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Application of 3D printing for personalized boluses in radiotherapy: a systematic review

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ABSTRACT

The goal of this study was to evaluate the current literature covering the topic of 3D-printed radiotherapy boluses in the context of fabrication methods, materials, and clinical outcomes.

This systematic review followed the PRISMA 2020 guidelines. Data were extracted for authors, publication details, application type, printing technique and materials, study type, radiation type, reported outcomes and implementation difficulties.

The search yielded 161 articles, 52 of which met the inclusion criteria. Publications on 3D printing for customized boluses have increased since 2014, with the most articles from the United States (21%). Most studies (80.8%) focused on manufacturing custom boluses and testing 3D printing materials, whereas 19.2% explored creating molds for boluses. CT scans were the primary method for defining the bolus area (88.6%). The publications included three study types: dosimetric evaluations, evaluations with anthropomorphic phantoms, and clinical case studies. Fused Deposition Modeling (FDM) was the most common printing technique (88.1%), with Polylactic Acid (PLA) being the most frequently used material (57.1%). Challenges included ensuring proper fit, assessing material properties, and managing printing time.

The outcomes of this review suggest that 3D printing technology holds significant promise for improving radiotherapy by creating custom-fit boluses. 3D-printed boluses demonstrated notable advantages, such as improved dose distribution, better bolus conformity, and reduced setup times. However, several limitations have been identified, including considerable variability in study designs, making it challenging to draw generalized conclusions. Some studies had small sample sizes or did not clearly report methodological details. Addressing these issues will help to optimize technology's implementation.

Keywords: 3D printing; three-dimensional printing; radiotherapy; 3D-printed bolus

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Introduction

With the development of advanced three-dimensional (3D) printing techniques, printers are increasingly used in medicine. The ability to manufacture complex shapes tailored to the patient's anatomy has created the possibility of using 3D printing to produce patient-specific accessories such as implants [1], applicators [2, 3], shields [4], stents [5] or boluses used in radiotherapy.

The build-up effect characteristic of high-energy external X-ray beams enables skin protection in irradiated patients. For superficial lesions or tumors located close to the skin, build-up prevents the administration of a full therapeutic dose, which may result in a reduced chance of obtaining local control.

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The use of a bolus allows delivery of the full dose to the clinical target volume (CTV). In radiotherapy, a bolus is referred to as a piece of tissue-like material placed on the skin to reduce the risk of local recurrence [6]. Compared with commercial sheet boluses, 3D-printed boluses can provide a better fit to the irregular surface of the patient's skin, reduce the volume of air gaps, and improve the repeatability of alignment in each therapy session [7]. Correct bolus placement is a prerequisite for achieving the planned dose distribution, consequently enhancing patient outcomes [8].

The aim of this paper is to systematically review the literature in terms of fabrication methods, materials, and research developments on the topic of manufacturing customized 3D-printed teleradiotherapy boluses. Another goal is to systematize the current knowledge and guide the introduction of this technique into more radiation oncology centers.

Methods

This systematic review was conducted in accordance with the updated Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA 2020) statement [9]. The data collection process was carried out by one of the reviewers and verified by other authors.

The PubMed database was searched for literature. The following keywords and phrases were used to create the search query: *radiotherapy AND bolus AND (3d printing OR 3d printer OR 3d printed OR polylactic acid OR PLA OR acrylonitrile butadiene styrene OR ABS OR flex OR thermoplastic polyurethane OR TPU OR fused deposition modeling OR FDM OR stereolithography OR SLA OR selective laser sintering OR SLS OR additive manufacturing)*. Online libraries of journals associated with radiation oncology and medical physics were also screened (Physica Medica, Journal of Applied Clinical Medical Physics, Medical Dosimetry, International Journal of Radiation Oncology, Biology, Physics, Advances in Radiation Oncology, Practical Radiation Oncology) with the following search terms: *radiotherapy AND 3D printing AND bolus*.

Expressions: *fused deposition modeling (FDM), stereolithography (SLA)* and *selective laser sintering (SLS)* refer to 3D printing techniques, whereas *polylactic acid (PLA), acrylonitrile butadiene styrene (ABS), flex* and *thermoplastic polyurethane (TPU)* are the most common materials used in medical applications of additive manufacturing technology.

We included papers published after January 1, 2000. All papers with full text available were found, covering research articles, review articles and short communications. During the search process, papers for which only the abstracts were published were excluded from the analysis. We allowed English-language publications only.

The primary identification allowed the rejection of duplicate articles. Each record was then subjected to screening of titles and abstracts. Each record related to the topic and potentially informative to the review was included for detailed analysis. The retrieved full-text articles were thoroughly reviewed to determine whether a study was eligible for inclusion in the review. Studies that did not focus on the use of 3D printing in individual bolus production or did not include a study of the properties of the materials being used in 3D printing were excluded.

The articles included in the analysis were ordered and analyzed with predetermined parameters. They included authors, country and year of publication, type of application (bolus or mold fabrication), printing technique and utilized materials, type of study (dosimetric evaluation of material properties, bolus evaluation on phantom, clinical cases), radiation type application, potential risks, difficulties or weaknesses of the method and outcomes.

