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Clinical Implementation of Adaptive Radiotherapy Bridging Precision and Personalization

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Abstract: Adaptive Radiotherapy (ART) is a fundamental shift from static dosimetry to a dynamic, customized procedure that is determined by the patient's daily biological and anatomical changes. Organs at risk (OARs) may become more toxic, or therapy efficacy may be compromised if these inter-fractional discrepancies are not addressed. AI-driven solutions are the most important part of making things useful. They make it possible how to adapt (Triggered OART) and cut down on the main problem, manual demarcation. To get around the problems with CBCT for proton treatment, employ Robust Planning or Deep Learning-based Synthetic CT (sCT). Dosimetric efficacy is consistently shown; high-level clinical evidence connecting these benefits to enhanced patient outcomes is still developing. Future research must concentrate on large-scale Randomized Controlled Trials (RCTs) and the inclusion of biological and functional MRI biomarkers.

Keywords: Adaptive radiotherapy, Learning-based synthetic CT, MRI biomarkers, Organs at risk, Randomized controlled trials, Triggered OART.

Abbreviations

ART-	Adaptive Radiotherapy
OART-	Online Adaptive Radiotherapy
OAR-	Organs at Risk
RCT-	Randomized Controlled Trial
IMRT-	Intensity-Modulated Radiation Therapy
SBRT-	Stereotactic Body Radiation Therapy
IGRT-	Image-Guided Radiation Therapy
CBCT-	Computed tomography Cone-beam CT
HU-	Hounsfield Unit
sCT-	Synthetic CT
MR Linac-	Magnetic Resonance Linear Accelerator
MRgRT-	Magnetic Resonance-Guided Radiotherapy
AI-	Artificial Intelligence
HNC-	Head and Neck
GTVp GTVn-	Gross Tumour Volume (Primary and lymph node)
CTV-	Cinical Target Volume
PTV-	Panning Target Volume
Pca-	Prostate Cancer
SV-	Seminal Vesicles
QA-	Quality Assurance
APT-	Adaptive Proton Therapy
RRS-	Range Robutness Settings
DWI-	Diffusion weighted Imaging
DL-	Deep Learning
NPC-	Nasopharyngeal Cancer
AUC-	Appropriate Use Criteria
LOP-	Learning of Plans
LUTS-	Lower Urinary Target Symptoms

I. Introduction

Adaptive Radiotherapy (ART) is a complex strategy in which a patient's radiation plan is continually updated to account for anatomical shifts that occurs during the treatment period. The major purpose of this strategy is to refine dosage administration, providing total tumor coverage while sparing neighboring healthy tissues, termed as organs at risk (OARs). This dynamic approach is vital since traditional, set treatment plans—even those using advanced technologies like as Intensity-Modulated Radiation Therapy (IMRT) or Stereotactic Body Radiation Therapy (SBRT)—fail to address daily physiological changes

By switching from a static, pre-planned dosimetry technique to a dynamic procedure that takes into account anatomical changes during treatment, adaptive radiotherapy (ART) constitutes a model shift in the treatment of cancer (Mastella *et al.,* 2025; Yan *et al.,* 1997, as quoted in Marwaha *et al.,* 2025). Because patient anatomy is dynamic, inter-fractional and intra-fractional alterations brought on by organ filling, tumour shrinking,

weight loss, or respiratory motion might result in considerable variances between the anticipated and delivered dose. ART can be performed at different intervals: offline (between treatment sessions using past data to adjust future plans), online (just before a session with quick imaging and plan modification), and real-time (adjusting the beam during treatment delivery).

A. CBCT-Based ART

Cone-beam CT (CBCT) imagers are utilized on the majority of conventional linacs (Oud *et al.,* 2025). The low picture quality, artifacts, and Hounsfield Unit (HU) limitations of CBCT, which are inadequate for direct dose calculation, greatly restrict this approach, despite its improved accessibility (Vestergaard *et al.,* 2025; Yeap *et al.,* 2024).

Because of its economy, ease of use, and compatibility with current processes, CBCT/CT is well regarded. technologies that enable CBCT-based ART, particularly the development of synthetic CT (sCT) for proton therapy.

B. Online ART

The OART process is fundamentally time-sensitive. The daily manual re-contouring of targets and OARs is a major bottleneck, often taking longer than all other steps combined (Konrad *et al.,* 2025). This extended time on the treatment table is not only a logistical strain on clinic resources but also degrades treatment quality by increasing patient discomfort and the likelihood of intra-fractional motion, which can invalidate the very plan being adapted (Konrad *et al.,* 2025). Gan *et al.* (2025): can an AI model be developed for "triggered OART" to automatically identify which fractions actually require a full adaptation.

