity in a patient with pathogenic heterozygosity in *FANCA*, while Adeline Granzotto *et al.* (2016) [126] showed that delayed nuclear translocation of ATM compromises repair—both examples of biomarkers for prior screening. Yasuhiro Ogawa (2016) [119] introduced the KORTUC II method, combining H_2O_2 modulation, and Sarah L. Kerns *et al.* (2018) [120] and John Kang *et al.* (2020) [117] explored RSI and GARD in association with TCP and NTCP models. E.J. Her *et al.* (2018) [121] highlighted the influence of α-parameter variability in brachytherapy, and Nathalie Arians *et al.* (2019) [111] demonstrated that carbon ions overcome HPV-induced resistance. Norbert Mészáros *et al.* (2019) [124] reinforced the value of cytogenetics, and V.F. Chekhun & E.A. Domina (2023) [114] expanded the discussion to systemic effects such as those associated with COVID-19. Mahdieh Dayyani *et al.* (2021) [125] compared ^{60}Co and ^{192}Ir sources in brachytherapy, while Cesare Cozzarini *et al.* (2022) [112] developed TCP models validated in post-prostatectomy cohorts. Marina Nikitović & Tatjana Stanojković (2022) [116] compiled molecular and clinical evidence, while Gerda M. Verduijn *et al.* (2022) [122] consolidated the COMPLETE protocol, integrating multiparametric imaging, radiomics, and machine learning. Recent studies expanded the translational basis with 3D spheroids (Raitanen *et al.*, 2023) [115], voxel-based mapping (McWilliam *et al.*, 2023) [123], pediatric radiobiology (Jazmati *et al.*, 2025) [113], functional proteomics (Perico & Mauri, 2025) [127], and FLASH-RT (Guo *et al.*, 2025) [15]. The central action of this class is to consolidate an individual risk

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matrix combining biomarkers and clinical data, transforming them into operational recommendations for dose, technique, and modality.

Class 4 – Radioresistance and Associated Mechanisms ocuses on identifying and neutralizing tumor mechanisms of resistance to radiation. Adeline Granzotto *et al.* (2016) [126] showed that delayed ATM phosphorylation kinetics compromises target activation, while Mery *et al.* (2018) [110] highlighted the role of hypoxia and *VHL* mutations in renal carcinoma, activating pro-survival pathways. Nathalie Arians *et al.* (2019) [111] demonstrated that in HPV-positive cervical cancer, the loss of cell-cycle control and degradation of p53 and Rb can be reversed through carbon-ion irradiation. Davide Perico and Pierluigi Mauri (2025) [127] expanded this framework through high-resolution proteomics, integrating axes of hypoxia, metabolism, stemness, viral integration, and enhanced repair. This class translates mapping into interventions such as high-LET modalities, repair inhibitors, and microenvironment modulators, effectively reversing resistant phenotypes and improving outcomes in poor-prognosis subgroups.

Class 5 – Advanced Technologies and Innovative Radiotherapy iis dedicated to the incorporation of next-generation modalities. Zhang *et al.* (2021) [105] demonstrated that ultrafast radiotherapy (FLASH-RT, ≥40 Gy/s) maintains tumor efficacy while preserving normal tissues and remodeling the immune microenvironment. Guo *et al.* (2025) [15] reinforced the clinical feasibility of FLASH-RT, identifying multiple protective mechanisms—including mitochondrial preservation and $CD8^+$ lymphocyte maintenance—provided it is accompanied by dosimetric standardization. Mahdieh Dayyani *et al.* (2021) [125] showed that the comparison of ^{60}Co and ^{192}Ir in brachytherapy allows for strategic adjustments, balancing biological efficacy and safety. This class integrates FLASH-RT, optimized brachytherapy, and voxel-based mapping into adaptive protocols that combine physical precision with biological selectivity.

The five classes together describe a pragmatic implementation plan for connecting precision radiotherapy to population-level public health delivery, and for Brazil's Unified Health System (SUS), the plan describes how standardized workflows, such as molecular diagnostics, biomarker-driven patient stratification, and adaptive radiotherapy protocols, can be implemented in a step-wise fashion, if and when clinically validated. Rather than promise immediate gains, the framework highlights the essential interfaces between biomarker discovery, dosimetric modeling, and outcome assessment, because once validated in pilot environments, these interfaces will enable more evidence-based decisions and rational distribution of limited resources.

Table 2 organizes these prospective metrics by class, describing how survival, toxicity, personalization, access, and cost-effectiveness indicators might be measured in pilot or registry-based studies. **Figure 2** presents a conceptual integration map that connects the plan's classes (blue nodes), measurable indicators (green nodes), and strategic health objectives (red nodes), illustrating a logical pathway from scientific discovery to policy evaluation rather than a proven causal link. This structure positions the plan as a dynamic and testable framework that links molecular biology, clinical radiotherapy, and health management in a coherent model open to validation through prospective cohorts and pilot programs within the SUS.

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Table 2. x – Integrated Precision Radiotherapy Plan.

Indicator	Related Plan Class(es)	Description and Measurement Method	Expected Public Health Impact
Overall survival (OS) at 1, 3, and 5 years	2, 3, 4, 5	Percentage of patients alive 1, 3, and 5 years after radiotherapy, stratified by tumor type and treatment protocol.	Improved longevity and reduction in cancer-specific mortality, particularly in high-risk tumors.
Progression-free survival (PFS)	2, 3, 4, 5	Mean time to recurrence or disease progression after personalized radiotherapy.	Greater disease control, reduced retreatment, and lower hospital costs.
Local and regional control ratel	1, 2, 3, 4	Proportion of patients without recurrence in the tumor bed or regional lymph nodes after 12 and 24 months.	Increased therapeutic efficacy and improved population prognosis.
Incidence of acute and late toxicities (grade ≥3)	1, 2, 3	Standardized reporting (RTOG/EORTC or CTCAE) of severe adverse events related to radiotherapy.	Reduced disabling side effects and improved post-treatment quality of life.
Rate of unplanned hospitalizations related to treatment	1, 3	Percentage of patients requiring emergency hospitalization due to radiotherapy complications.	Savings in hospital resources and reduced burden on inpatient units.
Percentage of patients undergoing molecular and functional stratification prior to treatment	1, 2, 3	Proportion of patients who underwent genomic, proteomic, or functional testing before radiotherapy initiation.	Greater precision in therapeutic planning and optimization of resource allocation.
Proportion of treatments with adaptive protocols	2, 3, 5	Percentage of patients whose radiotherapy plan was adjusted during treatment based on clinical response and/or biomarkers.	Reduced toxicity, improved efficacy, and more rational use of technology.
Complete and partial response rate	2, 4, 5	Percentage of patients with complete disappearance or significant reduction of tumor after treatment.	Direct indicator of personalized protocol effectiveness.
Average cost per patient with tumor control achieved	2, 5	Total treatment cost divided by the number of patients with sustained complete or partial response.	Increased economic efficiency of the public health system.
Mean hospital stay due to treatment complications	1, 3	Average number of days of hospitalization caused by radiotherapy-related adverse events..	Reduced hospital bed usage and expanded treatment capacity.
Geographic coverage of services with multi-omic and radiobiological capacity	1, 2, 3	Percentage of health regions with infrastructure for multi-omic testing and radiobiological integration.	Reduction of regional inequalities in access to advanced treatments.
Percentage of patients with access to advanced therapies in the public health system (SUS)	4, 5	Proportion of patients receiving modalities such as FLASH-RT, optimized brachytherapy, or particle therapy.	Equity in access to innovative technologies across the national territory.
Proportion of cases integrated into national registries with molecular and radiomic data	1, 2, 3, 4, 5	Percentage of patients with clinical, molecular, and imaging data stored in national repositories.	Strengthened epidemiological surveillance and translational research.

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Indicator	Related Plan Class(es)	Description and Measurement Method	Expected Public Health Impact
Utilization rate of machine learning in clinical planning	2, 3, 5	Percentage of cases planned or adjusted using validated AI models.	Standardization of evidence-based practices and increased outcome predictability.
Number of adaptive protocols validated and incorporated into national guidelines	3, 4, 5	Number of adaptive clinical protocols formally approved and implemented in the public health system	Continuous improvement of care quality and systematic technological updating.