Results

The search process resulted in the identification of 161 articles. The implementation of the selection protocol shown in the flow diagram (Fig. 1) resulted in the identification of 52 articles that met the predetermined inclusion criteria. A list of all the articles included in the review can be found in Supplementary File.

Over the past few years, there has been a noticeable upward trend since 2014 in the number of publications addressing different applications of 3D printing technology in the production of customized boluses (Fig. 2). Prior to 2014, there was no academic literature available concerning the use of additive manufacturing technology for the production of radiotherapy boluses. Considering the country

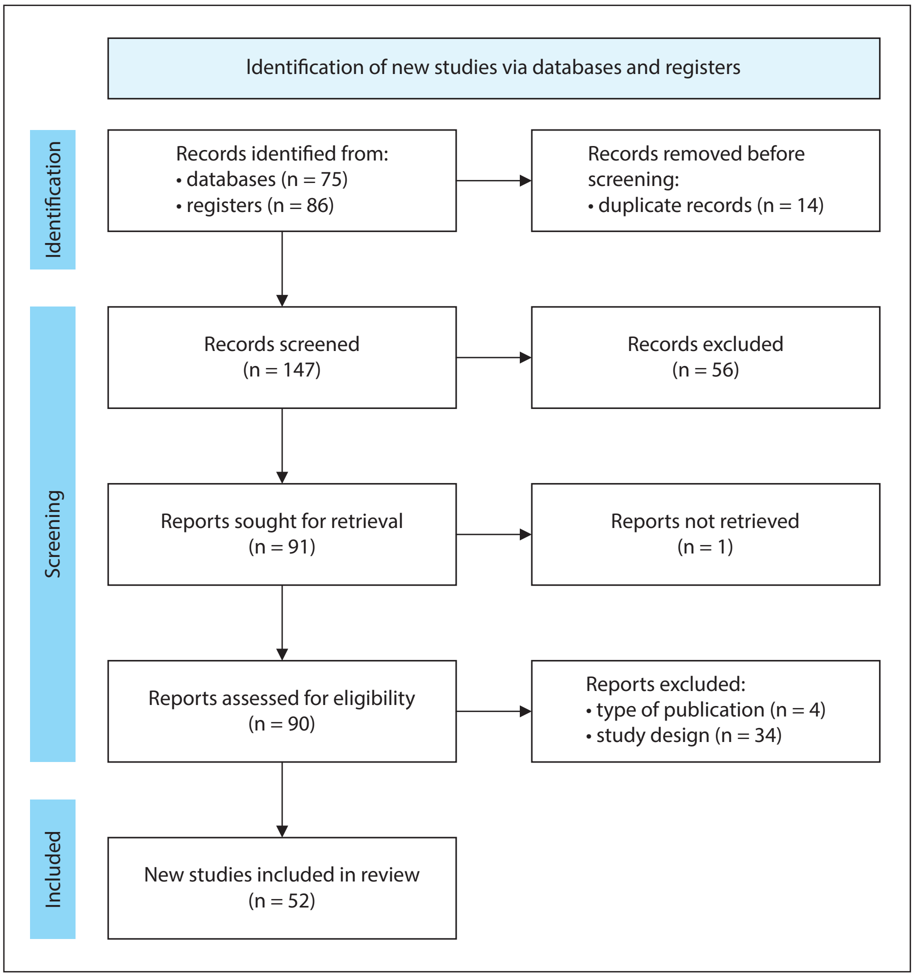
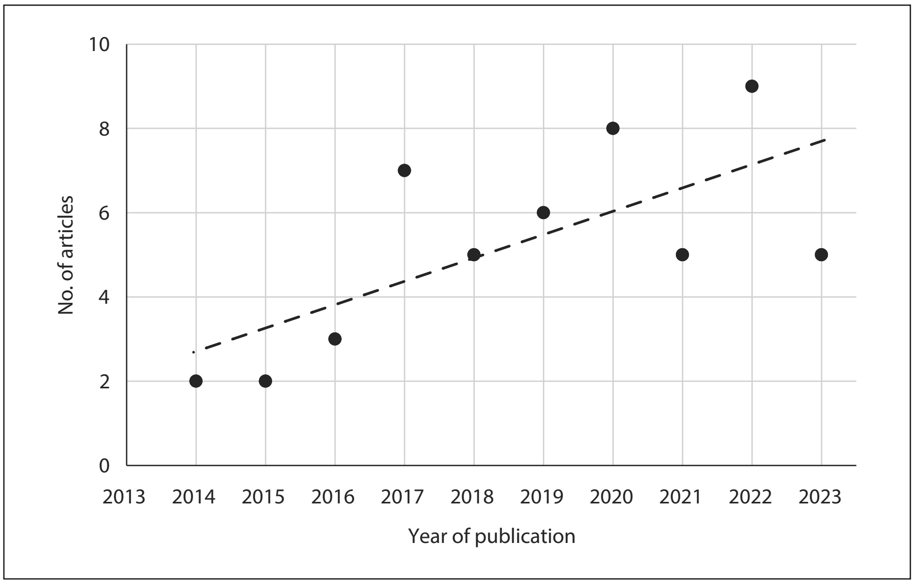