C. MR-Linear Accelerators (MR-Linacs)

MR-Linac offers exceptional soft tissue imaging and real-time tracking capabilities. MR-Linear Accelerators (MR-Linacs), such as the Elekta Unity and View Ray MRIdian, are used in Magnetic Resonance-Guided Radiotherapy (MRgRT) (Ma *et al.,* 2025; Marwaha *et al.,* 2025). For difficult locations like the brain and lung, MRgRT offers greater soft-tissue contrast without the use of ionising radiation, allowing for real-time tumour tracking and visualisation (Ma *et al.,* 2025; Marwaha *et al.,* 2025).

D. AI-Driven Workflow Optimisation for Efficiency and Practicality

Artificial Intelligence (AI) powers workflow automation. A manual OART procedure is excessively time-consuming, requiring daily picture acquisition, delineation, re-planning, and quality verification (Konrad *et al.,* 2025). By automating OAR and target delineation and treatment re-planning, AI is the primary enabler for making OART therapeutically feasible (Mastella *et al.,* 2025; Preziosi *et al.,* 2025).

II. Research Problem

A. Managing Geometric and Volumetric Changes

i. Head and Neck Cancer (HNC)

Patients with HNC often show considerable tumour and lymph node shrinkage, along with soft tissue alterations due to weight loss or edema. Research indicates that the primary clinical target volume (CTV) and affected lymph nodes can decrease in size by 6%–69% by the end of treatment.

ii. Prostate Cancer (PCa)

PCa is intensified by substantial, unpredictable fluctuations in bladder and rectal fullness, which cause the prostate to shift and deform, typically by more than 1 cm. This issue is exacerbated in high-risk PCa, because the complete seminal vesicles (SVs) must be included in the treatment field. Due to the SVs' significant motion, which is frequently unrelated to the prostate's movement, broad planned target volume (PTV) margins—roughly 8 mm—have historically been necessary to prevent the OARs from receiving hazardous doses.

B. Overcoming Limitations of Current IGRT and ART Workflows

i. High Workload and Low Throughput

The standard ART method is labour-intensive, involving considerable time and manpower for tasks like as manual contouring, plan review, optimization, and Quality Assurance (QA). For instance, on a MR-Linac without AI aid, the time necessary to manually repair multiple structures in HNC situations is a substantial hurdle to frequent adaption. MR-Linac sessions can span 45 to 60 minutes, even on quicker systems. This limits the number of patients that can be treated and increases the uncertainty due to movement throughout the session.

ii. Subjectivity and Lack of Standardization

Decisions regarding the time of generating a new adaptive plan are generally relied on the subjective assessment of radiation oncologists and medical physicists rather than on established, quantitative criteria. The dearth of standardized terminology and nomenclature also makes it difficult to compare and publish the findings of adaptive therapy experiments.

iii. Image Quality and Artifacts

CBCT/CT systems often lack the soft-tissue definition required for accurate delineation of tumors and OARs in the abdomen and pelvis, use of fiducials or surrogate markers. For

HNC, artifacts on CT/CBCT scans, such as dental fillings, can interfere with correct contouring. Although MR-Linac gives superior contrast, it needs the production of a synthetic CT (sCT) image for dose computation. This procedure presents uncertainties that some opponents claim invalidate the accuracy benefits of ART.

iv. Online ART Workflow

Konrad *et al.* (2025) and Preziosi *et al.* (2025) investigate this exact problem: quantifying the time saved by integrating AI into the OART workflow for prostate cancer. Clinical workload of having experts assess the need for adaptation every single day is unsustainable (Gan *et al.,* 2025). This leads to the problem investigated by Gan *et al.* (2025): can an AI model be developed for "triggered OART" to automatically identify which fractions actually require a full adaptation, thereby optimizing clinical resources.

CBCT is ubiquitous; its direct use for dose calculation is unreliable due to artifacts and, most critically, HU inaccuracies (Oud *et al.,* 2025; Vestergaard *et al.,* 2025). This issue is greatly exacerbated in Adaptive Proton Therapy (APT), where small density mistakes can result in large proton range errors, which can induce OAR over-irradiation or target misses (Oud *et al.,* 2025; Yeap *et al.,* 2024). Two aspects of the research challenge.