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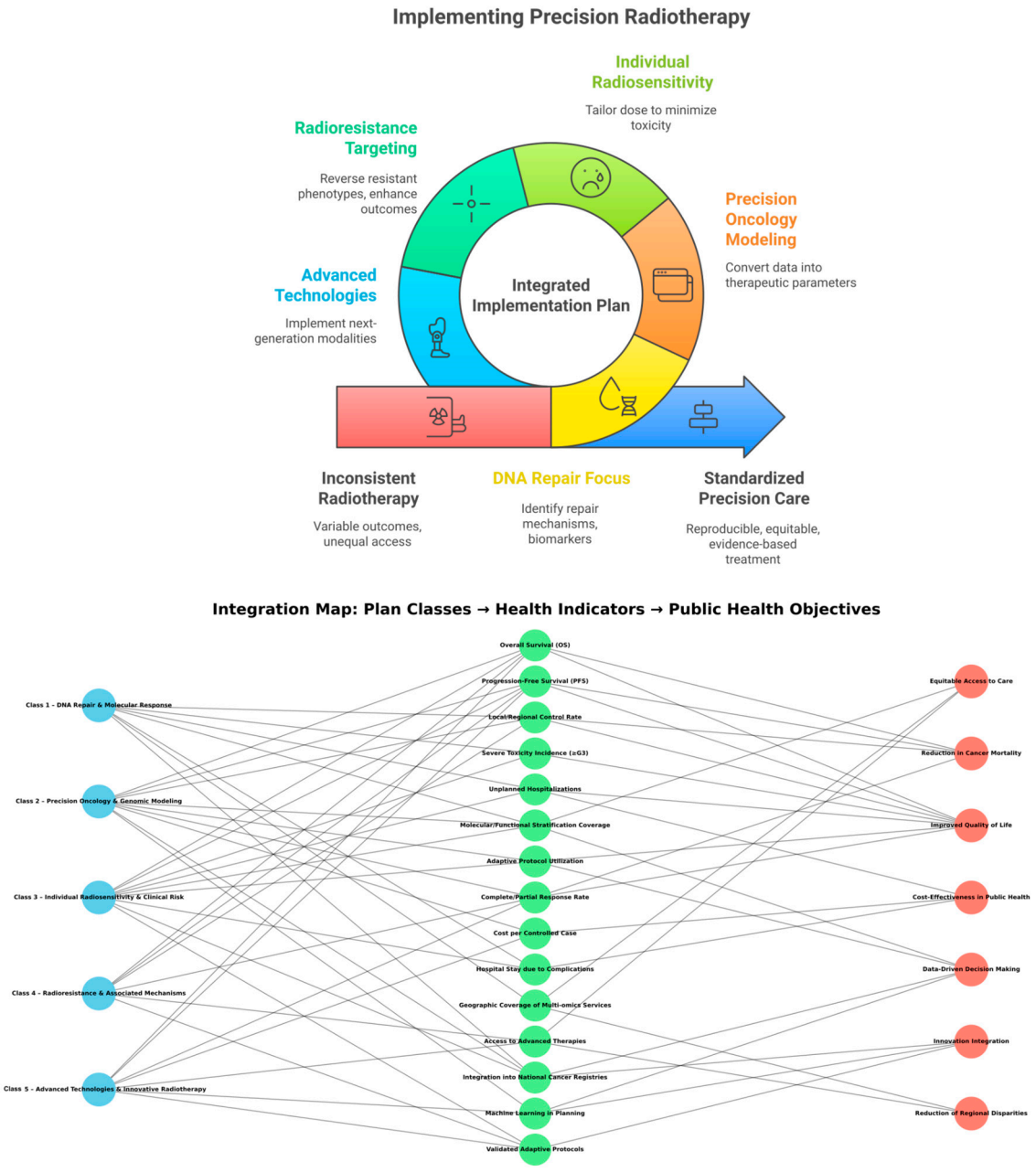

Figure 2. Integration between Plan Classes, Health Indicators, and Strategic Objectives. The figure illustrates how the five classes of the Integrated Implementation Plan in Precision Radiotherapy (blue nodes, left) connect with measurable health indicators (green nodes, center) and broader public health objectives (red nodes, right). The network highlights the translation pathway from technical and scientific actions—such as DNA repair characterization, genomic and proteomic modeling, individualized radiosensitivity assessment, targeting of radioresistance mechanisms, and adoption of advanced radiotherapy technologies—into quantifiable outcomes, including overall survival (OS), progression-free survival (PFS), local and systemic control, incidence of severe toxicity (G≥3), and cost per controlled case. These indicators converge toward collective health objectives within the Brazilian Unified Health System (SUS), promoting equitable access to care, reduced cancer mortality, improved quality of life, cost-effectiveness in oncology, data-driven decision-making, technological innovation, and the reduction of regional disparities.

3.3. Contributions, Practical Implications, Limitations, and Future Work

This paper provides a timely, simple, and humanistic account of how radiotherapy, radiobiology, and oncology have evolved and are evolving, based on the AI-based semantic and

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temporal analysis of 3,343 publications between 1964 and 2025. The most significant strength of this paper lies in its methodological integration: rigorous data cleaning and normalization (deduplication and lemmatization), powerful discovery tools (topic modeling and network analysis), and careful temporal mapping to reconstruct the conceptual architecture of the field, which, from this perspective, identifies two complementary axes that presently define the field.

The clinical-anatomical axis classifies disease sites, therapeutic modalities, and prognostic endpoints. In contrast, the mechanistic-molecular axis describes DNA damage and repair, biomarkers, and cellular radiation responses, and together, they describe a field that has matured from a collection of isolated silos into an interdependent system, where biological mechanisms and clinical decision-making inform one another in near real time.

The most practical contribution of this paper is the Precision Radiotherapy Implementation Plan, which operationalizes this integrated understanding into a practical framework, defining five classes - DNA repair and molecular response, precision oncology and genomic modeling, individual radiosensitivity and clinical risk, mechanisms of radioresistance, and innovative radiotherapy technologies - each integrating biomarkers, predictive models, and therapeutic strategies in support of individualized care.

Importantly, this is not a conceptual roadmap, but a practical bridge from data to bedside, structured to align AI-derived biological markers with real-world outcomes that matter to patients and healthcare systems: overall and progression-free survival, toxicity profile, and cost per controlled case, because, in the context of a scalability- and equity-oriented environment like Brazil's SUS, the framework describes how to integrate molecular diagnostics and predictive stratification in resource-sensitive, standardized pathways. It also describes a feasible path to the responsible implementation of high-end modalities such as FLASH-RT and hadron therapy by relating their deployment to measurable benefits and real-world feasibility.

The authors are forthright about the limitations of the study, because the dip in 2025, for instance, represents an indexing lag rather than an actual decline in research output. The authors also confined the primary analysis to 2014-2025 and used a controlled set of 15 standardised terms to keep the meanings consistent between sources, which improves internal consistency and semantic precision, but also means that the analysis captures less of the earlier historical record.

The deliberate exclusion of non-DOI records and pre-2014 literature, while improving data quality and comparability, may have omitted some historically important or recently under-indexed contributions. Nevertheless, this methodological choice has produced a clean, reusable baseline that can be expanded in future studies to encompass longer temporal horizons.

Some thematic clusters—particularly *Advanced Technologies*—suffered from limited sample sizes, resulting in wider uncertainty bands and validation challenges. Additionally, heterogeneous terminology and writing styles across sources posed difficulties for semantic alignment, especially when processed with models such as Llama-3 (8B). These challenges are intrinsic to large-scale, multilingual, and rapidly evolving biomedical corpora, and they define the natural constraints of first-generation integrative analyses.

Looking forward, the authors outline a clear roadmap for methodological refinement. First, coupling physical and biological models of ultrafast radiotherapy with high-Z nanotechnologies could enhance system-level dynamic modeling. Second, semantic supergraph analysis may uncover underexplored clusters, early signals, and strategic opportunities for funding and collaboration. Third, incorporating AI-derived biomarkers into adaptive, real-time radiotherapy planning will enable predictive systems that evolve with patient response, closing the loop between inference and action.

This work represents a milestone in computational oncology. It demonstrates that integrative synthesis in radiotherapy is not only feasible but transformative when paired with clinical expertise and public-health pragmatism. By weaving heterogeneous data into a cohesive, decision-ready framework, the study advances the field toward a *continuously learning ecosystem* where semantic

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analytics, molecular insights, and clinical innovation converge to deliver more precise, safer, and equitable cancer care.

