

Systematic Review

Artificial intelligence in adaptive radiotherapy for head and neck cancer: a systematic review of synthetic CT, automated segmentation and prediction of anatomical change and adaptive RT requirement

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ABSTRACT

Artificial intelligence (AI) is increasingly being explored to overcome the technical and workflow challenges of adaptive radiotherapy (ART) in head and neck cancer (HNC). However, the available evidence remains heterogeneous, with varying degrees of technical and clinical validation. This review evaluated the current role and clinical maturity of AI-enabled ART in HNC. A systematic literature search of PubMed, Scopus and EMBASE was performed from inception to 1 August 2026. Original prospective or retrospective human studies published between 1 January 2020 and 1 August 2026 were eligible. Studies were restricted to photon-based radiotherapy using CBCT, kVCT or MVCT. Eligible studies were classified into four domains: synthetic CT/image enhancement; AI-based auto-segmentation and deformable image registration; anatomical change prediction and adaptive planning; and prediction of ART requirement. Reporting quality was assessed using CLAIM 2024, QUADAS-2 was applied where appropriate. Out of 62 records screened, 25 studies were included. Sixteen studies addressed synthetic CT/image enhancement, seven addressed auto-segmentation/deformable registration, two evaluated anatomical change prediction/adaptive planning, and three investigated predictions of ART requirement, with some overlap between domains. AI consistently demonstrated technical improvements in image quality, CT-number accuracy, segmentation performance and dosimetric agreement. However, evidence for prospective prediction of anatomical change and ART requirement was considerably limited. CLAIM adherence ranged from approximately 68% to 88%, with a mean of 79.9%±5.8%. AI demonstrates substantial technical potential across HNC ART workflows, particularly for image synthesis, segmentation and registration. However, multicentre evidence demonstrating improved clinical decision-making and patient outcomes remains insufficient.

Keywords: AI in RT, Adaptive RT head neck cancer, Systematic review

INTRODUCTION

Radiotherapy for head and neck cancer (HNC) is a complex, highly conformal process in which anatomical changes during treatment can alter target coverage and

doses to surrounding organs at risk. Adaptive radiotherapy (ART) has therefore emerged as a strategy to account for tumour regression, weight loss, tissue deformation, and other interfractional changes. However, conventional ART remains resource-intensive because repeated imaging,

contouring, deformable registration, dose recalculation, and replanning require substantial clinical time and expertise.^{1,2}

Artificial intelligence (AI), particularly machine learning and deep learning, is increasingly being integrated into radiation oncology to automate image reconstruction, segmentation, registration, treatment planning, and predictive analysis.^{2,3} In ART, AI may facilitate rapid generation of treatment-quality images, automated delineation and registration, prediction of anatomical changes, and identification of patients who are most likely to benefit from adaptive replanning.^{2,3}

Despite rapid technological development, an important distinction remains between technical demonstration of AI performance and clinical validation of AI-guided ART. Existing literature includes diverse approaches ranging from synthetic CT generation and automated segmentation to predictive models for anatomical change and treatment adaptation, but these applications differ substantially in their validation strategies, clinical maturity, and applicability to routine practice.^{2,3} Therefore, this systematic review aimed to evaluate the current evidence for AI in adaptive radiotherapy for HNC, focusing on four clinically relevant domains: synthetic CT and image enhancement, AI-based auto-segmentation and deformable image registration, prediction of anatomical change and adaptive planning and prediction of the requirement for adaptive radiotherapy. We additionally assessed the methodological reporting quality and risk of bias of the available evidence to determine the current level of clinical maturity of AI-enabled ART.

METHODS

Study location and period

This systematic review was conceived at Department of Radiotherapy, Midnapore Medical College. The selected studies (published between 1 January 2020 and 1 August 2026) were shortlisted and analysed from 1st June 2026 to 31st August 2026.