- *The Correction Approach:* Can AI-based deep learning models generate a "synthetic CT" (sCT) from the daily CBCT that is dosimetrically accurate for proton planning? This is the central question for Vestergaard *et al.* (2025), Viar-Hernandez *et al.* (2024), and Yeap *et al.* (2024).
- *The Coping Approach:* Oud *et al.* (2025) investigate if using robust optimization with increased Range Robustness Settings (RRS) can effectively mitigate the dosimetric impact of CBCT errors, making adaptation feasible without a perfect sCT.

III. Result

A. Technological Platforms and Imaging Solutions

i. CBCT/CT

CBCT/CT systems are already widely available, more affordable, and clinical staff are familiar with X-ray imaging. Advanced CBCT technologies now provide significantly better image quality, approaching that of diagnostic CT, with rapid imaging that minimizes motion artifacts and enhances clarity. A major advantage of CBCT is its ability to perform direct dose calculations on the acquired image, which avoids the need for a synthetic CT (sCT).

ii. MR-Linac

MR-Linac systems provide unmatched soft tissue visualization, allowing for direct observation of tumours and OARs without relying on bony landmarks, which is common with older CT/CBCT technology. Advantage is their ability to perform continuous, real-time imaging as the radiation beam is on, enabling superior motion management and adaptive re-planning that static CBCT cannot achieve. Additionally, MR-Linac allows for the use of functional imaging biomarkers, such as Diffusion-Weighted Imaging (DWI), to potentially inform biologically guided treatments.

iii. Hybrid Approach

CBCT-based online ART on standard C-arm linacs has proven clinically viable for five-fraction PCa SBRT, successfully providing optimal target coverage in cases where non-adapted IGRT plans were inadequate in about 70% of fractions. This demonstrates that high-quality ART is not limited to dedicated MR-Linac or O-ring platforms. The CyberKnife robotic radiosurgery system, another example, uses an in-room CT-on-rails for daily plan adaptation paired with 2D KV imaging to track fiducials during treatment, showing its feasibility for SBRT in high-risk prostate cancer.

B. Workflow Automation and AI Integration

i. Auto-Segmentation (DL-Based)

Deep Learning (DL) models are crucial for speeding up contouring, the most time-intensive part of the workflow. In CyberKnife planning, DL-based auto-contouring was superior to deformable image registration for OARs (rectum, bladder) and seminal vesicles because it required less editing time and was more reliable when dealing with large anatomical shifts. For nasopharyngeal cancer (NPC) adaptive RT. DL auto-segmentation was highly accurate (mean DSC > 0.85) for most structures, though challenges persisted for the primary gross tumor volume (GTVp) and involved lymph nodes (GTVn).

ii. Synthetic CT (sCT) and Simulation-Free Workflows

The viability of creating sCT images from Cone-Beam CT scans using Cycle-GAN models has been established for adaptive RT in NPC. An even more innovative approach is a simulation-free MR-Linacs workflow for PCa SBRT, which showed that clinically acceptable adaptive plans could be created using routine diagnostic MRI scans as the reference, eliminating the need for a separate RT simulation appointment. This approach drastically shortens the treatment pathway, reduces costs, and lessens the burden on patients.

iii. AI-Driven Triggering

Machine learning models that use a mix of CT radiomics features (which quantify the shape and texture of tumours/organs) and dosimetric features have shown promise in creating an objective model for predicting the need for Triggered OART (Trigger-OART) in postoperative PCa, achieving a high AUC of 0.893. This solution tackles the issues of subjectivity and staff workload by automatically screening for fractions that require replanning.

iv. Quick Plan Templates

The Cyber Knife workflow was made faster by using "quick plan templates" that generate treatment planning parameters with fewer sample points. This reduced optimization time from about 10 minutes to roughly 3.5 minutes without compromising plan quality, directly addressing the time pressures of online adaptation.