4. Discussion

These analyses detail how modern radiotherapy has evolved historically, semantically and operationally into an interdisciplinary, data-driven ecosystem spanning radiobiology and oncology, because the computational workflow began with automated retrieval from Scopus, PubMed and Web of Science, followed by standardization, normalization and metadata integration, resulting in 3,343 unique records. The source imbalance, with PubMed as the major contributor, illustrates the field's biomedical origins, and the temporal profile of publication activity shows three phases: a low-output phase (1964-1990), steady growth phase (1991-2010) and high-output phase (2011 onwards) coinciding with the development of stereotactic body radiotherapy, proton therapy and predictive modeling, although the apparent decline in 2025 is best explained by indexing delay rather than a real decrease in output. A word cloud of titles and abstracts displays recurrent terms-cell, cancer, dose, treatment, radiotherapy-underscoring the continued interplay between mechanistic biology, dosimetry and clinical practice, and Latent Dirichlet Allocation revealed ten major topics across titles and abstracts, categorized into two interrelated axes, namely a clinical-anatomical axis containing tumor sites, treatment modalities and patient-centered outcomes, and a mechanistic-molecular axis including cellular responses, DNA repair, biomarkers, and toxicity pathways. Together, these axes form a translational continuum where experimental findings and clinical needs are informing each other iteratively, and the network topology of the co-occurrence supergraph has a high density (0.07), low modularity (0.15), and clustering coefficient (0.5), suggesting a strong semantic cohesion, because the central node cancer is directly connected to tumor, radiotherapy, particle, and breast, while the technological subfields (proton, stereotactic, and imaging) that anchor the methodological innovation are positioned at the periphery. The findings reveal a deep conceptual convergence across biology, medical physics, and clinical care in radiotherapy, marking its transition from siloed subdisciplines to an integrated translational science, and this model supports the following four working hypotheses: cancer and radiotherapy are the structural axes of recent radiotherapy scholarship, second, the increasing frequencies of cell, dose, effect, and treatment reflect the increasing focus on personalization and clinical efficacy, third, the cooccurrence of tumor, DNA, repair, and survival suggests that precision-medicine research has increased, and fourth, high density and low modularity reflect the transversal and integrative character of the field. Targeted database searches based on these hypotheses identified 61 articles of high relevance published between 2014 and 2025, which were grouped into five themes: DNA repair and molecular responses, precision oncology and genomic modeling, individual radiosensitivity and clinical risk, mechanisms of radioresistance, and advanced technologies and innovation in radiotherapy, and case analyses demonstrate how these themes complement each other, because DNA repair studies focused on complex damage from high-LET radiation, circadian alignment of therapy, and the modulation of the HR, NHEJ, ATM, and ATR pathways, while precision oncology studies integrated multi-omic data and AI models for dose calibration and genomic stratification, using indices such as RSI and GARD, and protein markers such as RAD51, PARP1, CHK1, and MAPK15. Individual radiosensitivity studies combined genetic and clinical data to develop personalized risk matrices based on TCP/NTCP modeling, and including imaging, radiomics, and machine learning, and the radioresistance studies highlighted the potential of high-LET modalities, repair inhibitors and proteomic mapping to reverse resistant phenotypes, whereas the technology studies reviewed the potential of FLASH radiotherapy and optimized brachytherapy for tissue-sparing effects and immune modulation. These studies provided the foundation for the Integrated Implementation Plan in Precision Radiotherapy, an operational framework of five interdependent blocks that connects molecular discovery to translational validation and clinical delivery, because it utilizes biomarker panels, genomic models and adaptive protocols to support biologically informed treatment planning, and is designed with Brazil's Unified Health System in mind, specifying measurable indicators-overall and progression-free survival, local

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control, grade ≥3 toxicity, unplanned hospitalizations and average cost per controlled case-that align with health-system goals to improve equity, reduce mortality, optimize resources and expand access to advanced technologies. Together, they form a practical, evidence-based pathway for oncology, and conceptually and methodologically, this study demonstrates that the combination of semantic mining, temporal modeling and network analysis can reconstruct the evolution of a complex biomedical domain, therefore radiotherapy is shown to be a coherent, interdependent system in which molecular biology, medical physics and clinical decision-making reinforce each other in a continuous learning loop. However, the authors note several limitations, including the likely index lag in 2025, the choice of analytic window (2014-2025) and the exclusion of non-DOI records, although these choices enhanced consistency and semantic precision at the expense of historical depth, heterogeneous terminology and limited published data for certain advanced technologies likely expanded the confidence intervals of certain results, and nevertheless, the Pearson values (>0.9) indicate the robustness of the main interpretations. Consequently, the implications of this study are substantial, because theoretically, the work provides a fine-grained conceptual map of modern radiotherapy, operationally, it provides a reproducible framework for the implementation of personalized, data-guided care pathways, and for health policy, it outlines a scalable model for the integration of advanced technologies within public healthcare systems, thus future directions include the development of coupled physical and biological models of ultrafast radiotherapy coupled with high-Z nanoparticle platforms, expansion of semantic supergraph analysis to surface underexplored clusters and embedding AI-derived biomarkers into adaptive, real-time learning protocols. Moreover, the confluence of semantic analytics, molecular modeling and clinical innovation described above leads to an ever learning oncology ecosystem that transforms data into safer, more precise and more equitable cancer care.

5. Conclusions

The current study demonstrates that AI-assisted semantic and temporal analysis of the scientific literature in radiotherapy, radiobiology, and oncology provides a sound and forward-looking foundation for a precision implementation agenda that bridges molecular science, clinical practice, and public health, because by analyzing 3,343 unique documents published between 1964 and 2025, the study reconstructs the historical trajectory and conceptual architecture of the field, showing how radiotherapy has transitioned from a fragmented domain to an integrated, interdisciplinary system, characterized by semantic cohesion and translational continuity.

The results delineate a mature scientific landscape located at the intersection of biology, physics, and clinical oncology, with strong semantic linkages among core concepts including cancer, radiotherapy, DNA repair, radiation dose, and patient outcomes, and two dominant research dimensions are identified: the first is clinical-anatomical, centered on tumor classification, therapeutic modalities, and prognosis, while the second is mechanistic-molecular, focused on DNA repair pathways, biomarkers, and cellular responses to radiation.

The convergence of these dimensions highlights the translational character of the field, in which molecular findings are rapidly operationalized into therapeutic and technological innovations with direct patient impact; therefore, the study outlines the Integrated Implementation Plan in Precision Radiotherapy, a structured model that operationalizes scientific evidence into an iterative cycle of discovery, validation, and clinical deployment.

The programme is structured around five operational classes: DNA repair and molecular response; precision oncology and genomic modelling; individual radiosensitivity and clinical risk; mechanisms of radioresistance; and innovative radiotherapy technologies, and each class incorporates biomarkers, predictive modelling, and therapeutic strategies to allow the development of personalized treatment plans with the overall objective of improving survival, reducing toxicity, and increasing equitable access to advanced technologies including FLASH-RT and hadron therapy.

The programme addresses the perennial problem of data silos in biomedical research by harmonizing heterogeneous data sets using AI-based modelling, thereby turning isolated findings

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into a coherent, decision-ready evidence base, thus placing AI at the heart of interpreting and integrating the complexity of modern science.

Overall, the programme suggests that radiotherapy, radiobiology, and oncology have reached a high level of interdisciplinary maturity that now supports the development of a dynamic and integrated framework for precision medicine, moreover, in addition to computational synthesis, the programme represents a conceptual advance in the organization and application of scientific knowledge allowing for decades of data transformed into a meaningful base for innovation, clinical decision-making, and more equitable care.

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Abbreviations

The following abbreviations are used in this manuscript:

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Abbreviation / Term	Meaning	Context / Explanation
≥3 Toxicity	Grade 3 or Higher Adverse Events	Represents severe clinical side effects per standardized toxicity grading.
≥40 Gy/s	Dose-Rate Threshold for FLASH-RT	Represents ultrafast radiation rate preserving normal tissue integrity.
0.291–0.669 (~0.378 span)	Range of Observed Cosine Scores	Captures the minimum-to-maximum similarity observed between LLM outputs.
0.5235 ± 0.0271 (95% CI 0.4964–0.5506)	Aggregate Similarity Statistics	Demonstrates moderate overall alignment and high reproducibility of language/semantic structure between models.
15 Standardized Terms	Controlled Vocabulary Set	Used for harmonizing semantic meaning across Scopus, PubMed, and Web of Science records.
2014 / 2015–2024 windows	Temporal limits of corpus	Ensure focus on contemporary, translational radiotherapy.
2014–2025 Analytic Window	Defined Temporal Scope of Corpus	Restriction ensuring semantic stability and consistent term usage across databases.
2D / 3D	Two-dimensional / Three-dimensional	Cell-culture models compared for radiation response.
3D Spheroids	Three-Dimensional Cell Cultures	In-vitro tumor analogues reproducing microenvironmental gradients and resistance.
60Co / ^{192}Ir	Cobalt-60 / Iridium-192 Isotopes	Common brachytherapy sources; compared for efficacy, RBE, and safety.
a	Abstracts Corpus	The suffix “a” in Topic_0a–Topic_9a refers to topic models generated from abstracts rather than titles.
Adaptive Clinical Protocols	Dynamically Updated Treatment Guidelines	Clinical pathways that adjust based on biomarker or imaging feedback.
Adaptive Radiotherapy Planning	Treatment Optimization Based on Patient Response	Future goal using AI-derived biomarkers for closed-loop, real-time dose adjustment.
Adjacency definition	Mathematical rule for linking nodes	Directed adjacency alters numeric scales of network metrics.
Advanced Radiotherapy Technologies	Emerging Modalities (FLASH-RT, Brachytherapy, Particle Therapy)	High-precision and/or ultrafast radiation technologies providing enhanced therapeutic index.
Advanced Technologies Cluster	Thematic Category in LDA Model	Identified area with limited samples causing wider uncertainty in validation.
AGENT	Therapeutic Agent	Denotes a drug, molecule, or compound used in combination with radiation therapy.
AI	Artificial Intelligence	Central methodological pillar of the study; refers to machine-learning and computational modeling approaches.
AI Models (Validated)	Certified Predictive Algorithms	Used to plan or adjust treatments, ensuring regulatory and scientific reliability.
AI synthesis	Artificial Intelligence synthesis	Refers to AI-based interpretation and summarization phase of the pipeline.