Study design

This systematic review evaluated the role of artificial intelligence (AI) in adaptive radiotherapy (ART) for head and neck cancer (HNC). The review was conducted and reported in accordance with PRISMA recommendations. Eligibility criteria, study-selection procedures, data-extraction domains, and methodological quality-assessment criteria were predefined before the final qualitative synthesis. The review specifically addressed AI applications supporting photon-based external beam ART using treatment-associated volumetric imaging, including cone-beam computed tomography (CBCT), kilovoltage CT (kVCT), and megavoltage CT (MVCT).

The review was designed to distinguish AI used for individual technical components of ART from AI intended to support the clinical decision to adapt treatment.

Review question

The primary research question was: What is the current evidence regarding the role of artificial intelligence in facilitating adaptive radiotherapy for head and neck cancer, particularly in synthetic CT generation, automated segmentation and deformable image registration, prediction of anatomical changes and adaptive planning, and prediction of the requirement for adaptive radiotherapy? The review additionally examined validation strategies, methodological quality, and clinical applicability of the available evidence.

Eligibility criteria

Studies were eligible if they met all predefined criteria: patients with HNC undergoing radiotherapy; evaluation of an AI, machine-learning, or deep-learning method directly related to ART; photon-based external beam radiotherapy; treatment-associated CBCT, kVCT, or MVCT; prospective or retrospective original research involving human data; publication between 1 January 2020 and 1 August 2026; and reporting of technical, dosimetric, predictive, workflow, or clinically relevant outcomes. Eligible AI applications included synthetic CT generation or image enhancement, automated segmentation and/or deformable registration, anatomical-change prediction and/or adaptive planning, and prediction of ART requirement.

Reviews and meta-analyses, narrative or scoping reviews, editorials, commentaries, letters, conference abstracts without sufficient methodological information, phantom-only or simulation-only studies, non-human studies, studies using other radiotherapy or imaging modalities, and studies addressing non-HNC sites without separable HNC data were excluded. Studies evaluating AI solely for diagnosis, prognosis, radiomics, or treatment planning without a direct ART application were also excluded, as were duplicate or secondary publications without additional relevant information.

Literature search and study selection

PubMed/MEDLINE, Scopus, and EMBASE were searched from inception to 1 August 2026. The search combined terms related to HNC, artificial intelligence, machine learning, deep learning, adaptive radiotherapy, CBCT/kVCT/MVCT, synthetic CT, auto-segmentation, deformable image registration, anatomical-change prediction, and adaptive planning. Database-specific strategies were adapted to the relevant indexing system. Reference lists of relevant reviews and included studies were screened for additional eligible publications.

Records were screened sequentially through identification, primary screening, secondary screening, eligibility assessment, and inclusion. Following removal of duplicates, titles and abstracts were screened, followed by full-text assessment against the predefined criteria. Reasons for exclusion at eligibility assessment were recorded. The study-selection process was presented using a PRISMA flow diagram. Of 62 identified records, 25 original studies fulfilled the eligibility criteria and were included in the qualitative synthesis.

Data extraction and domain classification

A structured extraction framework recorded first author, publication year, study design, sample size, tumour site, radiotherapy technique, imaging modality, AI methodology, clinical application, comparator/reference standard, training and testing strategy, principal technical and dosimetric outcomes, workflow measures, clinical applicability, and reported limitations. For synthesis, studies were classified into four predefined domains: AI-based synthetic CT and image enhancement; AI-based auto-segmentation and deformable image registration; AI-based anatomical-change prediction and adaptive planning; and AI-based prediction of ART requirement. Studies addressing more than one component could contribute to multiple domains.