Figure 1. The PRISMA flow diagram process for selecting papers



Figue 2. The number of articles published in recent years on the application of 3D printing technology to the production of radiotherapy boluses, along with the trend line. The years 2000--2013 were excluded from the graph due to lack of matching data

of publication, the highest number of publications originated from the United States (n = 11, 21%), followed by China (n = 7, 13%), Korea (n = 7, 13%), Australia (n = 5, 10%), and Canada (n = 4, 8%). The remaining publications were distributed across Poland (n = 3, 6%), Japan (n = 3, 6%), Switzerland (n = 2, 4%), Colombia (n = 2, 4%), and individual contributions (2%) from Italy, Turkey, the United Kingdom, Germany, the Netherlands, Thailand, Ireland, and Spain.

Significant heterogeneity among the included studies was detected. The vast majority of the articles (n = 42, 80.8%) covered the following topics: manufacturing custom boluses via 3D printing, testing the properties of the 3D printing materials and the printing parameters for their potential use in bolus manufacturing. The remaining 19.2% (n = 10) of the articles focused on the use of 3D printing in the process of creating a mold for a bolus, which was later filled with another material. In eight of them, the molds were filled with various types of silicone or silicon [6, 8, 10–15]; in one study, water and wax were used for filling [16]; and in one study, the authors tested a liquid polyurethane resin developed in the center [17]. This type of application of 3D printing in bolus manufacturing does not assume the direct production of boluses through additive methods in clinical practice, and as such, it was not considered for further analysis.

Data extracted from the examined articles revealed that in studies involving bolus production (n = 35), two methods were used to define the bolus area. The primary method used to obtain surface scans remains CT (n = 31, 88.6%); in four studies (11.4%), the authors utilized optical scanning methods [18–21]. One study focused on comparing the results obtained from both modalities [19].

The analyzed publications included three distinct study types, often overlapping in focus (Tab. 1). These studies include dosimetric evaluations examining the properties of materials with potential applications in bolus printing processes (n = 22, 52.4%), studies investigating both the material properties and dosimetric characteristics of printed boluses utilizing anthropomorphic phantoms (n = 19, 45.2%), and clinical case studies (n = 20, 47.6%). Notably, among the clinical cases, three cases of 3D bolus application in veterinary patients were identified [22–24]. A weakness of the available studies of this type may still be the relatively small group of papers that chose to implement 3D printing technology to produce boluses for a larger group of patients. A predominant majority of the clinical case reports (60%) included studies with no more than ten patients each (median across all investigations = 10). Furthermore, only seven of the acquired papers opted for in vivo dosimetry, presenting a comparative analysis of the resulting dosimetric data against the calculations of the treatment planning system (TPS). This approach is crucial for obtaining comprehensive insights into the precision of TPS calculations in the presence of inhomogeneities caused by partial bolus filling, accurate material density conversion, and the potential possibility of introducing individualized boluses into clinical application. One paper described the use of 3D-printed boluses across a substantial group of 360 cases, offering intriguing possibilities for drawing conclusions regarding the method's clinical implementation. However, dosimetric data from in vivo measurements were available for 27 cases within this extensive cohort [25]. In 15 papers focusing on phantom studies, the complete procedure for crafting an individual bolus for an anthropomorphic phantom was detailed. This also included the irradiation process, dose distribution measurements, and comparisons with treatment planning system calculations or data obtained for boluses utilized in conventional clinical practice. Only three papers did not cover the dosimetric measurement process. Instead, they focused on the comparative analysis of treatment planning system dose distribution calculations obtained for printed boluses and traditional and conventional boluses. One paper focused only on validating the conformity of the 3D-printed bolus to the surface of the phantom [18].

A detailed summary of 3D-printed boluses applications is provided in Table 2. With respect to the type of radiation beam used in the dosimetry measurement process, measurements using photon beams accounted for 61% of the papers (n = 25). Additionally, eight papers were identified in which the authors investigated either electron radiation exclusively or focused on both types of radiation.

The main topic of 55% of the works in which boluses were printed was the head and neck region. Another area of application of 3D-printed

Table 1. Number of articles falling within each designated type of study with subcategories, characteristics of the 3D printing methods employed in the studies (including the 3D printing technique, the materials used and the number of materials tested) and risk factors and challenges in implementing the 3D printing technique while producing individual boluses in clinical practice

Type of study	Number (n = 42)
Dosimetric evaluation of material properties	22 (52.4%)
Phantom study	19 (45.2%)
Dose measurements	15
TPS dose comparison	3
No measurements	1
Clinical cases	20 (47.6%)
Human	17
Veterinary	3
Sample size	
1–10	12 (60.0%)
11–50	6 (30.0%)
51–100	1 (5.0%)
> 100	1 (5.0%)
3D printing parameters	Number (n = 42)
3D printing technique	
FDM	37 (88.1%)
PolyJet	5 (11.9%)
SLA	2 (4.8%)
SLS	1 (2.4%)
> 1	3 (7.1%)
Not given	1 (2.4%)