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AI-assisted	Artificial Intelligence–Assisted	Denotes the use of AI in processing, interpreting, and modeling scientific literature.
AI-based	Artificial Intelligence-based	Refers to the study's computational modeling methods.
AI-based methods	Artificial-intelligence analytical techniques	Include topic modeling, text mining, and co-occurrence network analysis.
AI-based Modelling	Artificial Intelligence–Based Modeling	Framework for harmonizing heterogeneous datasets into unified evidence models.
AI-derived Biomarkers	Machine-Learned Predictive Molecular Indicators; Artificial Intelligence–Generated Predictive Features	Proposed for real-time, adaptive radiotherapy planning linked to patient-specific biological response; Used for adaptive treatment and real-time learning protocols.
Alpha/Beta (α/β)	LQ model tissue parameters	Reported in pediatric medulloblastoma for tailoring dose/fractionation.
ATM	Ataxia-Telangiectasia Mutated	DNA-damage response kinase; nucleoshuttling linked to tissue radiosensitivity.
ATR	Ataxia Telangiectasia and Rad3-Related Protein	Parallel kinase to ATM; monitors replication stress and coordinates DNA repair.
Average Degree = 9.5	Mean number of links per node	Quantifies average lexical connectivity.
Average Weighted Degree = 1962.2	Mean sum of edge weights	Captures total co-occurrence frequency per term.
BER	Base Excision Repair	DNA repair pathway correcting small, non-helix-distorting base lesions caused by ionizing radiation.
BIOLOGICAL	Biological Effect or Endpoint	Used in Topic_2a for biophysical modeling linking energy deposition to cellular effect.
Biomarker signature	Composite molecular indicator	Selection criterion for case-study inclusion and stratification.
Biomedical Stopwords	Domain-specific uninformative terms	Filtered to improve semantic precision.
Biomedical subject areas	Domain filter in Scopus	Restricts search to clinically relevant literature.
Blue–Red Color Bar	Visual encoding of co-occurrence strength	Blue = weak association; red = strong association.
BMAL1, CLOCK, PER, CRY	Core Circadian Genes	Regulate cellular timing of DNA repair; targeted in chronoradiotherapy to reduce toxicity.
Brachytherapy	Internal radiotherapy using implanted sources	Another advanced modality considered in the framework.
Brachytherapy dose escalation	Targeted increase of internal RT dose	Inclusion term; linked to voxel-level and TCP modeling.
Carcinoma	Cancer Type Originating from Epithelial Cells	Frequently used term in radiation oncology literature (breast, esophageal, prostate).
$CD8^+$ Lymphocytes	Cytotoxic T Cells	Immune effectors preserved after FLASH-RT, supporting anti-tumor immunity.

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Cell-Fit-HD	High-Density Cell Microbeam Technology	Experimental system quantifying DNA-damage kinetics and repair precision.
Central node	Highest-connectivity vertex	"Cancer" identified as the core of the radiotherapy supergraph.
cGAS–STING	Cyclic GMP–AMP Synthase / Stimulator of Interferon Genes	Cytosolic DNA-sensing pathway linking radiation damage to immune activation.
ChatGPT	Generative Pretrained Transformer (GPT-5 model, OpenAI)	AI-based language model used under human supervision to improve clarity, grammar, and precision during manuscript preparation.
Chronoradiotherapy	Time-Synchronized Radiation Delivery	Aligns irradiation with circadian repair peaks to enhance efficacy and minimize side effects.
CI	Confidence Interval	Statistical interval representing uncertainty around the mean cosine-similarity estimates (95% CI: 0.4964–0.5506).
CiteSpace	Citation Space Mapping Tool	Bibliometric software for co-authorship and trend analysis.
Classe 1 – DNA Repair and Molecular Response	Class 1 Category	Focused on DNA damage signaling, repair pathways (HR, NHEJ, NER, BER), and checkpoint activation; aligns molecular biology with therapeutic personalization.
Classe 2 – Precision Oncology and Genomic Modeling	Class 2 Category	Integrates genomic profiling, machine-learning models, and patient stratification to personalize radiation therapy.
Classe 3 – Individual Radiosensitivity and Clinical Risk	Class 3 Category	Addresses variability in patient radiation response, genetic predisposition, and predictive biomarkers.
Classe 4 – Radioresistance and Associated Mechanisms	Class 4 Category	Explores resistance mechanisms (hypoxia, metabolism, stemness, viral integration) and corresponding therapeutic interventions.
Classe 5 – Advanced Technologies and Innovative Radiotherapy	Class 5 Category	Encompasses next-generation technologies including FLASH-RT, hadron therapy, voxel-based analysis, and high-Z nanoparticle radiosensitization.
CLINICAL / ONCOLOGY / RADIOBIOLOGY / MEDICAL / DEVELOPMENT / ELSEVIER / RIGHT / RESERVED	Publishing or Institutional Terms	Topic_8a includes frequent non-scientific tokens derived from editorial metadata, likely due to text-parsing of abstracts from publishers (Elsevier, etc.).
Clinical trial phase	Trial stage indicator	Used to filter translational maturity of studies.
Clinical–Anatomical Axis	Axis describing patient- and site-specific features; Dimension grouping disease sites, therapies, and outcomes	Encompasses disease sites, therapy types, outcomes; Derived from topic modeling to describe clinical themes.

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Clustering coefficient	Likelihood that connected nodes form closed triangles	High value shows local semantic cohesion.
Co-Occurrence Supergraph	Graph of term co-appearances; Combined network of all significant co-occurring terms	Reveals structural relationships among concepts in the literature; Integrates molecular, clinical, and technological vocabularies into one semantic structure.
Combined modality	Multimodal treatment (e.g., RT + IO)	Inclusion term bridging lab and clinic.
COMPLETE (trial)	HolistiC early respOnse assessMent for oroPharyngeaL cancEr paTiEnts	Protocol integrating imaging and early-response assessment in oropharyngeal cancer.
COMPLETE Protocol	Combined Multiparametric Imaging, Radiomics and Machine-Learning Framework	Integrates imaging and omics data for personalized radiotherapy planning.
Computational Oncology	Field Integrating AI and Cancer Research	The disciplinary frame under which the study's integrative modeling approach is positioned.
COPPE	Instituto Alberto Luiz Coimbra de Pós-Graduação e Pesquisa de Engenharia	UFRJ's graduate engineering institute; associated with the Nanotechnology Engineering Program.
Cosine Similarity	Vector-Space Similarity Measure	Quantifies the semantic and lexical overlap between two text representations (range 0–1). Used here to assess alignment between outputs of different LLMs.
Cost per Controlled Case	Economic Indicator	Total treatment cost divided by number of patients with complete or partial sustained response; measures cost-effectiveness.
COVID-19	Coronavirus Disease 2019	Systemic factor influencing radiosensitivity and patient management.
Cross-Model Consistency	Comparative Validation Concept	Indicates methodological reliability by reproducing semantically equivalent results across distinct LLM architectures.
CSV	Comma-Separated Values	Log format for timestamped model inferences and auditing.
CTCAE	Common Terminology Criteria for Adverse Events	Global clinical-trial standard for grading radiotherapy-related adverse events.
Data Repositories	Centralized Databases for Clinical and Molecular Information	National archives enabling interoperability and machine-learning-based outcome prediction.
DAY	Treatment Day / Fraction Day	Represents time variable in radiotherapy fractionation (Topic_7a).
Decision-Ready Framework	Actionable Computational Infrastructure	Describes the output: a structured knowledge base usable for policy, funding, and clinical translation.
Deduplication	Removal of duplicate entries	594 records removed by ID and 25 by title → 3 343 unique publications.