Outcome measures and synthesis

Technical outcomes included image-quality measures, CT-number accuracy, MAE, PSNR, SSIM, segmentation and registration accuracy, and predictive performance. Dosimetric outcomes included target coverage, organ-at-risk doses, dose agreement, and gamma analysis. Adaptive outcomes included the ability to generate clinically usable images or contours, identify meaningful anatomical change, support replanning, or identify patients requiring ART. Workflow outcomes included processing time, reduction in manual contouring, clinician workload, and feasibility of online or offline implementation. Clinical outcomes were recorded when reported. Because substantial heterogeneity existed in AI architectures, imaging datasets, study populations, validation strategies, and outcome measures, quantitative meta-analysis was not performed. Findings were synthesized qualitatively within the four domains, with emphasis on technical performance, dosimetric relevance, workflow implications, external or independent testing, and clinical maturity. Particular attention was paid to whether studies evaluated AI on held-out or external datasets and whether technical performance was linked to an actual adaptive treatment workflow.

Quality assessment

Reporting quality was assessed using the Checklist for Artificial Intelligence in Medical Imaging (CLAIM) 2024 update. Each applicable item was recorded as Yes, No or Not Applicable, and adherence was calculated

descriptively as the proportion of applicable items fulfilled. This percentage was used as a measure of reporting completeness and not as a validated quality score.²⁹ Risk of bias and applicability were assessed using QUADAS-2 where applicable. The four domains patient selection, index test, reference standard, and flow and timing were classified as low, high, or unclear risk of bias, with applicability concerns assessed separately.³⁰ Because QUADAS-2 is primarily designed for diagnostic-accuracy studies, it was not mechanically applied to purely technical AI studies for which the framework was unsuitable. In such studies, CLAIM was complemented by structured assessment of dataset independence, testing strategy, reference standards, external testing, and clinical applicability.

RESULTS

Study selection and characteristics of included studies

The systematic search identified 62 records for screening. Following duplicate removal and sequential screening, 25 original studies fulfilled the predefined eligibility criteria and were included in the qualitative synthesis. The included studies were published between 2022 and 2026, with most appearing from 2023 onward, reflecting the rapid recent development of AI-enabled ART. All included studies were retrospective or retrospective technical/clinical dataset-based investigations; no prospective interventional clinical study meeting all criteria was identified. Sample sizes and unit of analysis varied considerably, with some studies evaluating individual patients and others evaluating large numbers of longitudinal CBCT examinations or image datasets (Figure 1).

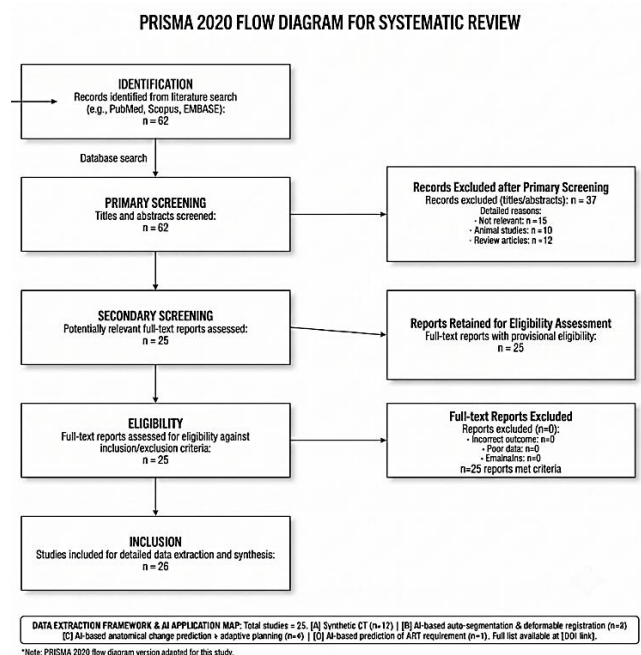


Figure 1: PRISMA flow diagram for the study selection.

CBCT was the predominant imaging modality, with selected studies evaluating kV-CBCT and MVCT. The AI approaches were heterogeneous and included convolutional neural networks, U-Net-based architectures, generative adversarial networks, transformers, recurrent networks, hybrid architectures, and diffusion-based models. Sixteen studies addressed synthetic CT generation or image enhancement (Domain A), seven evaluated AI-based auto-segmentation and/or deformable image registration (Domain B), two primarily addressed anatomical-change prediction and adaptive planning (Domain C), and three evaluated predictions of ART requirement (Domain D). Several studies contributed to more than one domain. Detailed characteristics and quantitative findings are presented in Tables 1-4.