Materials	
PLA	24 (57.1%)
TPU	11 (26.2%)
ABS	11 (26.2%)
Resins	4 (9.5%)
Other	5 (11.9%)
Not provided	1 (2.4%)
Number of materials tested	
1	29 (69.1%)
2	8 (19.0%)
3	3 (7.1%)
4	1 (2.4%)
Not provided	1 (2.4%)
Risk factors and implementation challenges	**Number (n = 42)**
Cost	12 (28.6%)
Printing time	18 (42.9%)
Material physical properties assessment	19 (45.2%)
Printing accuracy	9 (21.4%)
Bolus fit accuracy	26 (61.9%)
Materials biocompatibility	4 (9.5%)
Ease of bolus positioning	10 (23.8%)
Patient comfort	7 (16.7%)

TPS — treatment planning system; FDM — fused deposition modeling; SLA — stereolithography; SLS — selective laser sintering; PLA — polylactic acid; TPU — thermoplastic polyurethane; ABS — acrylonitrile butadiene styrene

boluses was the chest region, particularly in relation to the breast and postmastectomy chest wall, which constituted 20.6% of the retrieved studies. Additionally, 17.6% of the studies expanded their scope to bolus fabrication for several anatomical areas. Singular instances were identified where boluses were printed for the extremities [26] and the entire body [27], intended for use in total skin irradiation.

Fused deposition modeling (FDM) has remained the predominant 3D printing technique in the field, accounting for 88.1% of applications. In FDM, a thermoplastic filament is melted and extruded layer by layer through a heated nozzle to construct a three-dimensional object. Other employed techniques, quantified in Table 1, include PolyJet, Stereolithography (SLA), and Selective Laser Sintering (SLS). In both the PolyJet and SLA techniques, UV light is utilized for curing materials, which are liquid photopolymers or liquid resins, respectively. In SLS technology, powdered materials are sintered with laser light [28]. Notably, three works incorporated prints from various technologies [18, 28, 29], whereas one lacked information on the specific printing technique utilized [25].

The most common materials used in retrieved works were polylactic acid (PLA) (57.1%), thermoplastic polyurethane (TPU) (26.2%) and acrylonitrile butadiene styrene (ABS) (26.2%). A summarized presentation of the material data can be found in Table 1. For 18 papers (42.9%), at least one of the tested materials had elastic properties, which is highly desirable when a bolus needs to be applied to anatomical areas with very complex and irregular surfaces.

In nearly every paper, the authors addressed or considered at least one technical aspect or limita-

Table 2. Summary of articles involving studies which included 3D printed bolus fabrication (*if clinical cases were included)

Year of publication	Country	Description of research	Printing technique	Printing materials	Sample size*	In vivo dosimetry	Outcomes and conclusions	Authors
2021	Turkey	Measurements of the effects of printing parameters on characterization of 3D printed bolus	FDM	PLA	–	–	The dosimetric and physical properties of the printed bolus material significantly change with selected infill percentages, pattern and printing directions. PTV dose coverage in plan created with 3D-printed bolus was found to be significantly higher than that with commercially available bolus	Biltekin et al.
2022	China	Dosimetry and fit evaluation of the 3D printed bolus. Dose differences on the skin were evaluated and patient follow-up was conducted for possible skin side effects.	Not provided	Not provided	360	Yes	3D-printed bolus provided an optimal dose distribution, with HI = 0.07(0.06–0.17) and CI = 99.94% (97.41%–100%). Skin side effects occurred, but were similar to the incidences of radiation dermatitis caused by a traditional bolus	Wang et al.
2018	Switzerland	Investigation of the possible use of a surface-scanner to produce a 3D printed bolus prior to the planning CT.	FDM, SLA, PolyJet	PLA, ABS, Polymer resin	10	No	Phantom tests showed maximum bolus-to-skin air gaps < 0.6 mm for surface-scanned models, comparing with 1–2 mm for CT models. A breast bolus model based on images acquired in deep inspiration breath hold was also successful	Dipasquale et al.
2020	USA	Evaluation of a copper-plastic composite material for use as a custom fit 3D printed bolus with dose measurements of bolus fabricated for the temporal-frontal cranial region of an anthropomorphic phantom	FDM	PLA-PHA	–	–	0.4 mm thickness printed bolus remains flexible, yet providing half of the superficial dose enhancement of a traditional 5 mm thick bolus	Ehler et al.
2019	USA	Development and dosimetry validation of a patient-specific 3D printed bolus cap.	PolyJet	Photopolymer resin	1	Yes	New 3D-printing material (Agilus-60) proved to be suitable for use as scalp bolus. The average difference between TLD measured and planned doses for one patient was 5.3%	Baltz et al.
2022	China	Comparison of the dosimetry characteristics, NTCP, and acute toxicity for patients treated with VMAT PMRT using a 3D-printed bolus and a conventional bolus.	FDM	PLA	35	No	The use of a 3D-printed bolus in VMAT plans achieved better dose coverage and homogeneity in the PTV, while reducing in NTCP for the ipsilateral lung and heart	Zhang et al.
2014	Canada	Presentation of a Monte Carlo based algorithm for modulated electron radiation therapy that optimizes bolus design for conformation of the dose distribution to the PTV.	FDM	PLA	1	No	New algorithm enabled a reduction of mean dose by 38.2% in left kidney relative to standard bolus, while improving PTV dose coverage	Su et al.

