

Systematic Review

Dose Estimation by Geant4-Based Simulations for Cone-Beam CT Applications: A Systematic Review

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Abstract: The last two decades have witnessed increasing use of X-ray imaging and, hence, the exposure of humans to potentially harmful ionizing radiation. Computed tomography accounts for the largest portion of medically-related X-ray exposure. Accurate knowledge of ionizing radiation dose from Cone-Beam CT (CBCT) imaging is of great importance to estimate radiation risks and justification of imaging exposures. This work aimed to review the published evidence on CBCT dose estimation by focusing on studies that employ Geant4-based toolkits to estimate radiation dosage. A systematic review based on a scientometrics approach was conducted retrospectively, from January 2021, for a comprehensive overview of the trend, thematic focus, and scientific production in this topic. The search was conducted using WOS, PubMed, and Scopus databases, according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement. In total, 93 unique papers were found, of which only 34 met the inclusion criteria. We opine that the findings of this study provides a basis to develop accurate simulations of CBCT equipment for optimizing the trade-off between clinical benefit and radiation risk.

Keywords: cone-beam computed tomography; monte carlo simulations; Geant4; radiation protection; radiation exposure; dosimetry; systematic-review; bibliometrics



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1. Introduction

X-ray medical imaging has undergone tremendous technological advances for the diagnosis and treatment of a breadth of examinations and procedures [1]. In particular, due to its rich and robust image information and shorter examination time [2–5], cone-beam computed tomography (CBCT) has become standard in recent clinical applications as adaptive radiotherapy treatment [6], image-guided radiation therapy (IGRT) [6–12], maxillofacial applications [13–15], cone-beam breast tomography (CBBCT) [16–23], or proton computed tomography for particle therapy [24–28]. CBCT is a new technology using a cone-shaped beam and a detector that rotate 360° around the patient, able to acquire projected data in a single rotation [29].

Nevertheless, these advances have resulted in a rise in radiation dose, being the medical exposure to ionizing radiation from CT examinations a major issue of concern nowadays [30–36]. Ionization radiation exposure can induce harmful biological effects, depending on the radiosensitivity of the organ, radiation dose, dose distribution, age, gender, or genetic factors [37]. Due to the harmfulness of X-rays for living beings, the ALARA principle, “as low as reasonably achievable”, has become the criterion to apply for medical X-ray imaging [31,38]. This criterion has brought positive effects on protocol standardization [39–42].

Although CBCT imaging dose is known to be smaller than typical CT scan, it cannot be neglected. Indeed, an overuse of CBCT procedures may increase the risk of the secondary side effects [43]. Lifetime attributable risks (LARs) of cancer incidence for several solid tumors have been classified by patient age and time of exposure [44]. Statistically significant dependence of relative risk (RR) of leukemia and brain cancer incidence following CT scans in childhood was first reported by Pearce et al. [45] showing a linear-no-threshold risk hypothesis [46]. LARs and RR of cancer incidence for various organs in standard- and low-dose CBCT modes from a single scan were analyzed showing that the highest LARs are for incidence of colon and bladder cancers, while the highest RRs are for incidence of stomach and liver cancers for the abdominal CBCT [47]. Therefore, accurate evaluation of the dose delivered from CBCT scans is crucial to provide physicians' awareness of radiation risks [48].

One of the most common applications of CBCT is image-guided procedures during proton therapy [49]. This technique improves the accuracy of radiation therapy but significantly contributes to an extra radiation dose to cancer patients, thus increasing the risk of second malignant neoplasms [50,51] and other side-effects, as in Reference [52]. These effects are related to different factors as age at irradiation, type of irradiated tissue or volume, treatment technique, or previous radiological procedures [46,53]. Besides, the potential risks of second cancers from scattered proton radiotherapy for childhood cancers is a cause of major concern [54]. Indeed, the use of low-dose mode to avoid unnecessary radiation exposure is recommended in the particular case of pediatric IGRT [47].

In response to the increasing awareness, large-scale efforts have been made to develop new methodologies for improving radiation protection standards [55,56]. Monte Carlo (MC) simulations of the radiation transport and interaction are a powerful method for dose distributions calculations in complex geometries and the presence of extended spectra of multi-radiation sources [57–62]. Not only can they accurately predict the distributions of absorbed doses but also other amounts of interest in radiation procedures, as well as the evaluation of the image quality [8]. During the last few years, MC techniques have played a major role in dosimetry; however, until its development, any comprehensive dosimetric study was thought to be impossible and dangerous.

Current applications of the MC method in medical physics cover a wide variety of topics, such as radiation protection, diagnostic radiology, radiation therapy, nuclear medicine, and the design and optimization of imaging protocols. Nevertheless, there is still a wide need to adapt and validate the MC simulation codes in dosimetry studies in order to unveil its potential for testifying more radiation protection measures and also new techniques to reduce the high computational cost required.