Domain A: AI-Based Synthetic CT and Image Enhancement Sixteen studies evaluated AI-based generation or enhancement of treatment-associated volumetric images, predominantly CBCT, with objectives including improved image quality, CT-number accuracy, dose calculation, and facilitation of ART.

O'Hara et al compared deformable-registration-based conversion, bulk-density assignment, iterative HU correction, and CycleGAN-based synthesis. All approaches demonstrated clinically acceptable dosimetric agreement with repeat CT, while CycleGAN offered a favourable combination of accuracy and generation efficiency.⁴ Aouadi et al evaluated CycleGAN, pix2pix/cGAN, and U-Net approaches and reported improved image fidelity and dose agreement compared with uncorrected CBCT.⁵ Li et al evaluated RegGAN using data from different linear accelerators and included

an independent multi-linac test cohort, demonstrating maintained image and dosimetric performance across platforms.⁶ Khamfongkhrua et al reported improvement in MAE, RMSE, PSNR, SSIM and gamma-passing rates using supervised U-Net synthesis from kV-CBCT, with small dose differences in targets and organs at risk.⁷

Yoganathan et al. demonstrated favourable HU recovery, spatial fidelity, and dosimetric agreement using a self-attention residual U-Net.⁸ Hu et al combined a hybrid CNN-transformer synthesizer with a registration network and demonstrated improved image translation and dosimetric agreement in an independent test cohort.⁹ Lv et al demonstrated improved MVCT image quality and maintained dose-calculation accuracy using CycleGAN-based synthesis.¹⁰ Liang et al used a multimodal variational-autoencoder/transformer framework for image-to-image translation, while Peng et al developed a patient-specific score-based diffusion model that reduced dependence on large paired datasets.^{11,12} Yuan et al demonstrated synthetic CT generation from ultra-low-dose CBCT with preservation of dosimetric accuracy, addressing the potential imaging-dose burden associated with repeated ART imaging.¹³ More recent studies explored diffusion-based and generative approaches. Altalib et al reported improved HU accuracy, structural similarity, and preservation of anatomical boundaries using an equivariant conditional diffusion model, while Sánchez et al reported favourable image and dosimetric agreement with independent testing.^{14,15} Lye et al evaluated deformable-registration-derived synthetic CT within a directed ART workflow, extending image synthesis toward treatment adaptation rather than image-quality assessment alone.¹⁶

Table 1: Studies on Synthetic CT.

Study	Author	Year	Study design	Imaging modality	AI / ML method	Primary AI application	Clinical context / population	Main outcomes / metrics
3	Thummerr et al	2025	Retrospective	CBCT	ESRGAN / deep learning	Super-resolution / image enhancement	H&N RT / ART imaging	Image quality; dose reduction feasibility
4	O'Hara et al	2022	Retrospective	CBCT	CycleGAN / ML sCT	Synthetic CT generation	H&N ART planning	MAE, gamma, DVH, generation time
7	Aouadi et al	2023	Retrospective	CBCT	DRUnet / cGAN	Synthetic CT generation	H&N ART planning	MAE, gamma, dosimetric accuracy
8	Ki et al	2024	Retrospective	kV-CBCT	Deep learning / dual-encoder	Metal-artifact reduction	H&N RT / ART imaging	PSNR, SSIM, artifact reduction
9	Li et al	2023	Retrospective	CBCT	RegGAN	Synthetic CT generation	H&N ART	MAE, PSNR, SSIM;

Continued.

