# INFORMATION BRIEF (RAPID REVIEW)

# Integrated CT-LINAC

Malaysian Health Technology Assessment Section (MaHTAS)
Medical Development Division
Ministry of Health Malaysia
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# TITLE: INTEGRATED CT-LINAC

## PURPOSE

To provide scientific evidence on the effectiveness, safety and cost-effectiveness of integrated CT-LINAC following a request from the Deputy Director-General of Health (Research and Technical Support), Ministry of Health, Malaysia.

## BACKGROUND

Radiotherapy is an essential component in the treatment management of cancer patients, either alone or in combination with surgery or chemotherapy, and for both cure and palliation.[1] The accurate targeting of tumours with maximal sparing of normal tissues has been the foremost goal of radiotherapy practice.[2]

The treatment options are broadly categorised based on how the radiation is delivered including external beam radiation therapy (EBRT), internal radiation therapy and systemic radioisotope therapy.[3] The EBRT is the most common type of radiation therapy, where a machine outside the body delivers high-energy radiation beams to the tumour. External beam radiation therapy includes 3-dimensional conformal radiotherapy, intensity-modulated radiotherapy, stereotactic radiotherapy, image-guided radiotherapy, volumetric modulated arc radiotherapy, proton and heavy ion beam therapy, etc, with each individual modality having a specific advancements and adaptation for the tumour type and spatio-temporal dynamics.[3]

A conventional LINAC is a machine that delivers high-energy x-rays or electron beams to a tumour to destroy cancer cells while minimising damage to surrounding healthy tissue. However, tumours can shift and change position between treatment sessions due to patient movement, breathing, or changes in organ filling. This can make it challenging to ensure that the radiation is consistently targeting the tumour with pinpoint accuracy.[4]

To overcome such issue, Image Guided Radiation Therapy (IGRT) is introduced to improve accuracy by imaging the target right before treatment to account for patient and organ movement. This process can include target and normal tissue delineation, radiation delivery, and adaptation of therapy to anatomic, biological and positional changes over time in individual patients.[5] At the time of treatment delivery, IGRT is employed to determine the location of the target (and often the surrounding normal organs) at some predetermined frequency. The target location may be determined by a range of methods, from soft tissue volumetric imaging (eg, CT, ultrasound, MRI) to localisation of surrogates, such as bone, implanted fiducial markers or external surface markers or features (e.g by planar imaging or fluoroscopy, electromagnetic localisation or optical surface imaging).[5] The ability to achieve this goal has improved greatly through advances in imaging technology, specifically the development of computerised tomography (CT), magnetic resonance imaging (MRI), positron-emission tomography (PET) and fusion PET/CT.[2]

The CT-LINAC addresses this challenge by providing real-time or "on-board" imaging. The integrated CT scanner allows for a CT scan of the tumour to be taken immediately before each radiation treatment. There are two differing computed tomography (CT) imaging modalities i.e fan beam and cone beam, to be integrated with LINAC.

1. Cone-Beam CT (CBCT): This is the most common form of imaging on modern LINACS. A CBCT system uses a single X-ray source and a large-area detector to capture a volumetric image in a single rotation. While effective for image guidance, CBCT images typically have lower contrast and more scatter artifacts than diagnostic CT scans.
2. Fan-Beam Helical CT: It is a full-fledged, multi-slice diagnostic CT scanner (specifically, a 16-slice helical CT) that is mounted coaxially with the LINAC gantry. The fan-beam geometry and helical scanning motion are the same principles used in a regular diagnostic CT scanner in a hospital's radiology department.

Among CT-LINAC that have received approval for usage includes:

[redacted]

There were other emerging technologies combining LINAC with imaging technologies which include MR-LINAC, a linear accelerator with a magnetic resonance imaging (MRI) scanner or PET-LINAC, a linear accelerator with a Positron Emission Tomography (PET) scanner. The MR-LINAC is claimed to provide better soft-tissue visualisation[9] whereas PET-LINAC provides functional and metabolic information about the tumour, which can be used to tailor the dose based on the biological activity of the cancer cells.[10]

The pitfalls associated with IGRT include uncertainties in target volume delineation, image quality, longer acquisition times, high intra-fractional errors, and extra-dose delivery during daily imaging. Adaptive radiotherapy overcomes these limitations, where changes are made to the original radiation treatment plan during the course of hypo-fractionated radiotherapy based on changes in anatomical and tumour features/ biology.[3]