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Density	Ratio of existing to possible edges; Ratio of actual to possible edges	0.5 in the directed setup, signifying a tightly connected lexical field; Indicates a dense and cohesive co-occurrence network.
DER / SER / RBE	Dose Enhancement Ratio / Sensitization Enhancement Ratio / Relative Biological Effectiveness	Quantitative radiobiological indices comparing biological responses between radiation modalities.
Diameter	Longest shortest path in the network; Longest shortest-path length	Here equals 1 due to directed adjacency; reflects condensed connectivity; Reflects immediate connectivity among principal terms in a directed adjacency setup.
Directed / Weighted Graph	Graph with edge orientation and numerical weights	Models term co-occurrence frequency and directionality in the semantic network.
DNA	Deoxyribonucleic Acid	Central mechanistic concept related to damage, repair, and radiosensitivity.
DNA Repair	Deoxyribonucleic Acid Repair	Core biological process for maintaining genomic integrity after radiation exposure; Major research theme representing molecular response to radiation.
DOI	Digital Object Identifier	Persistent identifier ensuring record uniqueness and traceability.
Dose–Response Model	Quantitative relation between dose and effect; Mathematical link between dose and biological effect	Appears among inclusion keywords; supports mechanistic theme; Underpins LDA topics and clinical correlation analysis.
E2	HPV Regulatory Protein	Loss disrupts viral genome control; restoration of E2-associated checkpoints observed with carbon-ion irradiation.
Edge Thickness	Graph-visualization parameter	Increases proportionally with co-occurrence weight.
Editorial Workflow (“Llama → GPT-4o”)	Sequential Model Use	Denotes the pipeline where Llama3 generated drafts and GPT-4o refined phrasing, without altering data or analytic interpretations.
Effect	Biological or Clinical Outcome	Used to represent both therapeutic effects and adverse effects of radiation exposure.
ENERGY	Beam Energy	Physical parameter determining penetration depth and RBE of particle beams (Topic_2a).
EORTC	European Organisation for Research and Treatment of Cancer	European body with harmonized toxicity and clinical-trial reporting frameworks.
Eq.	Equation	Used to identify model equations from Eq. 11 to Eq. 20.
Equations 1–20 (Supplementary Information)	Numerical LDA Output Tables	Provide word probabilities and model parameters for transparency.
Equity / Access Metrics	Health Policy Indicators	Includes survival, toxicity, cost per controlled case, and hospitalizations for public health alignment.

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EXPRESSION / GENE / PROTEIN / BLOOD	Biomarker-related Terms	In Topic_6a, these describe molecular and clinical biomarkers used for radiosensitivity prediction.
Factor	Biological or Statistical Factor	Represents either biological modifiers (e.g., hypoxia) or regression factors in predictive models.
FANCA	Fanconi Anemia Complementation Group A	Germline carrier state linked to hypersensitivity to chemoradiation.
Feasibility / Translational Potential	Applied Assessment Metrics	Used to evaluate how physical models and clinical data can be realistically implemented within current technological and clinical constraints.
Feature Space	Multidimensional Representation of Texts	Conceptual domain in which cosine similarity evaluates orientation and semantic overlap between document vectors.
FIU	Florida International University	U.S. collaborator institution for computational and AI analysis.
FLASH	Ultrafast Radiotherapy (FLASH-RT); Ultrafast radiotherapy at ultra-high dose rates; Ultrafast (> 40 Gy s^{-1}) radiation-delivery technique; Ultrafast (≥ 40 Gy s^{-1}) radiotherapy	High-dose-rate radiation mode producing reduced normal-tissue toxicity; investigated for normal-tissue sparing and tumor control; one of the advanced technologies highlighted in Class 5; modern modality delivering high-dose-rate pulses with reduced normal-tissue damage.
FLASH Radiotherapy and Brachytherapy	Advanced Techniques	Explored for synergistic effects in tissue protection and immune modulation.
FRACTION	Dose Fraction	In Topic_9a, refers to division of total dose into multiple treatment sessions—key variable in radiobiological modeling.
Fraction / Fractionation	Division of Total Radiation Dose into Multiple Sessions	Appears among frequent title/abstract terms; optimization variable flagged by abstracts analysis.
Frequency Trimming	Vocabulary Cutoff Procedure	Eliminates extremely rare or overly common tokens.
G ≥ 3	Grade 3 or Higher Toxicity	Severe adverse-event category per CTCAE or RTOG/EORTC scales; measures safety profile.
GARD	Genomic Adjusted Radiation Dose	Integrates RSI and gene-expression data to personalize dose prescription.
Genomic / Proteomic Modeling	Molecular Data Integration Approaches	Computational modeling of genomic (gene-level) and proteomic (protein-level) datasets to predict radiosensitivity and outcomes.
Genomic Classifier	Model Assigning Molecular Subtypes	Used for precision oncology decisions.
Genomic Modeling	Predictive Modeling Based on Genetic Data; Mechanistic to Machine-Learning Frameworks	Used for individualized therapy planning in precision oncology; used to personalize radiotherapy (predict response/toxicity).
Gephi	Open-source Network-Analysis Software	Used for calculating density, diameter, clustering, and modularity of the co-occurrence network.

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GPT-4o	OpenAI's Multimodal Large Language Model (Omni Version)	Used to refine language, maintain consistency, and ensure terminological precision; served only in editorial and validation steps.
GPT-5	Generative Pretrained Transformer, Version 5	Model used within ChatGPT for generative text refinement and consistency checking.
Grammarly (v.2025)	AI-Powered English Language Writing Assistant	Utilized for grammatical and stylistic correction to ensure readability for international readers.
Gy	Gray	SI unit of absorbed radiation dose (1 Gy = 1 J/kg); frequent in topics 4a, 7a, 9a related to dosimetry and toxicity.
Gy / Gy s^{-1}	Gray / Gray per second	SI units of absorbed dose and dose rate.
H_2O_2	Hydrogen Peroxide	Central to radiosensitization concepts exploiting oxidative effects (low-LET contexts).
Hadron Therapy	Particle-Beam Radiotherapy (Protons, Carbon Ions); Particle-Based Radiotherapy (Using Protons or Heavy Ions)	Emerging high-precision radiation technique; advanced technology referenced in the framework as part of "Innovative Radiotherapy Technologies."
Head and Neck / Breast / Prostate Cancer	Disease-Site Descriptors	Define clinical–anatomical axes in Topic_0t and related clusters.
Heavy Charged Particles	Proton/Helium/Carbon/Oxygen Ion Beams	"Next-generation multi-scale" characterization and high-LET effects.
HIF	Hypoxia-Inducible Factor	Transcription factor activated by VHL loss; mediates hypoxia-related radioresistance.
High-End Modalities	Advanced Treatment Technologies	Includes FLASH-RT, hadron therapy, and other precision radiotherapy innovations.
High-LET	High Linear Energy Transfer	Radiation that deposits dense energy tracks (e.g., heavy ions); generates complex DNA lesions.
High-LET Modalities	Heavy-Ion or Particle Therapies	Used in Class 4 to reverse resistant phenotypes via dense-ionization damage.
High-LET Radiation	High Linear Energy Transfer Radiation	Mentioned indirectly in prior results, relevant here as part of the "system-level dynamic modeling" refinement.
High-Z	High Atomic-Number Elements	Nanoparticles used to enhance dose deposition and radiosensitization.
High-Z Nanoparticles	High Atomic-Number Nanomaterials	Act as radiosensitizers by amplifying local dose and reactive-species generation.
High-Z Nanotechnologies	High Atomic Number Nanomaterials	Proposed future pathway to couple with ultrafast radiotherapy for dose amplification and radiosensitization.
High-Z Platforms	High Atomic Number Platforms	Refers to nanomaterials designed to enhance radiotherapy through dose amplification.
Hospitalization Rate	Frequency of Radiotherapy-Related Admissions	Indicator of adverse-event management effectiveness.

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HPV	Human Papillomavirus	Oncogenic virus associated with cervical-cancer radioresistance; carbon-ion therapy shown to overcome it.
HPV / E2	Human Papillomavirus / Regulatory Gene	Integration/E2 disruption associated with cervical radioresistance; carbon ions reported to overcome it.
HR	Homologous Recombination	Accurate double-strand-break repair pathway; its inhibition increases radiosensitization.
Hybrid Modeling / Model Fusion	Combined Output Strategy	Not used in this study; models were compared for agreement, not merged to produce shared outputs.
Hypotheses 1–4	Structural Inferences Derived from Topology	Define conceptual axes: (1) cancer + radiotherapy centrality; (2) personalization trends; (3) biomarker emphasis; (4) transversal field integration.
ID Numbers	Unique Database Identifiers (e.g., PMID, DOI, EID)	Used for automated deduplication across sources.
IIPPR	Integrated Implementation Plan in Precision Radiotherapy	The overarching operational and translational framework structuring radiotherapy research into five classes with progressive integration into health policy.
IMA	Instituto de Macromoléculas Professora Eloisa Mano	UFRJ institute specializing in polymers and macromolecular science.
Imaging	Medical Imaging	Used for diagnosis, planning, and verification in radiotherapy (e.g., MRI, CT, PET).
Immunoradiotherapy	Radiotherapy Combined with Immune Modulation	Emergent interdisciplinary theme.
Immunotherapy	Immune-Based Cancer Therapy	Appears in Topic_5a; integration of radiation with immunotherapy strategies.
In vitro	Laboratory-Based Experiments	Denotes cellular studies that feed mechanistic insight.
Individualized Radiosensitivity Assessment	Patient-Specific Radiation Response Evaluation	Quantifies how individual genetic and biological profiles modify treatment tolerance and efficacy.
Integrated Implementation Plan in Precision Radiotherapy (IIPPR)	Translational Framework	Unifies molecular, clinical, and technological insights into five interdependent operational blocks for precision oncology and public-health integration.
Interdisciplinary Maturity	Cross-Disciplinary Integration	Refers to the field's evolution into a coherent system combining biology, physics, and clinical practice.
Ion	Ion Beam	Refers to charged particle beams (proton, helium, carbon, oxygen) used in particle radiotherapy.
ION / PARTICLE / PROTON / CARBON / PHOTON	Ion-Beam and Particle Radiation Terms	Terms appearing together in Topic_2a; describe physical particles used in hadron therapy.