Study	Author	Year	Study design	Imaging modality	AI / ML method	Primary AI application	Clinical context / population	Main outcomes / metrics
								multi-LINAC robustness
10	Khamfong khrua et al	2024	Retrospective	kV-CBCT	Supervised deep learning / U-Net	Synthetic CT generation	H&N ART	MAE, RMSE, PSNR, SSIM, gamma, dose
11	Hu et al	2024	Retrospective	CBCT	Hybrid CNN-transformer + registration network	CBCT-to-CT translation + registration	H&N ART	Image translation and registration performance
12	Lv et al	2024	Retrospective	MVCT	CycleGAN-based synthesis	MVCT image enhancement / synthetic CT	H&N ART	Image quality; dose accuracy
13	Liang et al	2025	Retrospective	CBCT/CT	VAE + transformer	Multimodal image-to-image translation / sCT	H&N RT	MAE, image quality, dosimetry
17	Peng et al	2025	Retrospective	CBCT	Patient-specific score-based diffusion model	Unsupervised synthetic CT	H&N ART-relevant imaging	MAE, SSIM, image quality
18	Yuan et al	2022	Retrospective	Ultra-low-dose CBCT	Deep neural network / U-Net variants	Synthetic CT from low-dose CBCT	H&N RT / ART	MAE, PSNR, SSIM, dosimetry
19	Altalib et al	2026	Retrospective / dataset-based validation	CBCT	Equivariant conditional diffusion model	Synthetic CT generation	H&N RT / ART	Image synthesis accuracy; generalizability
21	Yoganathan et al	2023	Retrospective	CBCT	Self-attention residual U-Net	Synthetic CT generation	H&N ART	MAE, PSNR, SSIM, DVH, gamma
22	Sánchez et al	2026	Retrospective	CBCT	UNet3+ GAN	Synthetic CT generation	H&N ART	MAE, gamma, PTV dose differences; independent test
24	Lye et al	2026	Retrospective	CBCT/CT	DIR-based synthetic CT	sCT from deformable registration / directed ART	H&N ART	sCT and directed adaptation feasibility

Continued.

Study	Author	Year	Study design	Imaging modality	AI / ML method	Primary AI application	Clinical context / population	Main outcomes / metrics
25	Fu et al	2025	Retrospective / technical clinical dataset	CBCT	MuTA-Net	Soft-tissue enhancement in synthetic CT	H&N ART imaging	Soft-tissue MAE / image quality

AI was also applied to image enhancement. Thummerer et al demonstrated improved image quality and spatial resolution using deep-learning super-resolution of low-dose CBCT, supporting the feasibility of dose-reduced treatment imaging.¹⁷ Ki et al developed a dual-encoder model for dental-metal artifact reduction in kV-CBCT and reported improved visualization of anatomical boundaries.¹⁸ Fu et al evaluated a multi-task attention network targeting regional CBCT enhancement, including soft-tissue and high-density structure preservation.¹⁹

Overall, Domain A represented the largest evidence base and showed relatively consistent improvement in image quality, HU accuracy, or dosimetric agreement compared with uncorrected treatment imaging. The evolution of

methods also suggested increasing attempts to improve generalizability through multicentre or multi-linac testing and to reduce dependence on perfectly paired datasets. Nevertheless, most studies remained technical evaluations; evidence that synthetic CT or enhanced images directly improve adaptive decision-making or patient outcomes was limited.

Domain B: AI-based auto-segmentation and deformable image registration

Seven studies evaluated AI-based segmentation, contour propagation, deformable registration, or combinations of these approaches, addressing a major time- and labour-intensive component of ART (Table 2).

Table 2: Studies on AI-based Auto-segmentation + Deformable Registration.