C. Adaptive Planning Strategies and Clinical Feasibility

i. Library of Plans (LOP)

Library of Plans (LOP) approach is the most common and clinically validated strategy for cervical cancer. It is often used with an Internal Target Volume (ITV) margin that accounts for variations in bladder and rectal filling. This method has successfully reduced the volume of OARs receiving radiation while ensuring target coverage and serves as an intermediate step between offline and daily online ART.

ii. Margin Reduction

Dosimetric studies indicate that for ART to provide a clinically meaningful reduction in dose to OARs in HNC, it must be performed alongside a synchronous reduction in PTV margins. Simulations demonstrated that reducing the margin by 3 mm resulted in an average dose-sparing effect of over 1 Gy/mm for several OARs, including the parotid glands, oral cavity, and larynx. If margins are not reduced, the dosimetric advantage is often minimal and may not be worth the required resources.

iii. Weekly Adaptive SBRT for High-Risk PCa

The X-SMILE study protocol is designed to assess the safety of weekly adaptive SBRT (in 5 fractions) for patients with intermediate- to high-risk PCa who were often excluded from past trials due to pre existing Lower Urinary Tract Symptoms (LUTS) or Prostate Hyperplasia (BPH). This less frequent, adaptive schedule is intended to lower the high risk of acute genitourinary (GU) toxicity that is associated with baseline LUTS and large prostate volumes.

D. AI-Driven Workflow Efficiency and Automation

i. MRgRT

Konrad *et al.* (2025) prospectively investigated the implementation of an in-house AI auto-segmentation tool for prostate cancer on a 1.5T MR-Linac. The results were dramatic: the AI-based workflow reduced the median online delineation time by 46%, from 9.8 minutes in the standard manual workflow down to 5.3 minutes. This time saving had a crucial secondary benefit: the frequency of needing to "readapt" (restart the planning process due to patient motion during the long contouring phase) was reduced from 16% in the standard group to just 5% in the AI group.

ii. CBCT-Based ART

Preziosi *et al.* (2025) analyzed an AI-integrated linac (Varian Ethos) for prostate OART, where AI automatically segmented OARs on the daily CBCT. This automation resulted in efficient median total session times of 25 minutes for prostate-only treatments and 32 minutes for prostate-plus nodes treatments. The study confirmed the dosimetric value of this workflow: the final AI-driven *adapted* plan showed vastly superior target coverage (e.g., a +10.4% to +11.8% improvement in PTV V95%) compared to the *predicted* plan (the original plan simply recalculated on the day's anatomy) (Gan *et al.,* 2025).

E. Dose Calculation for CBCT/Proton

- *Correcting the Image:* Synthetic CT (sCT) Generation Multiple studies have successfully used deep learning to generate high-quality sCT images from daily CBCTs.
- *DL for Proton sCT:* Vestergaard *et al.* (2025) used a 3D Cycle GAN (a deep learning network) to convert CBCT images to sCT images for prostate proton therapy. The generated sCTs demonstrated image quality and CT numbers comparable to conventional fan-beam CT. Most importantly, the dosimetric accuracy was validated: proton range differences were minimal (largest median difference of 1.9 mm), and the recalculated dose plans showed excellent target coverage (V95% 99.6%).
- *Advanced DL for sCT:* Viar-Hernandez *et al.* (2024) advanced this concept by synthesizing dual-energy CT (DECT) images from CBCTs, as DECT provides superior tissue characterization for proton stopping power calculations. They employed a novel 3D conditional denoising diffusion probabilistic model (DDPM), which demonstrated superior performance (MAE of 39.58 HU) and significantly reduced artifacts compared to traditional GAN-based methods.
- *Commercial sCT Solutions:* Yeap *et al.* (2024) evaluated two commercial sCT algorithms (Corrected CBCT and Virtual CT) for proton therapy across head-and-neck, thorax, and pelvis sites. They found the optimal algorithm was site-specific: "Corrected CBCT" was more accurate for head-and-neck, while "Virtual CT" (which relies on deformable registration) was better for the pelvis.

IV. Conclusion

A. Dosimetric Benefit

i. Target Coverage

ART reliably maintains or improves coverage of the CTV/PTV, especially when significant anatomical changes occur. For instance, CBCT-based online ART for PCa ensured V40 Gy≥95% compliance in 100% of sessions, whereas non adapted plans only achieved this in 30% of sessions.

ii. OAR Sparing

Decreases in the mean dose to OARs—such as the parotids and spinal cord in HNC, and the rectum and bladder in PCa—are consistently observed. Simulations have also shown that when ART is combined with a reduction in PTV margins (e.g., from 5 mm to 2 mm in HNC), it leads to clinically significant dose reductions of several Gray to multiple healthy structures.