Although there is a wide range of MC codes capable of simulating radiation transport [63–69], not all available codes are capable of precisely handling all radiation-induced aspects, and they require very high computational costs and advanced programming skill. Among all of the above, it is worth highlighting the software Geant4, GEometry And Tracking [68,69], which is a flexible set of tools for simulating the passage of particles through matter by iteratively calculating the trajectories and interactions between particles and atoms. One of the advantages of this toolkit is the capacity of simulating the most physical processes in the areas of high-energy physics, nuclear, space, and medical physics, among others [70–73]. In addition, due to its great functionality, there are other architectures based on Geant4 with specific applications for radiation therapy and dosimetry applications, such as GATE (Geant4 Application for Emission Tomography) [74–76], or GAMOS (Geant4-based Architecture for Medicine Oriented Simulation), which has a set of field-specific utilities for nuclear medicine, radiotherapy, hadrontherapy, and radiation protection [77–83].

Since CBCT is a quite novel development in clinical practice, data on radiation doses and possible effects of CBCT are still being gathered and analyzed. Therefore, it is worth elucidating knowledge on CBCT applications that estimate delivered dosage using Geant4 simulation toolkit.

Bibliometric analysis in academic medicine is a relatively new suitable method to analyze a large amount of information extracted from scientific databases by using quantitative tools [84–88]. The aim of this systematic review (SR) is to investigate the most impactful and influential studies on CBCT applications using Geant4 architecture to estimate the dose, unraveling the following research questions (RQ):

- RQ1: What are the most significant current publications estimating radiation dose using Geant4 in CBCT applications?
- RQ2: Which are the most common CBCT applications that use Geant4 simulations to estimate the dose and how have they changed over the years?
- RQ3: How advances in Geant4-based CBCT dose estimator may help to evaluate the risk of developing stochastic effects?
- RQ4: What are the current research trends and disciplines for prospective research on this topic?

A holistic understanding of these results may contribute to the development of new theoretical and applied works that can be used to support new research from this field.

The manuscript is organized as follows. Section 2 exposes the search methodology to find all relevant papers by defining a suitable search query in Section 2.1, the inclusion and exclusion criteria in Section 2.2, and the data extraction and analysis process in Section 2.3. Next, Section 3 presents individually the obtained results and the corresponding discussion where the above RQ are answered. Finally, the conclusions are presented in Section 4.

2. Methodology

2.1. Literature Search

A SR of electronic data bases was conducted retrospectively between January 1975 and January 2021. The identified studies were subjected to pre-identified inclusion criteria according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement based on key words and MeSH terms specific to publications indexed in PubMed, Web of Science (WOS), and Scopus databases.

The search strategy was restricted to English-language papers via WOS, Scopus, and Pubmed. To construct a suitable query and increase the sensitivity of the search strategy, the research question included the following combined terms and their synonyms and related topics: “Geant4”, “GATE”, “GAMOS”, “radiation dosage”, “radiation protection”, “dose*”, and “cone-beam computed tomography”.

For the purpose of this search, these terms were defined as:

- Geant4 OR GATE OR GAMOS to include all the toolkit based on these codes.
- Cone beam computed tomography according to medical subject headings (MeSH).
- Cone beam computed tomography as a generic term that refers to the medical imaging technique with a conic/pyramidal X-ray beam of radiation.
- Radiation dosage and radiation protection according to medical subject headings (MeSH).
- Dose OR Dosimetry as a generic term including all types of doses described by the International Commission on Radiological Protection (ICRP) [38].

The final analysis contained primary research articles estimating physician knowledge of radiation dosage of cone-beam computed tomographies based on Geant4. These results were supplemented by a literature hand search. The full query is displayed in Table 1.

Table 1. Search strings, keywords, and items per database.

Indexing Terms	Items (n)
Web of Science	235.997
#1 Geant4 OR GATE OR GAMOS	15.035
#2 Cone Beam Computed Tomography OR CBCT	1.32
#3 Radiation Dosage OR Dose* OR Dosimetry OR Radiation protection	4.814
#4 #1 AND #2 AND #3	87

Table 1. *Cont.*

Indexing Terms	Items (n)
Scopus	324.712
#1 Geant4 OR GATE OR GAMOS	23.097
#2 Cone Beam Computed Tomography OR CBCT	2.46
#3 Radiation Dosage OR Dose* OR Dosimetry OR Radiation protection	7.584
#4 #1 AND #2 AND #3	36
PubMed	23.473
#01 Geant4 OR GATE OR GAMOS	14.283
#02 Cone beam computed tomography	9.704
#03 Cone beam computed tomography [MeSH]	959.263
#04 Dose*	109.722
#05 Radiation Dosage	62.177
#06 Radiation dosage [MeSH]	30.678
#07 Radiation protection	12.216
#08 Radiation protection [MeSH]	14.283
#09 #2 OR #3 OR	1.02
#10 #4 OR #5 OR #6 OR #7 OR #8 OR #9	1.140
#11 #9 AND #10 AND #1	24

2.2. Inclusion and Exclusion Criteria

Research studies based on publications estimating radiation dose using Geant4 in different CBCT applications published in international peer-reviewed journals were included. Reviews, technical notes, conference proceedings, reports, and articles were considered.

The exclusion criteria were:

- not medical use;
- papers that do not focus on CBCT;
- studies that do not focus on humans; and
- papers that do not estimate the dose using Geant4-based toolkits.