Study	Author	Year	Study design	Imaging modality	AI / ML method	Primary AI application	Clinical context / population	Main outcomes / metrics
1	Zhao et al	2024	Retrospective	CBCT	Deep learning / LSTM-UNet	Progressive auto-segmentation	H&N online ART	Segmentation accuracy; longitudinal information
2	Liang et al	2023	Retrospective	CBCT	Deep learning + test-time optimization	Auto-segmentation	H&N CBCT-based ART	DSC, HD95, efficiency
5	Ma et al	2022	Retrospective	CBCT	Registration-guided deep learning	Auto-segmentation + registration	H&N online ART	DSC; registration-guided segmentation
11	Hu et al	2024	Retrospective	CBCT	Hybrid CNN-transformer + registration network	CBCT-to-CT translation + registration	H&N ART	Image translation and registration performance
14	Kakkos et al	2024	Retrospective	CT/CBCT	Attention U-Net / deep learning	Auto-segmentation	H&N RT / replanning assessment	DSC, Hausdorff distance
15	Lee et al	2026	Retrospective	Planning CT + weekly CBCT	3D CNN + self-attention + ConvLSTM	Spatiotemporal deformable registration	H&N ART	Registration accuracy; speed
24	Lye et al	2026	Retrospective	CBCT/CT	DIR-based synthetic CT	sCT from deformable registration / directed ART	H&N ART	sCT and directed adaptation feasibility

Zhao et al developed progressive auto-segmentation incorporating longitudinal information for CBCT-based online ART.²⁰ Liang et al used test-time optimization to incorporate patient-specific information during inference and improve segmentation while maintaining computational efficiency.²¹ Ma et al developed registration-guided deep learning incorporating registration information into a 3D U-Net, improving robustness in CBCT-based segmentation.²² Kakkos et al used an attention U-Net for parotid segmentation and serial assessment of volume and positional changes relevant to replanning.²³ Lee et al developed a spatiotemporal deformable-registration framework combining 3D CNNs, self-attention, and ConvLSTM. The approach improved registration accuracy and reduced processing time compared with conventional large-deformation registration.²⁴ Hu et al incorporated a registration network into CBCT-to-CT synthesis to address residual anatomical misalignment.⁹ Lye et al combined deformable-registration-derived synthetic CT with directed adaptive radiotherapy, linking registration and image synthesis with an adaptive workflow.¹⁶

Overall, AI-based segmentation and registration demonstrated potential to reduce the time required for

contour propagation and image registration while maintaining clinically relevant geometric performance. Longitudinal and patient-specific strategies were particularly relevant to online ART because they incorporated information from the same patient's treatment course. However, most studies assessed technical accuracy rather than demonstrating that automated contours or registrations consistently resulted in clinical adaptive plan implementation.

Domain C: AI-based anatomical change prediction and adaptive planning

Two studies primarily addressed prediction of anatomical change and its relevance to adaptive planning. Chen et al. developed TransAnaNet, a transformer-based anatomy-change prediction network using planning CT and serial CBCT to predict treatment-related anatomical changes. Performance was assessed using image-similarity and geometric measures, including MSE, SSIM, and Dice-based metrics.²⁵ Ishizawa et al developed a machine-learning model combining clinical factors, DVH parameters, and baseline radiomics to predict substantial volume reduction during treatment; nested cross-validation was used for model evaluation²⁶ (Table 3).

Table 3: Studies on AI-based Anatomical-change Prediction + Adaptive Planning.

Study	Author	Year	Study design	Imaging modality	AI / ML method	Primary AI application	Clinical context / population	Main outcomes / metrics
6	Chen et al	2025	Retrospective	pCT + serial CBCT	Transformer / TransAnaNet	Anatomical-change prediction	H&N ART	MSE, SSIM, Dice; predicted anatomy
16	Ishizawa et al	2023	Retrospective	Serial CBCT + clinical/DVH data	Random forest / SVM + radiomics	Volume-reduction prediction	H&N RT	AUC, sensitivity, specificity

These studies suggest a potential transition from reactive ART, in which adaptation follows established anatomical deterioration, toward predictive ART in which clinically important changes may be anticipated. However, direct evidence that predicted anatomy can reliably generate or improve an adaptive treatment plan remains sparse.