B. Clinical Benefit

i. HNC Toxicity

A systematic review revealed that although ART lowered doses to OARs (e.g., reducing the mean parotid dose by 0.4 to 7.1 Gy), its effect on long-term toxicity and disease control is still uncertain due to small sample sizes and inconclusive results from prospective trials.

ii. PCa Toxicity

Preliminary clinical findings for PCa SBRT using online adaptive methods are encouraging, indicating low toxicity rates compared to historical data. For PCa, ART's ability to enable safe ultra-hypofractionation (e.g., treatment in 5 fractions) is a major clinical achievement in itself, as it reduces the patient's burden of undergoing a multi-week treatment course.

iii. MRgRT Strategies

High-field MR Linacs is maturing from technical feasibility to clinical strategy validation. For high-grade glioma, the UNITED trial (Detsky *et al*., 2024) has provided critical prospective evidence that the margin reduction enabled by MRgRT is oncologically safe, validating a key theoretical benefit of the technology. For lung cancer, MRgRT's combination of real-time tracking, gating, and adaptation is enabling safe and effective SBRT for high-risk central and ultra-central tumors (Ma *et al.,* 2025).

C. The Technological Trade-Off: Fidelity vs. Practicality

i. MR-Linac and (Fidelity)

Technology offers superior soft-tissue definition, real-time tracking of tumor and organ movement, and the potential for biological adaptation. It is a more expensive, less common, and more resource-demanding platform with longer treatment sessions, which poses a barrier to its global implementation.

ii. CBCT/CT (Practicality)

This technology is widely accessible and more affordable, making it well-suited to meet the global need for ART. Recent improvements in CBCT image quality and its integration with C-arm linacs and robotic systems provide viable options for online adaptation, countering the idea that high-fidelity ART is exclusive to MR-Linacs.

iii. Workflow Burden

Contours and validating plans makes ART a time-consuming and labor-intensive process. The average duration of adaptive treatments is still long, ranging from about 20 to 68 minutes on various systems, which is much longer than non-adaptive treatments. This can reduce patient throughput and elevate the risk of movement during the fraction. The dependence on the subjective decisions of on-site experts is a key challenge that new AI driven tools, such as auto-segmentation and Trigger-OART, are starting to resolve effectively.

iv. AI is Practical OART's Engine

The idea of online adaptability is no longer merely theoretical. AI-driven automation is a therapeutically viable option that makes OART practicable, especially for auto-segmentation. Studies (Konrad *et al.,* 2025) show a 46% reduction in contouring time for MR-guided prostate ART, effectively addressing the main bottleneck of delineation time.

D. CBCT-Based Proton ART

- *The sCT Pathway:* Deep learning models, from GANs to newer DDPMs, are capable of generating synthetic CTs from daily CBCTs with high dosimetric accuracy, including for proton range calculations (Vestergaard *et al.,* 2025; Viar-Hernandez *et al.,* 2024).
- *The Robust Planning Pathway:* CBCT uncertainty by using increased range robustness settings (e.g., 10% RRS) during online planning is also a highly effective and practical strategy that improves coverage without compromising OAR safety (Oud *et al.,* 2025).

V. Scope for Further Work

A. Validation Through High-Level Comparative Clinical Trials

Randomized controlled studies (RCTs) that use reliable clinical outcomes like late toxicity, quality of life, and survival to compare ART against non-ART control groups are desperately needed. Adopting uniform reporting requirements for adaptive treatments, which address therapeutic intent, frequency, imaging parameters, segmentation methodologies, and dosage accumulation procedures, is an essential step for comparing results from these trials.

B. Achieving Full Workflow Automation and Efficiency

Future research should attempt to advance from automating single phases to building fully end-to-end automated ART workflows. This would reduce the need for clinical staff by include duties like automated plan assessment, QA, and auto-segmentation of structures. Before completely incorporated

into clinical practice to expedite the procedure, the effective AI-driven Triggered OART models need prospective validation across several institutions. Furthermore, more validation is required before simulation-free MR-Linac procedures can be applied to different patient populations.

C. Integration of Biological and Functional Adaptation

ART lies in extending beyond just geometric corrections by incorporating quantitative and functional MRI. Use of MRI biomarkers include monitoring early tumor response to guide biologically adaptive methods like dosage painting, and forecasting or tracking radiation-induced damage to better spare OARs.

Biological adaptation rather than merely physical adaptation holds the key to the future of ART. This "paradigm shift" is mentioned in the reviews by Ma *et al.* (2025). Future work should focus on combining functional imaging (like DWI accessible on MR-Linacs) and delta-radiomics (monitoring changes in imaging features over time) into the OART procedure.

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