**Figure 1: CT-LINAC Machine i.e the [redacted]. The machine combines a 16-slice CT scanner with a 6 MV X-ray linear accelerator on the same bed, allowing high-quality CT imaging and precise image-guided radiotherapy (IGRT) to be performed at the same time.[8]**

## EVIDENCE SUMMARY

A total of 143 titles were retrieved from the scientific databases via OVID, PubMed and general search engines [Google Scholar], using the search term; *Image-guided Radiotherapy/ or X-ray Computed Tomography/ or CT-LINAC.* The last search was conducted on 30th August 2025. Sixteen articles were found to be relevant which included five observational studies and one pre-clinical study for effectiveness. Whereas for safety, two Phase III randomised trials, two feasibility studies, one observational study, one risk assessment study, and one case report were included. For the cost, one cost evaluation study and one longitudinal cost analysis from a Phase III trial were included.

## EFFICACY/ EFFECTIVENESS

### 1) Dosimetric advantage

### Gynaecologic tumour

An observational study was conducted by Guberina et. al (2023) comparing online adaptive Intensity-Modulated Radiation Therapy (IMRT) or Volumetric-Modulated Arc Radiotherapy versus image-guided radiotherapy (IGRT) involving seven consecutive patients with gynaecologic tumour at the West German Cancer Center. Adaptive radiotherapy uses high-quality cone-beam computed tomography (CBCT) ART was performed based on a physician's choice. For each fraction, the researchers compared the dose distribution of the adapted plan with a scheduled plan that was optimised on the initial planning CT scan. The primary outcomes were target dose coverage with ART compared with IGRT for planning treatment volume (PTV) margins of 5 mm or less in terms of the generalized equivalent uniform dose (gEUD) without increasing the gEUD for the organs at risk (bladder and rectum). All patients received at least 1 treatment series of at least 5 dose fractions using the adaptive mode. Two patients received more than 1 treatment series to reduce the treatment volume as sequential boosts. A total of 45 of 61 fractions of the adaptive series were delivered with the ART plan (73.8% applied adaptive fractions) and the other 16 fractions were delivered as IGRT. The results demonstrated that for a clinical PTV margin of 5 mm, IGRT was associated with a median gEUD decrease in the interfractional clinical target volume of −1.5% (90% CI: −31.8% to 2.9%) for all fractions in comparison with the planned dose distribution. Online ART was associated with a decrease of −0.02% (90%CI: −3.2% to 1.5%), which was less than the decrease with IGRT ($P < 0.001$) and not associated with an increase in the gEUD for the bladder or rectum. Whereas for a PTV margin of 0 mm, the median gEUD deviation with IGRT was −13.1% (90%CI: −47.9% to 1.6%) compared with 0.1% (90%: CI: −2.3% to 6.6%) with ART ($p < 0.001$). The benefit associated with ART was larger for a PTV margin of 0 mm than of 5 mm ($p=0.004$) due to spreading of the cold spot at the clinical target volume margin from fraction to fraction with a median SD of 2.4 cm (90%CI: 1.9 to 3.4 cm) for all patients. It was shown that online ART was associated with a smaller median gEUD decrease in the interfractional clinical target volume (iCTV) compared to IGRT, particularly with PTV margins of 5 mm or less. This improvement was achieved without increasing the gEUD to the bladder or rectum. The author concluded that ART improves dose coverage and that its benefits are more pronounced with smaller PTV margins.[11]

An observational study by Peng et al. (2023) evaluating the dosimetric advantages and reliability of the accurate delivery of online ART involving six patients with uterine cervical cancer. The patients were scanned with uRT-Linac 506c KV-FBCT then the target volume (TV) and organs at risk (OARs) were delineated by doctors. The workflow involved obtaining the daily FBCT, delineating the target and organs at risk (OARs), and generating two plans per fraction: a virtual nonadaptive plan (VPlan) and an adaptive plan (APlan). Performance metrics such as target dose distribution (maximum dose: Dmax; the dose received by 98%, 95%, 50%, 2% of PTV: D98, D95, D50, D2), conformity index, homogeneity index, and coverage were measured. The result showed that Dmax, D98, D95, D50 and D2 of APlan were superior to those of VPlan, with significant differences ($p<0.05$), among which the D95 (5041.18±42.02) of APlan met the prescription requirements, while D95 (4972.67±159.17) of VPlan failed to meet the prescription requirements. Dose to OARs specifically rectum V40 and Dmax, bladder V40, and small-bowel V40 and Dmax were all reduced by APlan. In vivo 3D dose reconstruction yielded a mean γ-pass rate above 97%. The authors concluded that online ART significantly improves dose distribution and is a promising individualised precision radiotherapy technology.[8]