2.3. Data Extraction and Analysis

Three examiners performed the eligibility and quality assessment of relevant studies. To construct a query suitable for WOS, PubMed, and Scopus, we extracted the following important information: author, journal, year of publication, citations, country or region, source, keywords, and CBCT applications. We also searched the reference lists of the studies encountered. We examined key elements of their titles, abstracts, and keywords analyzing the obtained results. If this information did not give enough evidence about the eligibility, the full text was screened. Furthermore, the whole text was also screened if one of the authors detected that one of the inclusion criteria was not accomplished. We also individually extracted the simulation toolkit (source Geant4, GATE, GAMOS), as well as the specific application (breast imaging, proton therapy, IGRT, etc.) from each study. In case of the author's disagreement over the study selection or data extraction, the issue was solved by consensus discussion among the reviewers. The selected articles were ranked based on the total citations received from the three databases.

The screening of the results from the literature search, based on title and abstract reading, revealed that 41 papers were potentially eligible for full-text reading. After examination of the full texts, papers that did not meet the inclusion criteria were excluded. The principal reasons for exclusion were: studies did not focus on humans (1 article); not CBCT applications (1 article); dose was not evaluated by MC simulations (2 articles); dose was not estimated by Geant4 codes (1 article). Each stage of the search and the eligibility screening processes with the number of papers identified, included, and excluded is illustrated in Figure 1.

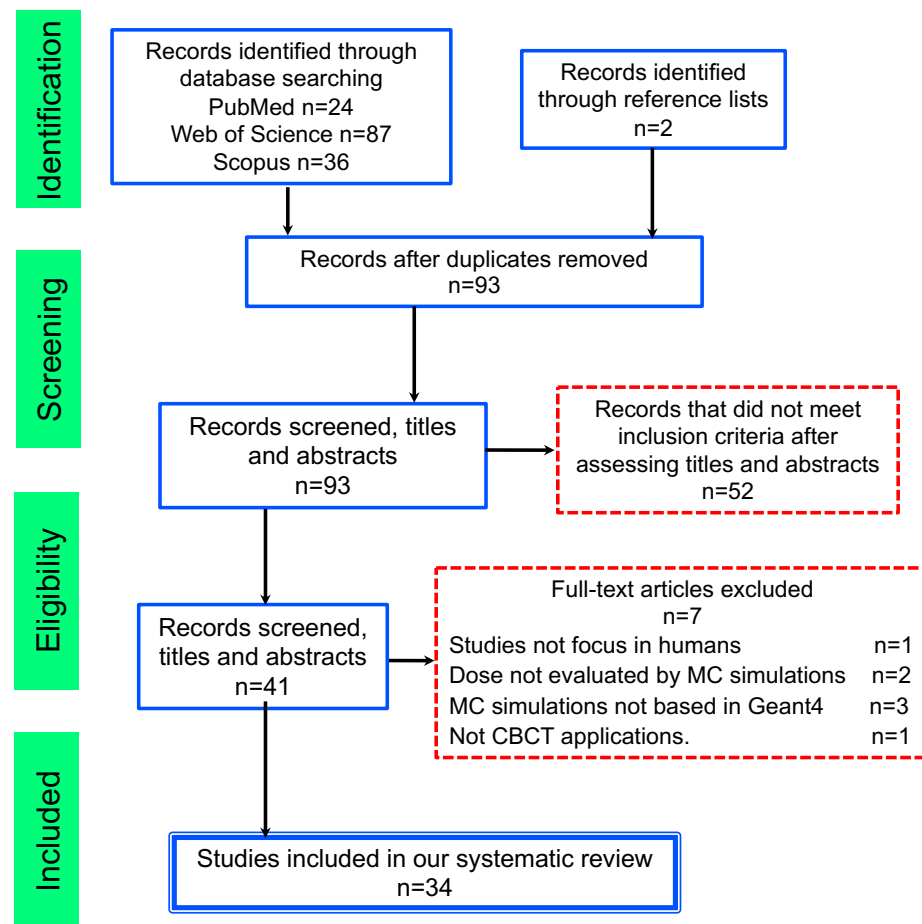


Figure 1. Flowchart consistent with preferred reporting items for systematic reviews (PRISMA) statement.

To answer the proposed research question, we performed a bibliometric analysis based on Bibliometrix R-package for scientometric factors and biblioshiny [89]. For visualization, the author's name, corresponding author's country, the total number of publications, author's keywords, and keywords plus were generated. For keywords, the co-occurrence of keyword and keyword plus and abstract phrases were evaluated. VOSviewer (version 1.6.16) was also used to perform a cluster analysis and construct a knowledge map of the topics.

3. Results and Discussion

Finally, we found 34 studies that satisfied the inclusion criteria coming from 14 different sources between 2008 and 2021. An overview of this information is shown in Table 2, which displays the main information about the selected papers, and Table 3, which presents the selected publications regarding author, application, and year of publication. Below, the studies from this selection will be discussed individually, addressing the aforementioned research questions.

Table 2. Main information about selected articles.

Results	
Timespan	2008–2021
Sources (journals, books, etc.)	14
Documents	34
Average years from publication	4.97

Table 2. Cont.