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Table 2. Summary of articles involving studies which included 3D printed bolus fabrication (*if clinical cases were included)

Year of publication	Country	Description of research	Printing technique	Printing materials	Sample size*	In vivo dosimetry	Outcomes and conclusions	Authors
2022	Ireland	A retrospective analysis of the first 60 cases treated using 3D printed bolus.	FDM	TPU	60	No	The 3D printed bolus using TPU best suited the head and neck and scalp regions and does not perform well in the pelvic region. It was also easily and quickly placed on a day-to-day basis and was preferred to using sheet bolus	Malone et al.
2020	USA	Comparison of 3D printed and standard bolus adherence for veterinary patients.	FDM	TPU	9	No	3D printing should be considered for superficial treatment areas of high irregularity. A significant difference in air gaps in patients receiving radiotherapy to the head ($p < 0.001$) was noted, but it was not significant for air gaps in caudal body sites ($p = 0.05$)	Martin et al.
2015	USA	Investigation of the potential of utilizing two 3D printing techniques for the fabrication of the electron bolus.	FDM, SLS	PLA, Polyamide	–	–	The average Euclidean distance between designed and fabricated bolus on the CT slices was found to be 0.84 ± 0.45 mm	Zou et al.
2017	Korea	In-vivo skin doses measurements for both conventional and 3D printed boluses for the chest wall with OARs doses comparison.	FDM	PLA	6	Yes	The precision of dose delivery was improved by 3% with the 3D-printed boluses. It also resulted in a reduction of the mean dose to the ipsilateral lung by up to 20%	Park et al.
2021	Spain	Dosimetric analysis of a 3D printed malleable ear bolus with comparison to a commercial bolus.	PolyJet	Photopolymer resin	–	–	PDD measurements showed that 3D printed bolus increase the surface dose effectively, comparably with a commercial bolus. PTV coverage for fabricated bolus was higher (D98% of 98.2% *vs.* 97.6%). Also the maximum dose was reduced by 6.6% and the minimum dose increased by 5.2%	Gomez et al.
2020	Switzerland	Fabrication and evaluation of 3D printed bolus for treatment and quality assurance in small animal irradiation.	FDM	PLA	–	–	3D printing can be very useful to produce geometrically accurate personalized boluses, in order to overcome issues caused by the build-up region for MV beams.	Koutsouvelis et al.
2014	Korea	3D printed bolus production both for Blue water and RANDO head phantom with its clinical feasibility evaluation.	FDM	ABS	–	–	For 3D printed nose bolus, the D_{max}, D_{min}, D_{mean}, $D_{90\%}$, and $V_{90\%}$ of the target volume were 101.3%, 90.0%, 95.5%, 91.6%, and 100.0%, respectively, indicating effective dose coverage.	Kim et al.
2020	China	Introduction of methodology for 3D printed bolus fabrication based on iPhone camera pictures.	FDM	ABS	–	–	The bolus printed based on the acquired images presented better PTV coverage comparing with flat bolus (CI = 817 *vs* 0.697, HI = 0.910 *vs*. 0.887)	Kang et al.
2019	Korea	3D printed bolus manufacturing with biological, physical, and dosimetric properties comprehensive assessment.	FDM	TPU	–	–	Z_{eff} for NinjaFlex material was calculated to be 6.08. It was also evaluated that 1.2 cm of this material is equivalent to 1.232 cm of water	Park et al.

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Table 2. Summary of articles involving studies which included 3D printed bolus fabrication (*if clinical cases were included)