Another observational study by Jiang et al. (2024) recruited 15 cervical cancer patients comparing online ART and a clinically implemented plan selection technique to quantify the added value of online ART performed for cervical cancer by using the FBCT-linac accelerator. The result showed that the PTV Dmax of the ART plan decreased by 1.23 Gy, the PTV D95 increased by 1.34 Gy, PTV V50 increased by 4.86%, CTV coverage rose by 3.02%. Meanwhile, doses to colon, rectum, and small intestine (PTV D2cc) were reduced by 1.1–1.3 Gy ($p < 0.01$). The procedure averaged ~21 minutes per fraction. Median follow-up was 28 months, with 3-year event-free survival (EFS) of 79.4% and overall survival (OS) of 92.9%. The authors concluded that online ART enables significantly better target coverage and OAR sparing than IGRT, with favorable survival.[12]

### Lung cancer

Another observational study by Onishi et. al (2003) evaluating a novel lung cancer irradiation technique combining a CT-linac, self-breath-holding technique, and a patient-directed beam-control switch on 20 lung cancer patients (mean age of 70 years old). All patients were instructed in the technique of breath-holding during the inspiration phase using visualisation of respiratory motion through fluoroscopy as a teaching aid. CT scans under patients' self-breath holding were repeated three times, and differences in tumor position on CT images were measured. The main outcome is the reproducibility of tumor position which was visually evaluated on electronic portal images (EPI). The result demonstrated that the reproducibility of tumor position during self-breath-holding was highly accurate, with mean maximum differences of 2.2 mm in the cranial-caudal direction, 1.4 mm in the anterior-posterior direction, and 1.3 mm in the right-left direction. In 480 treatment fractions, reproducibility of tumor position was classified as "good" in 302 (62.9%) fractions, "fair" in 168 (35.0%), and "poor" in 10 (2.1%). A patient-controlled switch connected to the linac console allowed individuals to synchronise the radiation beam with their breath-holding, a process delayed by less than 0.1 seconds. The author concluded that the system was found to be effective, offering reduced planned target volume (PTV), sufficient reproducibility, and decreased treatment duration compared to conventional methods.[13]

### Breast cancer

A dosimetric study reported by Musunuru HB et al (2022) comparing the planning quality of MR-guided and CT-guided radiation therapy for a new 3-fraction accelerated partial breast irradiation (APBI) schedule for breast cancer. A 3 mm margin was used to generate MR $PTV_{3mm}$ and CT $PTV_{3mm}$ plans, and a 10 mm margin was used for CT PTV $_{10mm}$. An APBI schedule delivering 24.6 Gy to the clinical target volume and 23.4 Gy to the PTV in 3 fractions was used. Organs at risk dose constraints were scaled down from existing 5-fraction APBI protocols. The result showed that average PTVs were 84.3±51.9 $cm^3$ and 82.6±55 $cm^3$ (p=0.5) for MR $PTV_{3mm}$ and CT $PTV_{3mm}$ plans, respectively. PTV V23.4Gy, dose homogeneity index, conformity index (CI), and R50 were similar. There was no meaningful difference in OAR metrics, despite MR $PTV_{3mm}$ being larger than the CT $PTV_{3mm}$ in 70% of the patients. Average PTVs for MR $PTV_{3mm}$ and CT $PTV_{10mm}$ plans were 84.3±51.9 $cm^3$ and 131.7±74.4 $cm^3$, respectively (p=0.002). Planned target volume V23.4Gy was 99%±0.9% versus 97.6%±1.4% (p=0.03) for MR $PTV_{3mm}$ and CT $PTV_{10mm}$, respectively. Dose homogeneity index, CI, and R50 were similar. MR $PTV_{3mm}$ plans had better ipsilateral breast (V12.3Gy, 34.8%±12.7% vs 44.4%±10.9%, p=0.002) and chest wall sparing (V24Gy, 8.5±5.5 $cm^3$ vs 21.8 ± 14.9 $cm^3$, p=0.004). The authors concluded that MR- and CT-based planning systems produced comparable plans when a 3 mm PTV margin was used for both plans. Whereas, MR $PTV_{3mm}$ plans produced better ipsilateral breast and chest wall sparing compared with CT $PTV_{10mm}$. However, the clinical relevance of these findings is not yet known.[14]