Domain D: AI-based prediction of ART requirement

Three studies evaluated prediction of whether patients would require adaptive radiotherapy. Rachi et al. developed machine-learning prediction programs using tumour geometry and body-shape changes in HNC VMAT and identified treatment-related variables associated with ART indication.²⁷ Iliadou et al evaluated early prediction of planning-adaptation requirement using volumetric

alterations and machine learning.²⁸ Ishizawa et al combined clinical, DVH, and radiomic features to predict substantial volume reduction, providing a potential basis for patient selection.²⁶

Collectively, these studies indicate that AI may facilitate patient-specific ART triage by identifying patients more likely to experience clinically significant anatomical change. This could potentially reduce unnecessary replanning while prioritising patients likely to derive greater benefit. The distinction is clinically important because ART itself introduces additional imaging, contouring, planning, and quality-assurance workload. However, the evidence remains limited and predominantly retrospective, and prospective evaluation of AI-based ART triggering was not identified (Table 4).

Table 4: AI-based prediction of ART requirement.

Study	Author	Year	Study design	Imaging modality	AI / ML method	Primary AI application	Clinical context / population	Main outcomes / metrics
16	Ishizawa et al	2023	Retrospective	Serial CBCT + clinical/DVH data	Random forest / SVM + radiomics	Volume-reduction prediction	H&N RT	AUC, sensitivity, specificity
20	Rachi et al	2023	Retrospective	CBCT + VMAT treatment data	Machine learning	Prediction of ART requirement	H&N VMAT	Prediction performance ; ART indication
23	Iliadou et al	2022	Retrospective	CBCT + radiomics	Machine learning	Early prediction of ART requirement	H&N RT	Prediction of volumetric alteration / ART indication

Methodological quality and risk of bias

CLAIM adherence across the included studies ranged from approximately 68% to 88%, with a mean adherence of 79.9%±5.8%. Reporting was generally strongest for AI methodology, imaging data, model architecture, and quantitative performance metrics. More recent studies increasingly reported independent testing or multicentre/multi-linac evaluation, indicating gradual improvement in methodological transparency. Nevertheless, external testing remained uncommon relative to internal or single-centre evaluation. The principal limitations in reporting related to patient-selection methodology, external testing, prospective evaluation, generalizability, model/data availability, and clinical implementation. Where QUADAS-2 was applicable, risk of bias was predominantly low for the index-test, reference-standard, and flow/timing domains. Patient selection was the principal area of uncertainty because consecutive or representative cohort selection was not consistently reported. No study demonstrated unequivocally high risk of bias across the principal domains. Overall, the quality assessment suggested that the literature is technically well developed but clinically less mature, with uncertainty concentrated around cohort selection and clinical generalizability.

Overall evidence synthesis

Across the four domains, the evidence demonstrated a progressive expansion of AI applications across the ART pathway. Synthetic CT generation and treatment-image enhancement represented the most extensively studied application, followed by automated segmentation and deformable registration. Evidence for anatomical-change prediction, adaptive planning, and prediction of ART requirement was substantially smaller. Thus, AI appears

technically capable of addressing several major workflow bottlenecks, particularly image generation, segmentation, registration, and early identification of anatomical change. However, prospective evidence demonstrating that AI-guided ART improves clinical decision-making, treatment efficiency, toxicity, or patient outcomes remains limited. The evidence therefore supports substantial technical feasibility but does not yet establish routine clinical superiority of AI-enabled ART over conventional adaptive workflows.