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Irradiation	Exposure to Ionizing Radiation	Common in Topics 6a and 7a; refers to experimental or clinical exposure processes.
k = 10 Topics	Number of LDA Topics	Defines model granularity; ten topics selected for interpretability and stability.
Kidney Cancer VHL/HIF Axis	von Hippel–Lindau / Hypoxia-Inducible Factor	Mechanistic route to pseudohypoxia and resistance.
KORTUC II	Kochi Oxidative Radiotherapy for Unresectable Carcinomas Type II	Technique using hydrogen peroxide (H_2O_2) to increase tumor oxygenation and radiosensitivity.
LaBioS	Laboratório de Biopolímeros e Sustentabilidade	Laboratory supporting the experimental and organizational phases of the study.
LabOPTIMA	Laboratory for Optimization, Data Analytics, and Artificial Intelligence in Materials Science	UFRJ-based lab responsible for data-centric analysis and computational modeling; mentioned as a contributor to data processing and validation.
LDA	Latent Dirichlet Allocation	Unsupervised topic-modeling algorithm used for semantic extraction of dominant research axes.
LDR	Low-Dose-Rate	Brachytherapy context (e.g., prostate cancer TCP modeling).
LDR Brachytherapy Sources ^{60}Co / ^{192}Ir	Cobalt-60 / Iridium-192	Compared radiobiologically (e.g., cervical cancer HDR; RBE differences).
Lemmatization	Word-Form Normalization	Reduces inflectional variants to base forms for stable modeling.
LET	Linear Energy Transfer	Energy deposition per track length; key in radiobiology and particle therapy.
LEVEL	Expression Level / Dosimetric Level	Indicates quantitative measurement of gene, protein, or dose levels (Topic_6a).
LINE	Cell Line	Experimental model system used for in-vitro radiation studies (Topic_1a).
Linear	Linear Model (Linear-Quadratic Model)	Refers to the linear component of the LQ model used to describe cell survival curves in radiotherapy modeling.
Llama-3 (8B)	Large Language Model (8 Billion Parameters); Open-Source Large Language Model (8 Billion Parameters)	Referenced as a semantic-processing model used during analysis, highlighting technical limitations and multilingual challenges; used for initial draft generation and offline semantic analysis; suitable for secure, local computation.
LLM	Large Language Model	AI model trained on massive text corpora; in this study, Llama-3 (8B) and GPT-4o were compared.
LLMs	Large Language Models	Used for semantic synthesis under fixed prompts; outputs logged for auditability; models (like GPT-type) used in PaperProcessor for semantic synthesis and summarization.

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Local Control / Systemic Control	On-Site vs Distant Tumor Suppression	Metrics evaluating therapeutic success at tumor site and metastasis prevention.
Machine Learning	AI Technique for Pattern Recognition and Prediction	Supports risk stratification, biomarker identification, and outcome modeling.
Mean (μ)	Arithmetic Average	Represents central tendency of similarity values (~ 0.52 overall).
Mean Clustering Coefficient = 0.5	Local Cohesion Metric	Reveals that many terms form tightly knit clusters (≈ 1140 triangles).
Mechanism / Molecular	Mechanistic and Molecular Basis	Indicates interest in the cellular and sub-cellular mechanisms of radiation injury and repair.
Mechanistic–Molecular Axis	Axis Describing Biological Mechanisms; Dimension Encompassing DNA Repair and Biomarkers	Encompasses cellular responses, DNA repair, and biomarkers; describes mechanistic research focus across decades.
Median Cohort	Summary Statistic in Cohort Analyses	Appears in abstract-level signals of methodological layer.
MeSH	Medical Subject Headings	Controlled vocabulary in PubMed employed for precise field-restricted searching.
Metadata	Supplementary Bibliographic Descriptors	Retained for reproducibility and cross-referencing (authors, year, source title, etc.).
MicroRNAs / Cytokines	Small Regulatory RNAs / Signaling Proteins	Linked to radiation toxicity and inflammatory responses in prostate cancer.
MMRd	Mismatch Repair Deficiency	Genetic defect leading to hypermutation; associated with increased immunogenicity and favorable prognosis.
Model	Computational or Predictive Model	Refers to mathematical frameworks (e.g., dose-response, LQ, biological modeling).
Modularity	Measure of Community Segregation; Community-Segregation Index	Low modularity indicates overlapping thematic communities; very low value (≈ 0.02) shows themes overlap strongly with one weakly connected component.
MOUSE	Animal Model	Indicates in-vivo preclinical testing in mice (Topic_7a).
Multi-Omic Biomarkers	Combined Genomic, Transcriptomic, and Proteomic Indicators	Used to stratify patients and personalize treatment strategies.
Multilingual Biomedical Corpora	Multi-Language Scientific Data Sets	Describes the heterogeneity of textual sources posing semantic-alignment challenges.
n	Sample Size	Number of text pairs analyzed per class (Class 1: n = 6; Class 2: n = 6; Class 3: n = 18; Class 4: n = 4; Class 5: n = 3).
NER	Nucleotide Excision Repair	DNA repair process that removes bulky helix-distorting lesions; important for radiation and oxidative stress responses.

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NER / SER / DER Metrics	Nucleotide Excision Repair / Sensitization Enhancement Ratio / Dose Enhancement Ratio	Quantitative parameters for evaluating biological amplification of radiation effects.
NHEJ	Non-Homologous End Joining	Fast, error-prone DNA repair mechanism; hyperactivation linked to radioresistance.
no_below = 2–5 / no_above = 0.5	Frequency-Trimming Parameters	Filter words appearing in fewer than 2–5 documents or in > 50 % of texts, ensuring vocabulary stability.
Node / Edge	Vertex / Connection	Represent keywords and their co-occurrence relations.
Normal	Normal Tissue	Opposed to tumor tissue; represents non-targeted biological matter whose protection is critical in treatment planning.
Normalization / Standardization	Data-Cleaning Processes	Harmonized author, title, and metadata formats across databases before merging.
NSCLC	Non-Small Cell Lung Cancer	Disease context in studies on radiotherapy benefits.
NSMP	No Specific Molecular Profile	Endometrial cancer subtype lacking defined genomic markers; used for risk-based treatment calibration.
O	Overall (e.g., Overall Survival – OS)	Shortened reference to clinical endpoints (Topic_3a); likely from expressions such as “overall survival.”
Offline Analyses	Local Computation Without Internet Connectivity	Performed using Llama-3 for data security, sovereignty, and reproducibility.
Omics Data	Integrated Genomic, Transcriptomic, Proteomic Datasets	Used across classes for multi-scale modeling of tumor behavior.
Oncology	Medical Field of Cancer Diagnosis and Treatment	Provides the clinical component in the interdisciplinary framework.
OpenAI	Artificial Intelligence Research Organization	Developer of ChatGPT; referenced for model attribution.
OS	Overall Survival	Proportion of patients alive at specified follow-up times (1 / 3 / 5 years) after radiotherapy.
P	p-value (Statistical Significance)	Appears in Topic_3a and 4a; denotes statistical significance in clinical or survival analyses.
PaperProcessor	LLM-Guided Semantic Extraction Script	Pipeline component for document-level summarization and tagging.
Parameter / Radiobiological	Model Coefficients / Domain Qualifier	Signal the quantitative calibration layer in abstracts.
Particle Therapy	Proton or Heavy-Ion Radiation Treatment	High-precision, high-LET modality for deep or radioresistant tumors.
passes = 10	Number of LDA Training Iterations	Controls convergence during topic-model optimization.
Pathway	Biological Pathway	Indicates molecular signaling cascades affected by radiation (e.g., DNA damage-repair pathways).

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Pearson Correlation Coefficient	Statistical Measure (r); Statistical Correlation Index	Indicates robustness of network stability across runs ($r > 0.9$); confirms stability of node/community ordering between directed and undirected graphs.
PENt	Programa de Engenharia da Nanotecnologia (Nanotechnology Engineering Program, COPPE/UFRJ)	Academic home of the AI and semantic-modeling pipeline described.
Peripheral Nodes	Lower-Degree Vertices at Network Edges	Terms like proton, stereotactic, imaging anchor technology subfields.
Personalized / Protocol	Individualized Plans / Standardized Procedures	Bridge terms in co-occurrence graphs linking themes.
PFS	Progression-Free Survival	Interval during which a patient remains free from tumor progression or recurrence.
PLAN / DOS	Treatment Planning and Dosimetry	In Topic_7a, “plan” and “dos” (truncated for dose or dosimetry) refer to planning and dose-distribution modeling.
PNG	Portable Network Graphics	Raster format for graphical visualization outputs.
POLE	DNA Polymerase Epsilon (Mutated Subtype)	Mutation defining a favorable genomic subtype in endometrial cancer; used in precision oncology stratification.
PORTEC-3 / PORTEC-4	Post-operative Radiation Therapy for Endometrial Carcinoma Trials	Landmark clinical studies incorporating molecular subtyping into radiotherapy decision frameworks.
Precision Oncology	Data-Driven Personalized Cancer Care; Data-Driven Personalized Cancer Treatment	Cross-cutting theme linking biomarkers to clinical protocols; integrates molecular profiling and computational modeling to guide clinical decisions.
Precision Radiotherapy	Data-Guided, Patient-Specific Treatment Framework	Conceptual endpoint of the integrated ecosystem.
Precision Radiotherapy Corpus	Consolidated Dataset	Final ≈ 45 deduplicated records informing thematic and network analyses.
Precision Radiotherapy Implementation Plan (PRIP)	Operational Framework; AI-Derived Operational Framework	Practical output of the study – translates semantic and molecular insights into five actionable clinical classes; translates computational and molecular insights into clinical strategies.
Preclinical	Preclinical Study; Experimental (Non-Clinical) Phase	Experimental phase prior to human clinical trials; linked to animal or in-vitro testing (Topic_5a); denotes laboratory or animal studies preceding human trials.
Prediction / Response / Normal	High-Centrality Nodes	“Semantic hinges” connecting mechanistic and clinical themes in the supergraph.