### 2) Quality assurance/ stability/ accuracy

A pre-clinical study by Wang T et al. (2025) analyses the performance of the URT-Linac 506C accelerator, which integrates a diagnostic helical CT scanner with a linear accelerator to facilitate advanced online adaptive radiotherapy. The study conducted a two-year quality control program from October 2022 to June 2024 to evaluate the physical stability and reliability of the unit, focusing on its 6 MV photon beams. The results showed that the absorbed dose was consistently within 102% of the benchmark value, and long-term patient dose verifications ranged from 99.6% to 100%. Flatness measurements for a 10 cm×10 cm field were within 105%, while for a 20 cm×20 cm field, they were within 103%. Symmetry measurements for both field sizes remained within 102%. The data on absolute dose, flatness, and symmetry were found to be stable, aligning with a normal distribution. The authors concluded that the URT-Linac 506C demonstrates high-dose stability, and that routine quality assurance is critical for ensuring the accuracy and reliability of this equipment, which is essential for precise treatment delivery. They also acknowledged that factors such as environmental conditions, power supply, and continuous operation can affect the machine's stability, highlighting the need for regular calibrations by physicists to maintain optimal performance.[15]

## Prostate cancer

A rando phantom study by Cheng CW (2003) evaluated the setup accuracy and uncertainties from organ motion of CT-LINAC for precise tumor localization on 30 patients with prostate cancer. The CT localisation procedure was carried out for five consecutive treatments. The following measurements were made on each CT slice containing the prostate gland: the anterior, the posterior, the left and the right aspects of the prostate gland as well as the anterior aspect of the rectum. Each measurement was mapped out on the beams-eye views (BEV) printouts. The change in the filling state of the rectum and its effect on the prostate shape and on the isocenter position relative to the anatomy can be clearly delineated from the daily CT scans. The result showed that the accuracy of movement of the CT scanner, as determined from the separation measured between the 10-cm markers in the most superior and inferior slices, was found to be within 1 mm for all repeated measurements. The distance between the wires in the left right direction in a given CT slice also agreed to within 1 mm with the distance measured on the phantom. By comparing the verification CT study of the Rando phantom with the hard copy printouts of the original plan, the radiation oncologist was able to determine the isocenter displacements to within 2 mm of the original position in all three directions for the three separate trials. The adjustment of the treatment couch in the left-right direction was minimal with more or less symmetric about the central axis and mostly 3 mm, well within the margin of coverage. However, the adjustments of the couch was significant in both the AP/PA and caudal-cephalic directions. In the AP/PA direction, 33% of the treatments required an adjustment of the couch in the range 3–5 mm, 18% in the range 5.1–10 mm, and 6% 10 mm with a maximum of 20 mm. In the caudalcephalic direction, about 26% of treatments required adjustment in the range 3–5 mm, 8% in the range of 5.1–10 mm, and 2% required an adjustment 10 mm. The direction of the prostate movement in the AP/PA direction appears to follow roughly the day-to-day variations in the rectal filling. Variations in the isocenter position may result in underdosage of the PTV if correction is not made for the change in the isocenter position as shown at day 3 while the CTV is adequately covered, the periphery of the PTV receives less than the prescribed dose (PD) in all 3 days. The author concluded that in-room CT-linac setup allows for the correction of organ motion before dose delivery, enabling the use of smaller planning target volumes (PTVs) and potentially allowing for dose escalation without increasing toxicity. The process adds approximately 15 minutes to each treatment using a 5-mm slice thickness.[16]