Results	
Average citations per documents	9.56
Average citations per year per doc	1.27
References	839
Articles	32
Conference papers	1
Meeting abstracts	1
Keywords plus	132
Author's keywords	107
Authors	150
Authors of single-authored documents	0
Authors of multi-authored documents	150
Documents per author	0.23
Authors per document	4.41
Co-Authors per documents	5.62
Collaboration index	4.41

Table 3. Overview of extracted data from papers regarding reference named by first author, applications, and year of publication.

Reference	Applications	Year
Tseng, H. W. et al. [90]	Cone-Beam Breast CT	2021
Cho, S. et al. [91]	Novel method to improve quality of CBCT images	2020
Principi S. et al. [92]	Comparison between LBTE methods against Geant4 benchmark	2020
Shi M. et al. [93]	GPU-based for proton simulation	2020
Lee, H. et al. [94]	Deep Learning-based scatter correction method	2019
Jia, S et al. [95]	Dental and maxillofacial CBCT	2019
Wang A. et al. [96]	Comparison between Acuros CTD against Geant4	2019
Ardenfors, O. et al. [97]	Proton Gantry-Mounted CBCT	2018
Ardenfors, O. et al. [98]	Proton Gantry-Mounted CBCT	2018
Gholami, S. et al. [99]	Stereotactic Radiosurgery with small radiation fields	2018
Maslowski, A. et al. [100]	Comparison between Acuros CTD against Geant4	2018
Leotta, S. et al. [101]	Image-Guided RadioTherapy	2018
Son, K. et al. [102]	Image-Guided RadioTherapy	2018
Zhu, J. et al. [103]	Adaptive Radiotherapy	2017
Benhalouche, S. et al. [104]	Simulated Mega-Voltage CBCT	2017
Myronaki, M. et al. [105]	Optimization of a Multilayer Imager Mega-Voltage CBCT	2017
Sakata, D. et al. [106]	Dual-Energy Computed Tomography	2017
Son, K. et al. [107]	Image-Guided RadioTherapy	2017
Marchant, T.E. et al. [108]	Radiotherapy	2017
Xu, M. et al. [109]	Cone-Beam Breast CT	2017
Shi, L. et al. [110]	Cone-Beam Breast CT	2016
Baldacci, F. et al. [111]	TLE method for low-energy X-ray irradiations	2015
Choi, J.H. et al. [112]	New dose point measurement method validated by Geant4	2015
Brochu, F.M. et al. [113]	Radiotherapy	2014
Li, X. et al. [114]	Perfusion and Interventional CBCT	2014
Hansen, D.C. et al. [115]	Proton Computed Tomography	2014
Son, K. et al. [116]	Image-Guided RadioTherapy	2014
Bartzsch, S. et al. [117]	Image-Guided RadioTherapy	2013
Lanconelli, N. et al. [118]	Cone-Beam Breast CT	2013
Fleckenstein, J. et al. [119]	Volumetric Modulated Arc Therapy	2013
Vedantham, S. et al. [120]	Cone-Beam Breast CT	2012
Sechopoulos, I. et al. [121]	Cone-Beam Breast CT	2010
Chen L. et al. [122]	Cone-Beam Breast CT	2009
Chen L. et al. [123]	Cone-Beam Breast CT	2008

3.1. RQ1: What Are the Most Significant Current Publications Estimating Radiation Dose Using Geant4 in CBCT Applications?

In order to answer this question, special attention is paid to the most influential references and the author's productivity and relevance. Productivity was measured by the number of publications of each author. Influence was taken into account by the number of total citations (TC) received by the articles included in our selection from documents indexed on the different bibliographic databases. Table 4 presents the top 10 cited articles per author and journal, comparing the TC, TC per year, and the Local citations (LC) and its percentage. LC are citations received by a certain article internally in our selection. The three most influential papers in dosimetry studies by Geant4 simulation were Sechopoulos I. et al. [121], with 63 TC, an average of 5.25 cites per year, 4 LC, and 6.35% of LC; Chen L. et al. [123], with 37 TC and an average of 2.64 cites per year; and Chen L. et al. [122], with 26 TC and an average of 2.0 cites per year. The main topic addressed in his authored and co-authored publications corresponds to Cone-beam breast CT applications.

Table 4. Top 10 cited articles per author and journal. TC column shows the total citations, TC per year are the total citations per year, and LC are local citations, while LC % are the percentage of local citations.

Paper	TC	TC per Year	LC	LC %
Sechopoulos I. et al., 2010, Med. Phys. [121]	63	5.25	4	6.35
Chen L. et al., 2008, Med. Phys. [123]	37	2.64	0	0.0
Chen L. et al., 2009, Med. Phys. [122]	26	2.0	0	0.0
Vedantham S. et al., 2012, Med. Phys. [120]	20	2.0	20	10.0
Shi L. et al., 2016, Med. Phys. [110]	19	3.17	0	0.0
Bartzsch S. et al., 2013, Med. Phys. [117]	19	2.11	0	0.0
Fleckenstein J. et al., 2013, Z Med. Phys. [119]	19	2.11	0	0.0
Maslowski A. et al., 2018, Med. Phys. [100]	15	3.75	2	13.33
Myronakis M. et al., 2017, Med. Phys. [105]	14	2.80	1	7.14
Marchant, T.E. et al., 2014 Med. Phys. [108]	11	2.20	0	0.00
Hansen D.C., 2014, Med. Phys. [115]	11	1.4	0	0.0

Figure 2 illustrates the progression of publications available in the selected databases in the period 2008–2020. Despite the fact that our research was conducted retrospectively from 1975, since CBCT is a quite new development in clinical practice, and Geant4 is a recent simulation toolkit, the first publications combining both technologies appear in 2008. There was an upsurge in publications, from just 2 documents published in 2008 to 7 documents in 2017. The main reason for this surge may be attributed to the increase in CPU power and the development of MC simulations integrating new techniques to reduce the high computational cost required as explained in References [90,93,94,96,99,100,104]. The dashed blue line denotes the average TC per year showing two peaks in 2010 and 2016 corresponding to the references [110,121], respectively.