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Prediction Models	Computational or Statistical Outcome-Forecasting Tools	Represent the data-driven dimension emerging after 2010.
Predictive Systems	AI-Based Forecasting Models	Refer to evolving models that anticipate treatment response and guide dynamic planning.
Progression-Free Interval	Time to Recurrence	Quantitative measure for disease stability post-therapy.
Proteomics	Large-Scale Protein Analysis	Identifies functional markers of radioresistance and therapeutic targets.
Proton / Ion Beams	Particle-Beam Radiotherapy Modalities	Core of hadron-therapy and dose-delivery-physics studies.
Proton Therapy	Particle-Based Radiotherapy; Proton Therapy; Charged-Particle Radiation Modality	Advanced technique using proton beams for accurate dose delivery with minimal collateral damage; part of the technological wave correlated with publication surge.
Public Health Integration	Application of Precision Frameworks to Health-System Policies	Links AI-guided radiotherapy models to equity and access.
PubMed	U.S. National Library of Medicine Database (MEDLINE)	Primary biomedical source queried with MeSH and free-text terms; provided ≈ 66 % of final records.
PubMed, Scopus, Web of Science (WoS)	Scientific Databases	Used for bibliometric data collection and harmonization.
Quantitative Metrics	Numerical Parameters or Indicators	Include dose, LET, RBE, similarity scores, or statistical validation values supporting model precision.
RAD51 / BRCA1	DNA Repair Genes	Over-expression correlates with radioresistance; potential biomarkers for therapeutic targeting.
RAD51, PARP1, CHK1, MAPK15	Key DNA Repair / Stress Response Proteins	Biomarkers and therapeutic targets integrated into proteomic and genomic modeling layers.
Radiat / Cell / Dose / Tumor / Patient / Cancer / Radiobiolog	High-Frequency Lexical Stems	Most recurrent words in the processed corpus; define thematic backbone.
Radiobiological	Related to Radiation Biology	Describes models or parameters linking radiation dose to biological effects.
Radiobiological Integration	Coupling Biological Models and Clinical Protocols	Incorporates biological parameters (e.g., radiosensitivity indices) into planning.
Radiobiological Modeling	Quantitative Biological Modeling of Dose–Response	Used to predict tissue effects and optimize treatment.
Radiobiology	Study of Biological Effects of Ionizing Radiation	Core discipline analyzed alongside radiotherapy and oncology.
Radiomics	Quantitative Image-Feature Extraction	Supports predictive modeling and risk assessment integrated into adaptive radiotherapy.
Radioresistance Mechanisms	Molecular and Cellular Resistance Pathways	Refers to signaling and repair mechanisms that make tumor cells less responsive to radiation.
Radiotherapy (RT)	Use of Ionizing Radiation to Treat Cancer	Central disciplinary axis in all queries.

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RadRes	Radiation Research (Journal)	Appears in a title summarizing 75 years of the field.
random_state = 42	Random-Seed Setting	Ensures reproducible topic-model results.
Rate (Dose-Rate)	Dose Per Unit Time	Critical radiobiological variable, particularly relevant for FLASH-RT and LDR contexts.
RBE	Relative Biological Effectiveness	Quantifies biological potency of one radiation type relative to another.
Repair	DNA or Cellular Repair	Biological process restoring damaged DNA or cellular integrity after irradiation.
Reproducibility	Methodological Consistency; Methodological Standards	Refers to achieving consistent quantitative and terminological results across independent AI systems; ensures that pre-processing and modeling steps can be independently verified.
RESPONSE	Biological or Clinical Response	Describes radiation-induced effects, gene-expression responses, or treatment outcomes.
Risk / Volume	Dosimetric and Anatomical Covariates	Terms indicating planning and outcome modeling foci.
RSI	Radiosensitivity Index	Genomic predictor of individual radiosensitivity used for dose calibration.
RT	Radiotherapy	Appears in several topics and class definitions.
RTOG	Radiation Therapy Oncology Group	U.S. co-operative group providing standardized toxicity and outcome reporting criteria.
SARS-CoV-2 / COVID-19	Virus / Disease	Examined for potential changes in individual radiation sensitivity.
SBRT	Stereotactic Body Radiotherapy	Highly conformal, high-precision modality for small or lung tumors; advanced form of external beam radiotherapy delivering high-precision doses to small tumor volumes (directly referenced in Topic_4t).
Scopus	Elsevier's Multidisciplinary Abstract and Citation Database	Used for automated retrieval of bibliographic records on radiotherapy, radiobiology, and oncology.
Scopus / PubMed / Web of Science (WoS)	Major Bibliographic Databases	Primary data sources for corpus construction (1964–2025); used for refining, validating, and harmonizing corpus selection.
SD / ±	Standard Deviation	Expresses the dispersion of cosine-similarity values within each class.
Semantic Supergraph Analysis	Advanced Network Modeling Approach	Suggested future technique for identifying underexplored or emerging clusters within the scientific corpus.
Stereotactic Body Radiotherapy (SBRT)	High-Precision, Image-Guided Radiation Technique	Marks transition to modern radiotherapy (post-2010 growth phase).
Stopword Filtering	Removal of High-Frequency Function Words	Biomedical-specific list applied before modeling.

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Supergraph	Global Integrated Co-Occurrence Network	Encompasses molecular, clinical, and technological domains.
Supergraph Inset	Central Visual in Fig. 1	Depicts term relationships with colored weighted edges (blue = weak, red = strong).
SURVIVAL	Cellular or Patient Survival	Appears in Topics 1a and 3a, referring to both cell-survival assays and patient outcome metrics.
SUS / Unified Health System (SUS)	Sistema Único de Saúde (Brazil's Unified Health System)	Framework for pilot implementation, ensuring scalability, equity, and cost-effectiveness; Brazil's public-health system alignment target.
SVG	Scalable Vector Graphics	Visualization format for network maps.
t	Titles Corpus	The suffix "t" in Topic_0t–Topic_9t designates topics derived from article titles rather than abstracts.
Table 2 / Figure 2	Plan Visualization Elements	Table summarizes indicators; figure visualizes network linking plan classes, health metrics, and strategic goals.
TARGET	Radiation Target Volume	Anatomical or biological region receiving prescribed radiation dose (Topic_7a).
TARGETED (THERAPY)	Molecularly Targeted Therapy	Used in Topic_5a; describes agents designed to act on specific molecular pathways.
TCGA	The Cancer Genome Atlas	Genomic classification system defining molecular subtypes across cancers; applied for adaptive radiotherapy.
TCP / NTCP	Tumor Control Probability / Normal Tissue Complication Probability	Radiobiological models estimating treatment success vs. toxicity.
Temporal Evolution Curve	Publication-Frequency Over Time	Depicts output growth and term-usage expansion (sharp post-2010 increase).
Term-Frequency Curve	Temporal Plot of Keyword Occurrence	Used to link bibliometric evolution to network topology.
TF-IDF	Term Frequency–Inverse Document Frequency	Weighting scheme representing documents numerically for cosine-similarity computation; emphasizes discriminative words.
Therap / Radiotherapi (Radiotherapy Lemmatized Form)	Lemmatized Word Stems	Generated during text preprocessing before word-cloud and LDA analysis.
Therapeutic Window	Efficacy–Toxicity Balance	Keyword guiding selection of translationally relevant articles.
Tissue / Normal	Biological Material (Tumor vs. Normal)	Distinction between targeted tumor tissue and healthy tissue, relevant to toxicity models (Topic_9a).
TITLE-ABS-KEY	Title–Abstract–Keyword Query Field in Scopus	Syntax specifying that Boolean terms be searched in all three metadata fields.
Topic_0a–Topic_9a	Abstract-Based LDA Topics	Capture methodological and biological dimensions (e.g., FLASH-RT, RBE, immunotherapy).
Topic_0t–Topic_9t	Title-Based LDA Topics	Identify clusters such as tumor sites, radiation types, or molecular mechanisms; each topic represents a