### Relapsed B-cell lymphoma

A case reported by Ababneh HS et. al (2024) on adaptive bridging radiation therapy (ABRT) using CT-LINAC for a 57-year-old female with relapsed aggressive B-cell lymphoma before she underwent CAR T-cell therapy. The patient had a recurrence in her retroperitoneal and umbilical masses after initial chemotherapy. She received a single 5 Gy fraction of RT on a CT-linac, which allowed for real-time adjustments to the treatment plan to account for changes in her tumor anatomy. This single fraction resulted in a significant reduction in tumor volume in both masses, and due to this rapid response and the early availability of the CAR T-cells, no further RT was needed. Following the treatment, the patient experienced manageable toxicities common to CAR T-cell therapy, including Grade 1 cytokine release syndrome and Grade 3 immune effector cell-associated neurotoxicity syndrome. Follow-up scans confirmed a complete metabolic response, with no signs of disease recurrence at months 3 and 6 post-infusion. The authors conclude that this case demonstrates the feasibility and success of ABRT as a bridging strategy, highlighting its potential to personalize treatment and minimize toxicity before CAR T-cell therapy.[17]

A feasibility study by Ababneh HS et al (2025) evaluating CT-based adaptive bridging radiation therapy (ABRT) using CT-LINAC (Varian Ethos) involving ten relapsed or refractory large B cell lymphoma patients before CAR-T treatment. Patients were given once weekly, computed tomography-based adaptive radiation therapy at a dose of 5 Gy per fraction for up to 5 fractions over 5 weeks. The outcome is the percentage of patients being able to undergo ABRT, the adverse events and the overall response rate. The result showed that eleven sites were irradiated for palliative purposes, achieving an overall symptomatic response rate of 100%. Of the 40 total ABRT sessions, 26 fractions were delivered (65%). For 8 of the 11 target volumes treated, ABRT was held after the first 1 or 2 fractions. The in-field responses during ABRT pre-CAR T were: complete response (n = 3, 30%), partial response (n = 6, 60%), and in-field progression (n = 1, 10%). After CAR T cell infusion, the best overall response rate was 70% (n = 7), all of whom achieved complete response.[18]

### Abdominal or pelvic tumour

A feasibility study conducted by Gong W et. al (2022) integrating CT-LINAC (uRT-linac 506c from United Imaging Medical Technology) with deep-learning method called Content-Noise Cycle-Consistent Generative Adversarial Network (CNCycle-GAN) on 76 patients with abdominal and pelvic tumours to evaluate the quality of the low-dose CT network restoration images (RCT) through the objective evaluation parameters of the images, automatic delineation performance and dose calculation accuracy to judge whether the restored images can be applied to the ART workflow. The study included who underwent both low-dose and normal-dose CT (NDCT) scans. The network was trained on data from 70 patients and validated on the remaining six. The results showed that the restored CT (RCT) images significantly improved in quality compared to the LDCT images, reducing mean absolute error (MAE) from 34.34 ± 5.91 to 20.25 ± 4.27; increasing peak signal-to-noise ratio (PSNR) from 34.08 ± 1.49 to 37.23 ± 2.63; and increased structural similarity (SSIM) from 0.92 ± 0.08 to 0.94 ± 0.07, ($p<0.01$). It was also reported that the RCT images demonstrated accurate automatic delineation of organs at risk like the bladder, femoral heads, and rectum, with Dice similarity coefficients (DSC) of 0.98, which similar to manual delineation by doctors. The authors concluded that this deep learning approach provides a clinically feasible solution for low-dose

FBCT adaptive radiotherapy of abdominal and pelvic tumors, effectively reducing radiation dose while maintaining image and dosimetric quality.[19]

Zhu et al. (2025) investigated the integration of electronic portal imaging device (EPID)–based in vivo dose validation with fan-beam CT (FBCT) guidance on a CT-LINAC system (uRT-linac 506c) in 26 patients with early-stage breast cancer undergoing postoperative breast-conserving radiotherapy. Image-guided radiotherapy (IGRT) significantly improved γ-pass rates compared to non-IGRT ($p < 0.05$). Further improvement was seen in the FBCT group compared to IGRT (specifically at the 5%/3 mm level, $p < 0.05$). Additionally, inter- and intra-fractional variations significantly affected dose distributions in regions like PGTV D95, PTV D95, heart Dmean/V5, and lung V5 (all $p < 0.05$). The authors concluded that EPID in-vivo dose validation combined with FBCT guidance offers precise real-time dose evaluation, with superior accuracy versus conventional methods.[20]

## SAFETY

Some CT LINAC have obtained regulatory approval such as [redacted][8].