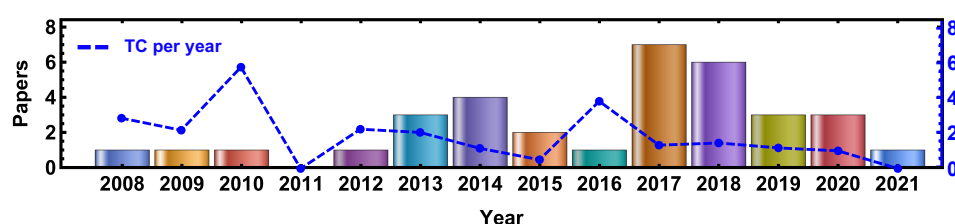


Figure 2. Annual publication trend of selected documents retrieved from WOS, PubMed, and Scopus in the period 2008–2021. The blue dashed line correspond to the average TC per year.

A further insight into the most relevant publications in terms of author's productivity, author's co-citation network, collaboration countries and co-occurrence average citation of the most relevant author's keywords is described in the Supplementary Material.

3.2. RQ2: Which Are the Most Common CBCT Applications that Use Geant4 Simulations to Estimate the Dose, and How Have They Changed over the Years?

To identify the main research themes, the co-occurrence keyword network map shown in Figure 3 was created by selecting co-occurrence as the target variable [87]. The size of a node is determined by the frequency of its occurrence as a keyword, while the line thickness connection of two terms shows how frequently they co-occurred as keywords. The most frequent keywords, such as “MC simulation”, “CBCT”, “dosimetry”, “computed-tomography”, “radiotherapy”, or “Geant4”, have the biggest sizes. We can distinguish 5 different intertwined nodes sharing the most common terms, but which, in turn, are grouped into more specific topics. The annual tendency show that around 2010 (blue-green colors) the articles were related to “breast imaging”, “mammography”, and “image-quality”, while, around 2015 (green-yellow colors), the main topic was “dosimetry” involving “mc simulations” and “radiotherapy” and “geant4” by 2017. The latest articles (orange-red colors) are related to “validation”, “cancer”, and “radiation dose”.

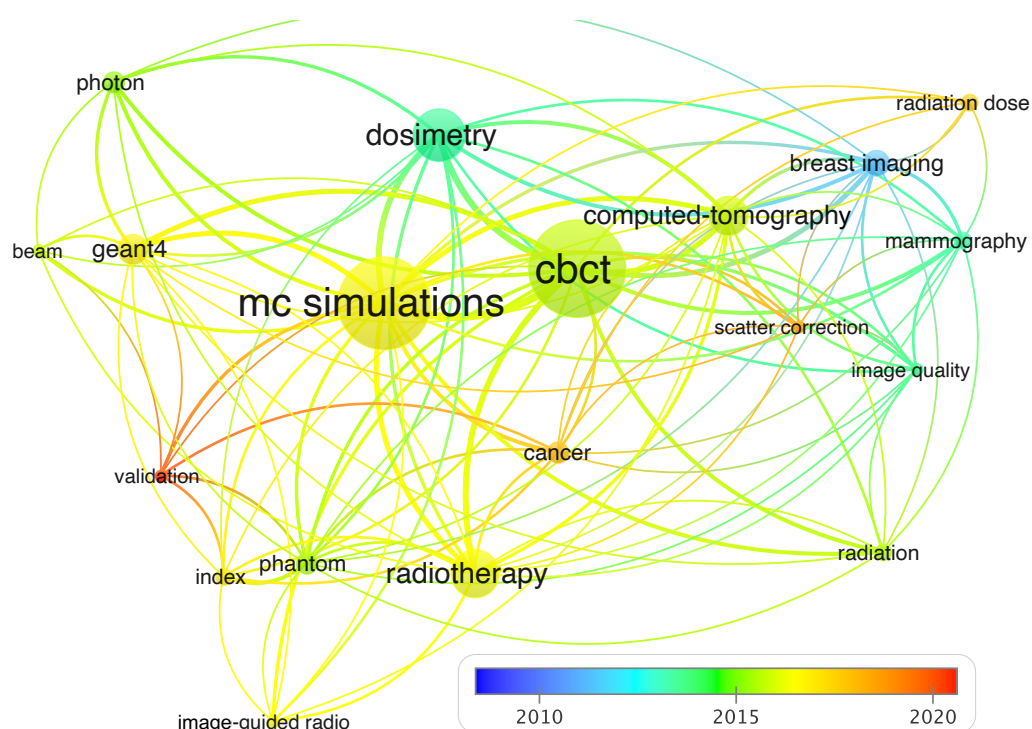


Figure 3. Co-occurrence network of keywords. The thicker line indicates a strong association between those keywords, while thinner lines depict weak association