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		statistically derived keyword cluster from titles.
Toxicity	Measure of Treatment-Induced Adverse Effects	One of the outcome indicators for therapy optimization.
TP53 / p53abn	Tumor Protein 53 / Abnormal TP53 Subtype	Gene regulating cell cycle and apoptosis; mutation indicates poor prognosis in endometrial and cervical cancers.
Translational Continuity	Bridging Experimental and Clinical Domains	Describes how findings progress from bench to bedside within a single analytical cycle.
Translational Publication Types / Translational Trials	Research Bridging Lab and Clinic / Studies Bridging Lab Findings and Clinical Implementation	Filters applied in PubMed to maximize relevance; reflected by terms “clinic,” “trial,” “meta,” “evalu.”
Transparency	Disclosure of AI Tool Use	Explicitly described to comply with academic-integrity and reproducibility standards.
Two-Dimensional Thematic Landscape	Dual-Axis Conceptual Map	Represents integration of clinical and molecular radiotherapy research.
UFRJ	Universidade Federal do Rio de Janeiro (Federal University of Rio de Janeiro)	Institutional affiliation of multiple authors.
Undirected, Thresholded Version	Simplified Graph with Bidirectional Edges and Minimum-Weight Cutoff	Used to test robustness of results.
VHL	von Hippel–Lindau Gene	Mutation induces pseudohypoxia and pro-survival signaling in renal carcinoma.
Vitro (from in vitro)	In-Vitro Studies	Laboratory studies conducted outside living organisms, often in cell cultures, used to study radiation-response mechanisms.
VOSviewer	Visualization of Similarities Viewer	Software for bibliometric and co-occurrence network visualization.
Voxel / Voxel-Based Analysis / Voxel-Based Mapping / Voxel-Level Analytics	Volumetric Pixel and Spatial Dose–Response Modeling Methods	Voxel = smallest unit in 3D medical imaging and dosimetry; used for dose/response mapping and adaptive planning; links radiobiological effects to 3-D anatomical regions for spatially resolved optimization.
Weakly Connected Component	Subgraph with at Least One Directional Path Between All Nodes	Indicates overall semantic unity of the dataset.
Web of Science (WoS)	Clarivate’s Multidisciplinary Citation Index	Used with direct keyword search to complement PubMed and Scopus coverage.
Weighted Degree	Sum of Edge Weights for a Node	Counts total co-occurrence frequency rather than binary presence.
Word Cloud	Frequency-Scaled Visual Representation of Keywords	Summarizes lexical prominence from titles and abstracts.
α-Parameter	Linear Component of the LQ Model	Represents cell-killing probability per unit dose in radiobiological modeling.

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α/β Values	Linear–Quadratic Model Parameters	Describe tissue-specific radiation response; used in pediatric and comparative modeling.
γH2AX	Phosphorylated Histone H2AX	Biomarker of DNA double-strand breaks; persistence indicates inefficient repair.

Appendix A

Appendix A.1. Topics from Titles (t)

Topic_0t = 0.090*"cancer" + 0.050*"radiotherapy" + 0.049*"patient" + 0.038*"head" + 0.037*"neck" + 0.022*"breast" + 0.018*"prostate" + 0.013*"toxicity" + 0.011*"advanced" + 0.010*"treatment" Eq. 1

Topic_1t = 0.075*"radiobiology" + 0.040*"radiotherapy" + 0.036*"clinical" + 0.031*"radiation" + 0.026*"therapy" + 0.019*"radiobiological" + 0.016*"treatment" + 0.015*"oncology" + 0.013*"perspective" + 0.010*"new" Eq. 2

Topic_2t = 0.050*"cancer" + 0.042*"radiotherapy" + 0.021*"patient" + 0.021*"breast" + 0.018*"carcinoma" + 0.014*"treatment" + 0.013*"prostate" + 0.012*"cell" + 0.010*"esophageal" + 0.009*"comparison" Eq. 3

Topic_3t = 0.097*"radiation" + 0.046*"oncology" + 0.023*"therapy" + 0.022*"biology" + 0.020*"mechanism" + 0.014*"molecular" + 0.011*"medical" + 0.011*"injury" + 0.011*"effect" + 0.011*"clinical" Eq. 4

Topic_4t = 0.058*"stereotactic" + 0.033*"body" + 0.031*"therapy" + 0.029*"lung" + 0.028*"cancer" + 0.028*"radiotherapy" + 0.027*"cell" + 0.025*"radiosurgery" + 0.023*"tumor" + 0.021*"radiation" Eq. 5

Topic_5t = 0.044*"radiation" + 0.042*"cancer" + 0.040*"therapy" + 0.024*"cell" + 0.021*"tissue" + 0.020*"normal" + 0.018*"beam" + 0.018*"ion" + 0.013*"proton" + 0.013*"effect" Eq. 6

Topic_6t = 0.039*"radiotherapy" + 0.029*"tumor" + 0.020*"cancer" + 0.016*"radiation" + 0.015*"therapy" + 0.015*"patient" + 0.015*"brain" + 0.012*"model" + 0.011*"imaging" + 0.011*"preclinical" Eq. 7

Topic_7t = 0.049*"tumor" + 0.034*"cell" + 0.026*"dna" + 0.023*"repair" + 0.022*"factor" + 0.019*"cancer" + 0.014*"lung" + 0.013*"targeting" + 0.013*"radiotherapy" + 0.013*"pathway" Eq. 8

Topic_8t = 0.093*"cell" + 0.039*"human" + 0.028*"effect" + 0.023*"expression" + 0.022*"radiation" + 0.018*"gene" + 0.017*"carcinoma" + 0.016*"line" + 0.015*"vitro" + 0.014*"irradiation" Eq. 9

Topic_9t = 0.089*"dose" + 0.033*"radiotherapy" + 0.030*"rate" + 0.029*"brachytherapy" + 0.018*"high" + 0.016*"radiobiology" + 0.016*"prostate" + 0.015*"model" + 0.013*"linear" + 0.012*"radiobiological" Eq. 10

Appendix A.2. Topics from Abstracts (a)

Topic_0a = 0.033*"model" + 0.013*"dose" + 0.012*"tumor" + 0.012*"imaging" + 0.009*"flash" + 0.009*"feature" + 0.008*"clinical" + 0.008*"image" + 0.007*"parameter" + 0.006*"volume" Eq. 11

Topic_1a = 0.070*"cell" + 0.021*"tumor" + 0.014*"effect" + 0.013*"dna" + 0.009*"repair" + 0.009*"response" + 0.009*"damage" + 0.008*"line" + 0.007*"mechanism" + 0.006*"survival" Eq. 12

Topic_2a = 0.033*"proton" + 0.025*"ion" + 0.022*"rbe" + 0.021*"beam" + 0.016*"particle" + 0.014*"carbon" + 0.014*"energy" + 0.014*"biological" + 0.013*"therapy" + 0.012*"photon" Eq. 13

Topic_3a = 0.044*"patient" + 0.016*"rt" + 0.015*"survival" + 0.015*"tumor" + 0.011*"p" + 0.008*"surgery" + 0.008*"local" + 0.008*"rate" + 0.008*"overall" + 0.007*"o" Eq. 14

Topic_4a = 0.056*"patient" + 0.019*"toxicity" + 0.015*"p" + 0.011*"breast" + 0.010*"risk" + 0.010*"grade" + 0.010*"gy" + 0.010*"month" + 0.008*"sbrt" + 0.008*"treated" Eq. 15

Topic_5a = 0.033*"study" + 0.028*"therapy" + 0.022*"clinical" + 0.017*"trial" + 0.015*"preclinical" + 0.012*"tumor" + 0.012*"immunotherapy" + 0.011*"targeted" + 0.010*"agent" + 0.010*"promising" Eq. 16

Topic_6a = 0.023*"expression" + 0.019*"cell" + 0.017*"gene" + 0.012*"response" + 0.012*"patient" + 0.011*"tumor" + 0.008*"level" + 0.007*"irradiation" + 0.007*"protein" + 0.006*"blood" Eq. 17

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Topic_7a = 0.026*"dose" + 0.023*"gy" + 0.020*"irradiation" + 0.014*"cell" + 0.013*"tumor" + 0.012*"plan" + 0.011*"dos" + 0.009*"day" + 0.009*"target" + 0.008*"mouse" Eq. 18

Topic_8a = 0.016*"clinical" + 0.012*"therapy" + 0.012*"oncology" + 0.008*"radiobiology" + 0.007*"patient" + 0.006*"right" + 0.006*"reserved" + 0.006*"medical" + 0.006*"development" + 0.006*"elsevier" Eq. 19

Topic_9a = 0.039*"dose" + 0.020*"tumor" + 0.014*"fraction" + 0.013*"tissue" + 0.012*"model" + 0.012*"effect" + 0.011*"gy" + 0.009*"normal" + 0.008*"rate" + 0.008*"cell" Eq. 20

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