A phase III randomised clinical trial (the MIRAGE trial) was conducted to compare magnetic resonance imaging (MRI)-guided stereotactic body radiotherapy (SBRT) with computed tomography (CT)-guided SBRT for the treatment of clinically localised prostate adenocarcinoma. The primary objective was to assess whether a more aggressive margin reduction using MRI guidance could significantly reduce acute genitourinary (GU) toxic effects of grade 2 or higher, as compared to CT guidance. The results showed that the incidence of acute grade 2 or greater GU toxic effects was significantly lower in the MRI group (24.4%) compared to the CT group (43.4%) ($p=0.01$). Acute grade 2 or greater gastrointestinal (GI) toxic effects were also significantly reduced with MRI guidance (0.0%) versus CT guidance (10.5%) ($p=0.003$). Patient-reported outcomes also favored the MRI-guided approach. At one month, a significantly smaller percentage of patients in the MRI group (6.8%) reported a clinically relevant increase in their IPSS compared to the CT group (19.4%) ($p=0.01$). Additionally, a significantly lower percentage of MRI patients (25.0%) experienced a clinically significant decrease in EPIC-26 bowel scores at one month compared to CT patients (50.0%) ($p=0.001$). The authors concluded that MRI-guided SBRT substantially reduced acute physician-scored toxic effects and patient-reported quality-of-life decrements. They also noted that longer-term follow-up is needed to determine if these benefits persist.[21]

A phase III randomised trial (Postoperative Adjuvant Radiation in Cervical Cancer, PARCER TRIAL), compared late toxicity after image-guided intensity-modulated radiotherapy (IG-IMRT) with three-dimensional conformal radiation therapy (3D-CRT) in women with cervical cancer undergoing postoperative radiation. Three hundred patients were randomly assigned to receive either IG-IMRT (n= 151) or 3D-CRT (n=149) after stratification for the type of hysterectomy and use of concurrent chemotherapy. The primary end point was 3-year grade ≥ 2 late GI toxicity assessed using Common Toxicity Criteria for Adverse Events v 3.0 and estimated using time-to-event, intention-to-treat analysis. The median follow up was 46 months. The result showed that the 3-year cumulative incidence of grade more than 2 late GI toxicity in the IG-IMRT and 3D-CRT arms were 21.1% versus 42.4% (hazard ratio [HR] 0.46; 95% CI: 0.29 to 0.73; $p < 0.001$). The cumulative incidence of grade more than 2 any late toxicity was 28.1% versus 48.9% (HR 0.50; 95% CI: 0.33 to 0.76; $p < 0.001$), respectively. Patients reported reduced diarrhoea ($p = 0.04$), improved appetite ($p = 0.008$), and lesser bowel symptoms ($p = 0.002$) with IG-IMRT. However, no difference was observed in the time by treatment interaction. The 3-year pelvic relapse-free survival and disease-free survival in the IG-IMRT versus the 3D-CRT arm were 81.8% versus 84% (HR 1.17; 95% CI: 0.68 to 1.99; $p = 0.55$) and 76.9% versus 81.2% (HR 1.03; 95% CI: 0.62 to 1.71; $p = 0.89$), respectively.[22]

An observational study was conducted by Guberina et. al comparing online adaptive Intensity-Modulated Radiation Therapy (IMRT) or Volumetric-Modulated Arc Radiotherapy versus image-guided radiotherapy (IGRT) involving seven consecutive patients with gynaecologic tumour at the West German Cancer Center. Six patients have already received their first follow-up examination (4 of 7 patients who received the ART course and both patients who received the IGRT course). The median monitoring period of these patients was114.8 days(range, 104 to 133 days), with no toxic effects reported.[11]

According to feasibility study by Ababneh HS et al (2025) evaluating CT-based adaptive bridging radiation therapy (ABRT) using CT-LINAC (Varian Ethos) involving ten relapsed or refractory large B cell lymphoma patients before CAR-T treatment. Patients were given once weekly, computed tomography-based adaptive radiation therapy at a dose of 5 Gy per fraction for up to 5 fractions over 5 weeks. Among all 10 patients, 3 experienced in-field recurrence after start date of BRT. Among those with immune effector cell-associated neurotoxicity syndrome (n = 6), grade 3 immune effector cell-associated neurotoxicity syndrome occurred in 50% (n = 3). No grade 3 or higher cytokine release syndrome events were reported. At the time of the last follow-up, 9 patients (90%) were still alive, and 1 patient (10%) died due to disease progression.[18]