Regarding Table 3, the most common application of Geant4-based toolkit are dedicated to breast imaging, such as CBCCT [90,109,110,118,120–123]. Tseng et al. found a potential for radiation dose reduction estimating the normalized glandular dose coefficients (DgN^{CT}) that provide air kerma-to-mean glandular dose conversion factors by GATE software, version 8 [90]. GATE was also used in Reference [109] simulating a multi-energy spectrum to radiate same-size built-in calcifications and lump breast motifs under the condition of the same number of particles, while References [110,118,120–123] investigate the feasibility of Geant4 codes to estimate the dose in CBBCT.

The second most common application corresponds to IGRT [101,116,117]. In the first publication in 2013, S. Bartzch et al. present a novel analytical method that can be employed in a fast treatment planning system for kV photon dose calculations in IGRT [117]. They validate their results by simulations performed with the Geant4 toolkit and found that dose calculation times can be significantly reduced in convolution-based algorithms. In 2018, S. Leotta et al. evaluated organ doses in IGRT due to CBCT and therapeutic MV irradiation in head-neck, thorax, and pelvis districts through GAMOS simulation toolkit [101]. After

verification by comparing with experimental quality indexes, they found that scattered radiation in therapy was one to two orders of magnitude larger than that diffused by CBCT. GAMOS toolkit was also used for a deeper understanding of late toxicity risk in external beam radiotherapy patients by simulating dose depositions integrated from different sources over the entire treatment plan in the reference [113].

Besides, using GATE simulation tool, dose deposited during MV-CBCT procedure was simulated and compared to measurements obtained with dedicated detectors in References [104,105], being able to reconstruct imaged volumes and to estimate doses deposited by simple and complex irradiation fields. GATE was also employed by K. Son et al. to investigate the imaging radiation dose delivered to radiosensitive organs from IGRT [116] and the imaging radiation doses resulting from six different acquisition protocols for the adult and pediatric numerical XCAT phantoms [107]. In the first article, they calculated the absorbed doses of head-and-neck, chest, abdomen, and pelvis regions, in both standard CBCT scan mode (125 kVp, 80 mA, and 25 ms) and low-dose scan mode (125 kVp, 40 mA, and 10 ms). They found that the reduction in the radiation dose in the low-dose mode compared to the standard mode was about 20%. In the second article, they provide a platform for developing a new kV-CBCT scanning protocol in conjunction with a low-dose capability. A few years later, the same first author successfully demonstrated the feasibility of incorporating a tube current modulation method in a kV-CBCT system for IGRT to optimized dose reductions without degrading image quality [116]. Thus, the results from these studies would significantly facilitate decisions regarding the administration of extra imaging doses to radiosensitive organs and may reduce the occurrence probability of adverse effects on health derived from radiation exposure.

Proton therapy is a promising high resolution image reconstruction modality applied to CBCT that maintain the improved stopping power estimation of proton CT. Hansen et al. [115] propose a method to overcome the problem of limited angles using a dual modality reconstruction combining the proton data with a CBCT. However, it does not fully achieve the quality of a 360° proton CT scan. In 2018, O. Ardenfors et al. accurately characterized a proton gantry-mounted CBCT system. To examine the influence on organ doses from different acquisition modes and repeated imaging, they used two MC codes: MCNP6 and GATE. They found that organ doses significantly fluctuated depending on the acquisition mode, recommending posterior scans [97,98]. T.E. Marchant also proved that the CBCT imaging doses simulated by GATE depend greatly on the imaging isocenter location, patient sex, and partial rotation angles [108].

A method to estimate dose accuracy in volumetric modulated arc therapy treatment plans by MONACO, an independent Geant4-based dose calculation algorithm, is presented in Reference [119]. J.H. Choi et al. propose new dose point measurement-based method to characterize the dose distributions and the mean dose from a single partial rotation of a CBCT system over a stationary, large, body-shaped phantom validated by a Geant4 simulation [112].

From 2018 to 2020, some publications have been dedicated to developing new software tools for rapidly and accurately estimating scatter in x-ray projection images by solving the deterministic linear Boltzmann transport equation (LBTE) [92,96,100]. These methods use Linear Discontinuous Finite Elements, Multigroup, and Discrete Ordinates methods to maintain the accuracy of a continuous solution. To solve the high computational complexity and achieve the speeds required for clinical utilization, implementation in CUDA allowed to exploit the parallel computing capabilities of GPUs. M. Shi et al. propose a novel strategy to accelerate simulations by also using a Geant4-based GPU code for photon transport for the simulation of an MV-CBCT [93].

3.3. RQ3: How Advances in Geant4-Based CBCT Dose Estimator May Help to Evaluate the Risk of Developing Stochastic Effects?

Estimating potential risks of developing stochastic from a CBCT scanning protocol requires analysis of both the radiation dose to specific organs and the risk of developing health effects as a result of this dose. To this aim, we study the quantities of interest that

provided organ doses [124] reported in our bibliographic dataset for the most common applications described in the previous section.