DISCUSSION

Artificial intelligence is increasingly being incorporated into different components of adaptive radiotherapy for head and neck cancer. The present systematic review demonstrates that the strongest evidence currently exists for AI-assisted image synthesis, image enhancement, automated segmentation, and deformable image registration, whereas evidence for AI-guided prediction of anatomical change and, particularly, prediction of which patients actually require adaptive radiotherapy remains comparatively limited. This suggests that the field is progressing from technical automation toward more clinically oriented adaptive decision-making, but this transition is not yet complete.^{34,35}

Taken together, the 25 studies indicate that AI has demonstrated considerable technical potential across multiple components of HNC adaptive radiotherapy, particularly image synthesis, segmentation and registration. However, the evidence becomes progressively thinner as the AI application moves from technical automation toward prospective clinical decision-making.^{31,32,35} Thus, the current evidence supports a transition from: AI-assisted technical automation toward, AI-supported adaptive decision-making, but the latter remains insufficiently validated.²⁹⁻³³

Strengths of the review

A major strength of this review is its focused clinical scope. Rather than broadly evaluating AI in radiotherapy, the review specifically addressed AI applications relevant to adaptive radiotherapy in HNC and restricted inclusion to photon-based treatment with CBCT, kVCT or MVCT. This provides greater clinical homogeneity and ensures that the included evidence has direct relevance to the contemporary ART workflow.³⁴

Another strength is the four-domain framework, which allowed heterogeneous AI applications to be organized according to their position within the adaptive pathway: synthetic CT/image enhancement, automated segmentation and deformable registration, anatomical change prediction/adaptive planning, and prediction of ART requirement. This approach facilitates comparison between technically mature and clinically emerging applications.

The review also incorporated CLAIM 2024 and QUADAS-2, providing complementary assessment of reporting quality and risk of bias. The generally good CLAIM adherence and predominantly low risk of bias in technical evaluation domains support the methodological robustness of much of the available literature. At the same time, the frequent uncertainty regarding patient selection highlights limitations in generalizability.^{29,30} Importantly, this review deliberately did not perform a meta-analysis. Given the substantial heterogeneity in AI architectures, imaging datasets, validation methods and outcome measures, qualitative synthesis was considered more appropriate than pooling technically incomparable performance metrics.

Limitations of the review

Several limitations should be acknowledged. First, the review was based predominantly on retrospective studies, and the absence of substantial prospective clinical validation limits the ability to determine whether technically successful AI models translate into improved adaptive treatment decisions or patient outcomes.³¹⁻³³

Second, considerable heterogeneity existed between studies in terms of patient populations, imaging protocols, AI architectures, reference standards and performance metrics. Although the four-domain framework facilitated structured synthesis, direct comparison between individual studies remains limited.³⁴

Third, the review included only photon-based radiotherapy and CBCT/kVCT/MVCT-based applications. This deliberate restriction improved clinical specificity but may have excluded potentially relevant AI approaches using other imaging or treatment modalities.

Fourth, although CLAIM and QUADAS-2 provided structured methodological assessment, QUADAS-2 is

primarily designed for diagnostic-accuracy studies and is not ideally suited to every technical AI study. It was therefore applied selectively where considered appropriate, with CLAIM providing the principal assessment of AI reporting quality.

Finally, the evidence base remains relatively recent and rapidly evolving. Consequently, some potentially promising AI approaches may not yet have sufficient longitudinal or external validation to establish their clinical utility.³⁴

CONCLUSION

Overall, this systematic review indicates that artificial intelligence has moved beyond experimental proof-of-concept applications and demonstrates substantial technical potential across several components of adaptive radiotherapy for head and neck cancer. The strongest and most consistent evidence is currently available for AI-based synthetic CT generation, image enhancement, automated segmentation, and deformable image registration. However, the evidence becomes considerably less mature when AI is used to predict future anatomical changes, determine the need for adaptive replanning, or directly support clinical adaptive decision-making. Thus, while AI appears capable of addressing several major time and labour-intensive steps of the adaptive radiotherapy workflow, its role in routine clinical ART remains incompletely established. The principal gap is the lack of prospective, externally validated and multicentre evidence demonstrating that AI-guided adaptive radiotherapy improves clinically meaningful outcomes rather than merely technical performance. Future research should therefore shift from demonstrating whether AI can perform individual ART tasks toward establishing whether AI can safely, reproducibly and efficiently improve the selection, timing and delivery of adaptive radiotherapy in clinical practice.

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