A risk assessment study using Failure Mode and Effect Analysis (FMEA) identified potential hazards in all-in-one (AIO) workflows and proposed mitigation strategies to strengthen clinical safety. In addition, a case report of CT-based oART in NPC confirmed that daily adaptive planning was feasible, improved coverage, and was delivered safely without acute toxicities.[23]

## COST/COST-EFFECTIVENESS (If any)

There was very limited evidence retrieved on cost-effectiveness of CT-LINAC. The sale price of a CT LINAC machine ranges from [redacted].[24]

A cost evaluation study by Parikh et al. (2021) compared the cost of CT-guided versus MR-guided stereotactic body radiotherapy (SBRT) for prostate cancer using a time-driven activity-based costing (TDABC) approach. By mapping the workflow, personnel time, and equipment utilisation, the direct costs for a 5-fraction course of prostate SBRT were found to be USD1,497

(MYR 6287) (1USD = 4.20MYR) higher with MR-imaging-guided radiation therapy (MRgRT) compared to computed-tomography-guided radiation therapy (CTgRT), mainly due to a $1,542 (MYR 6476) increase in space and equipment costs for MRgRT. The higher costs associated with MR-guided SBRT were largely attributable to longer treatment times, increased personnel involvement, and reliance on specialised MRI-linac technology. While MR-guided SBRT may provide clinical advantages such as improved soft tissue visualisation and the potential for adaptive planning, these benefits came at a significant cost premium. The authors concluded that CT-guided SBRT offers a more favorable cost profile and may be considered more cost-effective from an institutional perspective, unless the added clinical benefits of MR guidance can be shown to improve patient outcomes in a way that justifies the additional expense.[25]

Hande et al. (2024) analysed the longitudinal costs of image-guided intensity-modulated radiotherapy (IG-IMRT) compared with three-dimensional conformal radiotherapy (3D-CRT) in the Phase III PARCER trial, which evaluated treatment of locally advanced cervical cancer in an Indian setting. The study assessed direct medical costs, including radiation delivery, imaging, and management of treatment-related toxicities over the long term. The analysis showed the sum of average costs of toxicity management in the 3D-CRT and IG-IMRT arms were 1,926,753.94 INR (RM 91,172; 100 INR = 4.73 MYR) and 1,287,595.57 INR (RM60928.22), respectively, indicating a 1.50 times higher average toxicity-related cost burden for 3D-CRT patients. From longitudinal follow-up data and morbidity management, the average yearly financial impact per patient developing GI or GU toxicity of grade more than 2 was 2,124,336.44 INR (RM100522) in the 3D-CRT arm and 1,473,625.57 INR (RM69731) in the IG-IMRT arm, providing a ratio of 1.44:1.00. The author concluded that although the initial cost of IG-IMRT is higher, this is eventually recovered over time through reduced toxicity interventions, compared with 3D-CRT. Over a longer time frame, investing in high-precision technology for managing cervical cancer would result in lower costs for health policymakers.[26]

## CONCLUSION

Based on the review conducted, limited evidences retrieved demonstrated that integrated CT-LINAC shows promising potential in enhancing the precision and adaptability of radiotherapy across multiple cancer types. Current studies, including randomised controlled trials, observational studies, and feasibility assessments, suggest that CT-LINAC offers dosimetric advantages, particularly through adaptive radiotherapy approaches, leading to improved tumour coverage and sparing of organs at risk without compromising treatment efficacy. The evidence also indicates stability and accuracy in dose delivery, supporting its role in ensuring treatment reliability. Safety outcomes from comparative and feasibility trials highlight reduced acute and late toxicities with image-guided and adaptive techniques compared to conventional radiotherapy, thereby improving patient-reported quality of life. While short-term data support the tolerability of CT-LINAC-based treatments, longer-term follow-up is still required to establish sustained safety benefits. From an economic perspective, the current literature is limited but suggests that although initial investment and operational costs may be higher, CT-guided techniques may offer long-term cost savings through reduced toxicity-related interventions, particularly when compared with older conformal techniques. Overall, integrated CT-LINAC appears to be an effective, with acceptable safety profile, and potentially costsaving, however further high-quality trials with long-term clinical and economic outcomes are essential to guide its wider adoption.

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