Year of publication	Country	Description of research	Printing technique	Printing materials	Sample size*	In vivo dosimetry	Outcomes and conclusions	Authors
2018	Canada	Fabrication and evaluation of 3D printed boluses for patients undergoing chest wall radiation therapy in terms of the accuracy of fit and in vivo dosimetry of surface dose.	FDM	PLA	16	Yes	The accuracy of bolus fit was improved significantly. The frequency of air gaps ≥ 5 mm reduced from 30% to 13% and maximum air gap dimension diminished from 0.5 ± 0.3 to 0.3 ± 0.3 mm on average. Surface dose was within 3% for both standard sheet and 3D printed bolus. Setup time was also reduced from 104 to 76 seconds	Robar et al.
2016	Korea	Comparison of dose distribution under 3D printed and commercial bolus using an anthropomorphic female phantom with varying breast volumes.	FDM	PLA	–	–	The 3D-printed bolus can minimize daily setup uncertainties and address dose discrepancies caused by unintended air gaps in breast cancer radiation therapy. However, the 3D-printed PLA bolus could not fit bigger breast attachments because of its rigid form	Park et al.
2019	Canada	Presentation of results and in-house experience in 3D bolus printing based on surface scanning and digital design for patients with complex surface anatomy.	FDM	PLA	10	No	Estimated uncertainty of 3D printed bolus accuracy was on the order of < 1 mm None of the patients reported any discomfort in using the bolus during therapy	Sasaki et al.
2015	USA	Characterization of printing materials (PDDs and tissue maximum ratios) and dose measurements for a 3D printed bolus on head phantom.	FDM	PLA, ABS	–	–	For a treatment plan with printed nose bolus, with gamma criteria of 5% dose difference and 3 mm DTA, 95% points passed	Burleson et al.
2017	Japan	3D printed bolus fabrication and evaluation of its clinical feasibility in photon radiotherapy.	FDM	ABS	–	–	The dose coverage in the build-up region provided by the 3D-bolus was equivalent to the commercial-bolus	Fujimoto et al.
2017	Korea	A phantom study of application of surface scanner for 3D printed boluses fabrication.	PolyJet	TangoPlus	–	–	3D printed bolus was fabricated successfully, giving satisfactory surface dose comparable with that of a commercial one	Park et al.
2022	China	A theoretical retrospective analysis of the influence of modulated electron 3D printed bolus in PTV conformity OAR dose.	FDM	PLA	27	No	The median maximum dose to the LAD and the ribs decreased by 6.2% and 4.5% respectively, as well as other dosimetric parameters of the ipsilateral lung	Lee et al.
2020	USA	Presentation of clinical workflow and implementation of 3D printing technology in clinical practice.	PolyJet	TangoPlus	10	Yes	3D printed boluses improve plan conformity (CI = 0.993 (0.962-0.993) *vs* 0.977 (0.601-0.991)) and reduce air gap volume in irregular superficial areas comparing to flat bolus. In vivo measurements confirmed that the delivered superficial dose was within 1% of the intended prescription	Dyer et al.
2017	Poland	Comparison of 3D printed boluses with paraffin boluses in electron beam radiotherapy.	FDM	ABS	11	No	3D-printed boluses can be used accurately and safely for electron beam therapy as they have a better fit to irregular surface of the skin and show greater homogeneity over a paraffin bolus	Łukowiak et al.

Table 2. Summary of articles involving studies which included 3D printed bolus fabrication (*if clinical cases were included)

Year of publication	Country	Description of research	Printing technique	Printing materials	Sample size*	In vivo dosimetry	Outcomes and conclusions	Authors
2021	UK	Fabrication of a flexible bolus for head phantom as substitute to standard gel bolus.	FDM	TPU	–	–	TPU bolus resulted in significantly smaller air gaps while maintaining comparable PTV dose coverage. It was also noted, that it was easier to position and setup compared with commercial bolus	Robertson et al.
2019	Korea	Evaluation of the effectiveness of patient-specific 3D printed bolus in electron beam chest wall radiotherapy.	FDM	PLA	28	No	The use of 3D printed bolus reduced the mean heart dose by 2.39 Gy in comparison when no bolus was applied. It also allowed to decrease both low and high-doses delivered to the ipsilateral lung	Yang et al.
2017	Canada	Clinical application of 3D printed bolus for nasal septum, pinna and upper half of the face	FDM	PLA, TPU	3	No	Only minimal air gaps between bolus and skin were present at CT, even in the case of the intracavitary bolus	Zhao et al.
2018	USA	Evaluation of time required to create a 3D printed bolus, both with fit of the bolus and verification of skin surface dose in veterinary.	FDM	PET-G	14	Yes	Regardless of tumor location, bolus was generated and used for treatment within a 12 h window of time. The dose measured under the bolus within 5% agreement of expected dose was in 88% of the measurements	Ehler et al.
2016	Korea	Evaluation of the application of a 3D printed ear bolus in clinical practice.	FDM	ABS	1	No	The 3D-printed bolus provided a good fit to the ear area, with air gaps of less than 5 mm. The surface dose of the auricle and ear canal was successfully enhanced, however, the use of a rigid material was associated with patient experiencing pain	Park et al.
2019	USA	Case study of a patient where 3D printed, customized bolus was produced covering both legs.	FDM	TPU	1	No	Setup images showed a maximum air gap of < 2 mm in most visible seams of multiple parts of the bolus	Obeid et al.
2020	Japan	Dosimetric comparison of materials used in 3D bolus printing.	FDM, SLA	PLA, polyurethane resin	–	–	The dose differences between the calculations and measurements for PLA and Polyurethane resin bolus at 1, 5, 10 and 20 cm (X6) were: –0.83%, 0.06%, 0.39%, –0.82% and –0.33%, 0.20%, 0.50%, –0.39%	Aoyama et al.
2023	Colombia	Comparison of multiple materials and technologies in terms of radiotherapy bolus producing.	FDM	PLA	1	No	Mean Hounsfield Units value for a 3D printed PLA bolus with 100% infill = –9 ± 105 HU	Diaz-Merchan et al.
2023	China	Investigation of the effectiveness of 3D printing total skin bolus for total skin tomotherapy	FDM	TPU	1	Yes	3D printed bolus enabled a better PTV dose coverage in comparison with other studies where diving suits were used as boluses. The entire printing process (using two printers) took 5 days	Wang et al.