Radiological doses from CBCT are closely related to the field of view, the imaging detector, and voxel sizes used for scanning and can be borderline between low (<1 mGy) and high radiological doses (5–100) mGy [125]. The potential health effects from radiation do not just depend on the absorbed dose but also on how sensitive a certain organ is to radiation [37]. The use of daily standard mode CBCT can result in up to 1.5–2 Gy to some critical organs and an effective dose of 600–800 mSv to the body, which may induce an additional secondary cancer risk of 3–4% [126]. As an example, a daily standard mode CBCT for a prostate of 35 fractions protocol may deliver an additional effective dose of 800 mSv to the patient, which could induce an additional secondary cancer risk of 4%. If only weekly standard mode CBCT were done, the additional risk of secondary cancer would be 0.8%. A chest treatment of 25 to 30 fractions with daily standard mode CBCT can result in an additional effective dose of 600–700 mSv, which could induce an additional secondary cancer risk of 3–3.5% [126].

High-precision radiotherapy is crucial when the surrounding tissues are highly radiosensitive [127]. IGRT can reduce the treatment margin and reduce normal tissue exposure, but it also adds a dose to patients, and its contribution has to be assessed and minimized [126]. The dose delivered, in both standard CBCT scan mode and low-dose scan mode, was studied in different treatment sites as the head-and-neck, chest, abdomen, and pelvis regions [116]. The reduction in the radiation dose in the low-dose mode compared to the standard mode was about 20%. The average absorbed doses in standard mode doses of the organs in the head and neck and chest regions 40.9–82.8 mGy and 43.0–74.8 mGy for the abdomen and pelvis region, while, for low-dose, ranged 16.1–18.9 mGy and 7.9–18.5 mGy, respectively. The variation in organ doses between the different imaging protocols is a consequence of the employed imaging parameters. The average organ doses from 360° scans for the head, thorax, and pelvis protocols were calculated with values between 6–8 mGy, 15–17 mGy, and 24–54 mGy, respectively [98]. Absorbed doses to organs located inside the FOV ranged between 6–54 mGy per 360° scan translating into cumulative doses from repeated daily CBCT imaging of 0.2–1.6 Gy.

Organ doses in IGRT in head-neck, thorax, and pelvis districts were also evaluated due to CBCT and therapeutic MV irradiation [101]. The results showed that the scattered radiation during therapy (MV range) is larger than that diffused by CBCT by one to two orders of magnitude; therefore, it allows to optimize the dose delivery, and it also does not cause excessive dose absorption to the organs at risk. Similarly, the imaging organ doses for the six different CBCT scanning protocols doses were calculated to range from 0.1–24.1 mGy for the adult phantom, and up to 36.8 mGy for the pediatric phantom in Reference [107]. In contrast, the imaging dose to the pediatric phantom in the chest region turns out to be 1.5–2 times higher than that of the adult phantom. For the female organs in the pelvic region, such as the ovary, uterus, and vagina, the imaging doses for the pediatric phantom were calculated to be 1.6–2.24 times higher than those for the adult phantom. These results may shed light on this issue, providing reference data for clinicians to make better decisions on the related clinical procedures, particularly for the pediatric patients. Furthermore, the feasibility of implementing a tube current modulation method to provide optimized dose reductions without degrading image quality has been successfully proven in a kV-CBCT system for IGRT [102].

On the other hand, breast cancer is becoming increasingly common among young women [128]. CBBCT improves breast cancer detection and characterization providing high-quality images with the potential to better visualize overlapping breast tissue compared to mammography or ultrasound [129–131]. However, there is a lack of standardized operation criteria in CBBCT [109]. The mean glandular dose using the CBBCT automatic tube current settings can vary from 5.5–17.5 mGy, depending on the breast size and composition [121]. The glandular dose distribution inside the breast can vary by up to 50% of the mean value, while, for a typical mammographic acquisition, the glandular dose

distribution varies from 15–400% of the mean. Lower dose values can be achieved if lower tube current settings are selected instead of those automatically suggested by the system, although the image quality may be reduced, as well. Chen et al. proposed that it is possible to selectively image a VOI with a reduced breast dose and scatter effect [122]. Furthermore, Lanconelli et al. [118] found that the more energetic beams provide a more uniform dose distribution than at low energy. Dose values within a PMMA phantom ranged from 0.28–0.46 mGy (at 50 kVp), and 0.44–0.60 mGy (at 80 kVp), while the 50 kVp beam presented an almost double coefficient of variation (ratio between the standard deviation and the mean of the distribution) than that for the 80 kVp beam. A recent study proposed a CBBCT system with an offset detector that estimates the normalized glandular dose coefficients with a potential dose reduction [90].

Let us remark that it is necessary to consider the tradeoffs between image quality and radiation dose. The ALARA principle does not necessarily mean the lowest radiation dose, an accurate diagnosis must be achieved. Conventional methods for improving image quality (scatter and artifacts reduction) based on physical equipment or measurements may lead to a dose increase. S. Vedantham et al. proposed a method that fulfills the necessary conditions for data sufficiency employing a circle-plus-line trajectory instead of a single circular trajectory with less than 0.18% increase in average glandular dose to the breast per projection [120]. In addition, a precomputed scatter library-based software approach to suppress scatter without a dose or scan time increase has been recently proposed by M. Shi et al. [110]. However, a very promising solution based on deep learning-based methods which uses MC simulations results as real data to train a CNN for image restoration and scatter correction has demonstrated high efficiency, accuracy, and reliability [132].

3.4. RQ4: What Are the Current Research Trends and Disciplines for Prospective Research on This Topic?

We conducted an analysis of the trending topic based on the author's keywords from the dataset. Author's keywords are generally related to such publication content and, hence, adequate to derive thematic aspects of a certain topic [133,134]. Despite the fact that several authors' keywords have been shown in the network map of Figure 3, a further insight is given in Figure 4. A hierarchical classification of the topics is shown in this map, representing the log (frequency) of the authors' keywords over the years. In this case, we have analyzed all the authors' keywords regardless of their frequency. For instance, in 2017 and 2016, computed tomography was the most discussed topic, followed by simulation in 2017. The dosimetry, photon, cancer, and radiotherapy topics were also quite cited from 2015–2018. In 2020, the term “validation” appears, suggesting that the last tendency point to the development of new methods for dose estimator is dedicated to the validation and effectiveness of new simulations codes suitable for the current technologies.

Finally, it is worthy of mention that, based on the most recent advances, new promising dose estimator algorithms involves Deep-Learning-based methods [135]. Deep Learning is a subfield of machine learning that employs algorithms inspired by the brain function and structure called artificial neural networks. The work of each neuron is entwined in a distributed manner to collectively learn from the input in order to optimize its final output [136,137]. In particular, convolutional neural network (CNN) architectures have witnessed rapid growth in medical physics [138,139]. Although CNNs were primarily used in the field of image pattern recognition [140], they can be also applied to accurately determine a dose distribution from an approximated simulated input dose [141–145]. In this framework, H. Lee et al. [132] proposed the use of a CNN combined with MC simulations for a CBCT equipment to generate the training data.

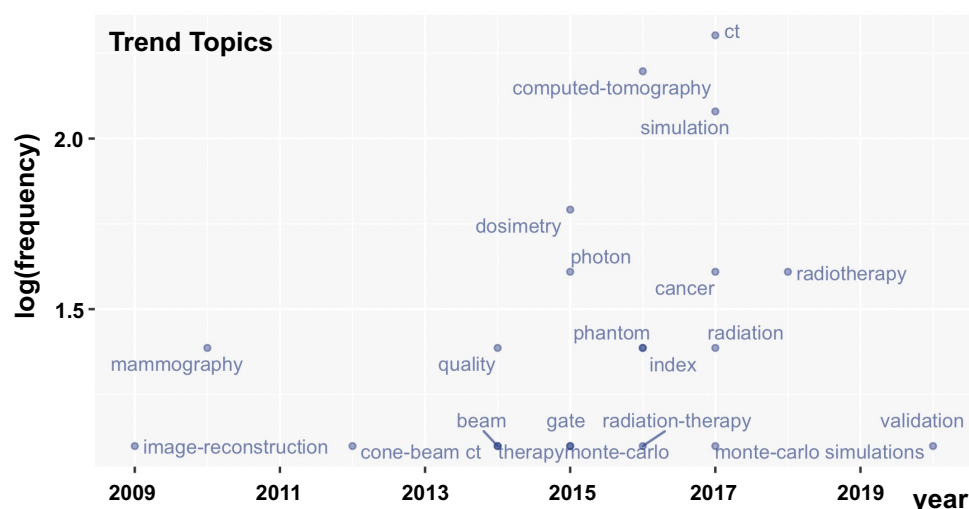


Figure 4. Trending topics between 2008 to 2021.

4. Conclusions

CBCT has emerged as a key technique for patient positioning and target localization in radiotherapy and other types of procedures; hence, the radiation exposure of human beings has been increased. An accurate estimation of ionizing radiation dose from CBCT procedures is of great importance to quantify the derived risks and for the justification of imaging exposures.

A significant number of publications have emerged in this field with several different approaches investigated due to different devices, medical applications, protocols, dose estimation methods, metrics of comparison, and treatment planning systems being discussed in the different studies. Due to the lack of standardization in dose estimator methods for CBCT applications, large-scale efforts have been made to develop new methodologies for improving radiation protection standards. Simulations based on MC have become one of the most accurate methods to predict the distributions of absorbed doses and other quantities of interest in radiation treatments.

In this systematic review we have adopted a scientometrics approach to investigate the most impactful and influential studies in the field of Geant4-based toolkits dose estimator for CBCT applications. An effective application of bibliometric tools can help for quantitative research and further insight of the state of the art. We opine that the findings of this study provides a helpful direction for medical physicists to elaborate new theoretical and applied works that can be used to develop accuracy simulations for radiation protection of patients and workers, while optimizing the trade-off between clinical benefit and radiation risk.

Supplementary Materials: The following are available online at <https://www.mdpi.com/2076-3417/11/13/6136/s1>, Figure S1: Top Author's Productivity over time, Figure S2: Author co-citation network, Figure S3: Rate of collaboration between countries based on authors' affiliations, and top 12 countries of publication based on corresponding author's country, Figure S4: Co-occurrence average citation of the most relevant author's keywords and dynamic view over time.

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