ABS — acrylonitrile butadiene styrene; CI — conformity index; CT — computed tomography; $D_{90\%}$ — dose received by 90% of the organ or volume as a percentage of the prescription dose; D_{MAX} — maximum dose; D_{MEAN} — mean dose; D_{MIN} — minimum dose; DTA — distance to agreement; FDM — fused deposition modeling; HI — homogeneity index; LAD — left anterior descending artery; NTCP — normal tissue complication probability; OAR — organ at risk; PDD — percentage depth dose; PET-G — polyethylene terephthalate glycol; PLA — polylactic acid; PMRT — postmastectomy radiotherapy; PTV — planning target volume; SLA — stereolitography; SLS — selective laser sintering; TLD — thermoluminescent dosimeter; TPU — thermoplastic polyurethane; $V_{90\%}$ — percent of the volume receiving 90% of the prescribed dose; VMAT — volumetric modulated arc therapy; Zeff — effective atomic number tion crucial for the implementation of 3D printing technology in bolus manufacturing within clinical practice (Tab. 1). The most frequently described aspect, present in 61.9% of the papers, focused on the accurate assessment of proper bolus fit to the phantom surface or patient's skin. The evaluation methods included assessing adherence on CT images (46.2%), measuring air gaps between the printed bolus and the intended surface visible on CT or cone beam CT (CBCT) images (46.2%), visual evaluation (3.9%), and, in a singular case, a method involving virtually applying a CT scan of the bolus to the patient's CT image (3.8%).

Another key aspect involves the assessment of the physical properties of printing materials (45.2%). This includes the analysis of Hounsfield Units (HUs) of boluses on CT images (63.1%), the evaluation of the impact of radiation on the material in terms of damage and degradation (10.5%), and the examination of hardness, deformation, or wrapping possibilities. Printing time, as an important factor influencing the bolus preparation process, was reported in 42.9% of the papers, especially when boluses intended to cover a large area were produced, along with considerations of printing cost (28.6%). The accuracy of the printing process itself has emerged as a major source of failure, and uncertainty has been addressed. In 21.4% of the papers, the authors compared the dimensions of the printed bolus and its virtual model physically or based on its imaging. The factors directly influencing the clinical use of printed boluses include ease of positioning on the patient (23.8%), patient convenience and comfort (16.7%), and the biocompatibility of the materials used in the printing process (9.5%).

Discussion

In this systematic review, we synthesized evidence from 52 studies focusing on the application of 3D printing technology in the manufacturing of individualized boluses used in radiotherapy. Across the reviewed literature, two direct major applications emerged. The first involves the production of customized boluses through 3D printing, either by assessing the characteristics of 3D printing materials and the printing parameters for potential use in bolus manufacturing or by directly manufacturing custom boluses. The second application centers around utilizing 3D printing to create molds for boluses and subsequently fills these molds with another material. Regardless of the diverse applications of 3D printing explored, most authors have pointed to the advantages of 3D printing technology in bolus preparation. These included enhanced dose distributions with potential direct implications for treatment effectiveness, improved bolus adherence achieved through its customization for individual patient needs, a possible reduction in treatment costs, and even facilitation of the bolus positioning process on the patient's skin during therapeutic sessions. However, despite these gains and positive results, the reviewed literature also acknowledged the associated risks, weaknesses of the technology, and the demanding multistep process involved in its introduction into clinical practice applications.

The initiation of utilizing 3D printing boluses involves a fundamental phase of testing materials intended for the printing process and selecting optimal printing parameters that meet the requirements in the context of radiotherapy boluses. Van der Walt M. et al. conducted a comprehensive investigation of tissue equivalence and radiological properties, focusing on the widely used 3D printing filament, PLA [30]. By printing PLA samples with different infill percentages and measuring their dosimetric properties, the authors identified parameters that could prove suitable for effective bolus production. Importantly, they also emphasized the need for individualized studies by each radiotherapy department intending to implement 3D printing. A similar analysis was carried out by Dąbrowska-Szewczyk et al. In this paper, the authors expanded their research to include a material showing elastic properties, which is a commonly available TPU [31]. An interesting direction emerging in the topic of 3D printing of boluses in radiotherapy is the use of the patient's optical scan as input for designing the bolus model, thus eliminating the need for a CT scan. This innovative approach would allow the patient to avoid additional imaging scans and, as a result, reduce their exposure to ionizing radiation. Sasaki et al. demonstrated the step-by-step process of creating and printing a bolus via a structured light scanner [19]. Their work detailed the quality assurance procedures, ensuring the safe implementation of this new technology, with obtaining mean shape errors of less than 0.5 mm in all cases. Another paper also reported a very good fit of the bolus based on the optical scan to the surface of the phantom [18]. The air gaps observed between these boluses and the phantom in the CT scans did not surpass 0.6 mm, which was notably smaller compared to data obtained for boluses based on CT images (2 mm). An intriguing concept presented by Kang et al. involved replacing commercial optical scanners with mobile phones [20]. They presented a paper showcasing the use of an iPhone camera for optical scanning, resulting in satisfactory bolus outcomes. A comparison of treatment plans with a printed bolus versus a standard flat bolus revealed better coverage of the planning target volume (PTV) area with 95% of the prescribed dose (95.65% *vs.* 88.39%), along with increased both homogeneity and conformity indices (0.887 *vs.* 0.697 and 0.910 *vs.* 0.817, respectively). While described as a cost-effective method, they recommended its primary use for skin cancers, where tumor lesion areas can be defined upon appearance or dermoscopic assessment.

This review also highlights the effectiveness of 3D printing in the production of boluses for particularly challenging anatomical areas. Employing a flexible rubber-like bolus during total scalp irradiation, a procedure often associated with severe skin irritation and pain in patients, once again led to a significant improvement in bolus conformity to the patient's body, resulting in a double reduction in the size of the maximum air gap [32]. Nevertheless, in cases where a patient has highly sensitive skin or an open wound, the process of fitting a bolus directly onto the patient's body can be painful and lead to inaccuracies in placement [33]. An alternative approach, suggested by Burleson et al., involves 3D printing specific parts of the patient's body and then fitting the bolus onto the printed positive mold instead of directly onto the patient [34]. This method ensures precise placement and a form-fitting bolus, eliminating air gaps and mitigating any discomfort for the patient. Malone et al. performed an analysis across four different treatment sites to determine if specific sites demonstrate a preference for a 3D-printed approach and whether the quality of fit varies during the treatment process [35]. Among the 627 fractions assessed, the head and neck, scalp, and extremity regions predominantly favored a 3D-printed bolus approach. Additionally, there were no apparent changes in the quality of fit for 3D-printed boluses observed throughout the entire course of treatment across all the examined fractions.

On the other hand, despite the numerous advantages that 3D printing has brought to the radiation therapy field, it is crucial not to forget the existing challenges and drawbacks of this method, which still should be taken into account. One primary concern is the need for significant reductions in printing time [36]. For instance, the fabrication of a single bolus designed to cover the breast or chest wall can extend beyond 12 hours [33, 37]. A case presented by Obeid et al. involved the printing of a bolus covering the patient's entire legs, which required an extensive period of nearly 70 hours [27]. In another study, the concept of 3D printing a total skin bolus was introduced [27]. Using two printers simultaneously, the entire printing procedure took five days, which is a workable situation for a single research case but is not feasible in standard, routine clinical practice. Importantly, the time invested in producing each bolus encompasses not only the actual printing duration, which can extend to several hours but also additional factors such as model creation, segmentation, and file preparation in a format compatible with the printer [22]. These challenges underscore the importance of addressing the time-intensive aspects associated with 3D printing in radiation therapy to optimize its practical feasibility and efficiency. Nevertheless, despite the considerable time required for bolus production, it is worth noting the advantages in terms of the reduction in the time spent setting up patients for treatment. In a specific study involving chest wall irradiation, the average setup time decreased from 104 to 76 seconds, showcasing some time savings compared with the use of a sheet bolus [37].

Another crucial factor to consider is the cost of producing an individual bolus. 3D printing technologies provide a cost-effective alternative for fabricating personalized boluses. The cost of printing such a bolus can be more than five times lower than that of standard boluses [22] , [38, 39]. Although the cost of printing materials is usually low, the price of printer and staff training should also be taken into consideration [28]. Despite the relatively low cost of materials commonly used in 3D printing, the prices of those specifically designed for medical applications can be considerably greater because of the large number of tests and strict manufacturing standards. Due to safety considerations, some centers have opted to assess the biocompatibility of the materials employed. Park et al. presented very thorough sequential biological stability tests, such as cytotoxicity, skin irritation and sensitization tests, for one of the TPU materials, ensuring its safe application in patients [40]. An interesting approach to address these concerns was presented by Burleson et al., who employed plastic wrap around the bolus before its application on patients' skin [34]. This practice aimed to maintain sanitary conditions and create a sterile environment for each treatment.

In summary, as we interpret the results of this review, widespread introduction of 3D-printed boluses has the potential to personalize treatment approaches, optimize dose delivery, and improve overall treatment outcomes. Nevertheless, challenges such as standardization, cost-effectiveness, and integration into routine clinical practice need to be addressed for extensive implementation of this technology in clinical practice.

Conclusion

The use of 3D-printed boluses in radiotherapy represents a significant advancement in personalized approaches to treatment. By enhancing the accuracy of dose delivery, improving treatment planning, and optimizing patient comfort, 3D-printed boluses may contribute to more effective and efficient radiotherapy outcomes. As technology continues to evolve, the widespread implementation of 3D-printed boluses in radiotherapy holds the promise of further development and provides opportunities for further research. This promising technology is still in the early stages of development. It can be hoped that in the near future, the limitations of some important constraints related to the preparation and use of 3D boluses should be resolved. In particular, boluses made of flexible materials will be more widely used.

Conflict of interests

Authors declare no conflict of interest.

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