Adaptive MV portal imaging for head and neck cancer, a model for countries with limited resources

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Abstract:

Background: Setup error had a considerable effect on treatment-related uncertainty in head and neck cancer. Through this study, we examine adaptive setup verification protocol using MV portal imaging in these patients.

Methods: A prospective phase 2 trial was conducted on 55 patients with advanced head and neck cancer from 2018 till 2021. Patients received intensity-modulated radiotherapy using Varian© RapidArc. Online verification was done, and setup error data were used to direct the frequencies of verification events. One-year local failure representing geometrical miss and overall local control were calculated. Patients' setup accuracy data were collected, analysed and used for calculation of the overall mean displacement (M), the population systematic (∑), random (σ) errors and the van Herk formula (2.5 ∑ + 0.7 σ) for PTV margin estimation. Local control where explored based on the frequency of setup events.

Results: A total of 55 patients between 2018 and 2020, with 678 setup events and 1356 Portal Vision verifications, were included in this study. Half of the patients experienced reduced frequency of setup verifications, while 25.4% required increased setup frequency. The 12-month RT field border failure rate was 3.6%. The 12-month control rate of all patients was 74.5%; it was 69.2%, 76%, 76.9% for patients with increased, reduced and non-changed setup frequency. The PTV margins were 3.5, 4.6, and 3.8 mm for vertical, lateral, and longitudinal axes, respectively.

Conclusion: Despite the lack of CBCT imaging, adaptive megavoltage PortalVision™ verification was effective in evaluation setup accuracy in head and neck cancer patients.

Keywords: Set up verification, KV portal vision head and neck cancer, set up error, head and neck cancer.

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Introduction:

Head and neck cancer are always challenging. The proximity to critical organs and the necessity to delivering a high dose to the tumours mandated the extreme cautions for setup error quantification in every local radiotherapy unit [1]. Several studies have pointed to the hazards of geometrical miss secondary to setup error. The calculated magnitude of loss in tumour control probability aggravated enormously when VMAT therapy was used instead of IMRT [2]. MV CBCT failed to show any additional benefit compared to two-dimensional MV portal imaging [3].

In contrast, KV imaging allowed easier and better setup verification compared to MV imaging. In addition, KV imaging harbours a better tissue contrasting, subsequently reducing the interobserver

variability. Therefore, the current practice depends on routine KV CBCT and KV portal imaging to verify setup and guide systemic corrections whenever necessary [5]. Unfortunately, KV imaging (two-dimensional or CBCT) is not always available in many medical care services working in low-socioeconomic countries. This usually leaves other methods such as online MV portal imaging as the best way to evaluate setup errors and patient positioning. This trial examines the feasibility of using adaptive verification for patients with advanced head and neck cancer.

Patients and Methods:

Study design

We conducted a phase two study on 55 patients with head and neck cancer between 2018 and 2020. The study evaluated the feasibility of using MV portal imaging in adaptive verification and its impact on the risk of geometrical miss and tumour control. The study was a part of a larger project that currently evaluates the feasibility and outcome of using intensity-modulated therapy in different head and neck cancer.

Patient and tumour characteristics

A total of 55 patients with different head and neck cancers have participated in this study. The majority of patients were laryngeal squamous cell carcinoma (41.8%). Concurrent chemotherapy was offered to 83.6% of the participants (Table 01).

Radiotherapy techniques

Patients led down supine and immobilised with head and shoulder thermoplastic immobilisation system (Klarity©, R461ST White S-Type, 42% perforation, 3.2mm) and patients were scanned without contrast by CT simulator for 3 mm slice thickness. The scan started from the vertex to the level of the carina. For patients planned to receive RT to upper mediastinal nodes, the scan level reached below the diaphragm. Varian © ARIA 13.6 version was used for target contouring and treatment planning. RapidArc plans were calculated using two 360 degrees arcs, a single isocenter, and energy of 6 MeV. One-plan VMAT was adapted where the prescribed dose of 70Gy in 35 fractions was delivered to gross disease, while high risk and low-risk areas for subclinical disease received 64Gy/35 fractions and 54Gy/35 fractions, respectively. All plans were optimised and normalised, where 98% of the volumes received at least 95% of the prescribed dose. Digital reconstructed radiographs were calculated using the following parameter (HU -16.0 – 126.0, weight 2.0 and HU 10.0 – 1000, weight 10.0). This allowed enhanced bone visualisation on a light background for soft tissue. All plans were verified by OCTAVIUS® 4D phantom and underwent 3D Gamma Volume Analysis before the approval of starting radiotherapy.

Image-guided radiotherapy

Set-up verification protocol depended on obtaining MV portal images for the initial two fractions, then twice weekly for every patient. The images were taken only after properly positioning the patients and aligning the in-room lasers on the marks drawn on the thermoplastic meshes. Afterwards, the verification was initiated by capturing two images for every setup event, taken at 0oand 270o. Usually, every patient would have 14 setups events (28 images). Each image was taken by exposing the patient, at plan isocenter, to an open-field of 30 x 30 mm to a dose of 1 motor unit. Thus, the exposures would add additional 24 MU all over the course and increase the dose delivered to the plan isocenter and all nearly exposed organs by roughly 24 cGy (0.34% of the prescription dose). Setup corrections were made before treatment if the error was more significant than 2 mm in any direction (Fig 1, 2, and 3).

If the mid-weekly verification should be acceptable setup positioning, the frequency of capturing portal images was reduced to weekly upon the third, fifth, sixth and seventh week (Fig 1). On the other hand, if the setup verification showed concerning signs of significant systemic error ≥ 4 in one direction, the patient was treated, and additional setup events would be initiated the next day. If significant errors were persistent in the following setups, a discussion was brought up with the clinical oncology team for restimulating the patient again with a more fitting thermoplastic mesh.

The outcome of this study

The primary endpoint was disease failure due to geometrical miss. A geometric miss was defined as a persistent or newly developed disease at or within 5 mm from the radiotherapy field border. Secondary endpoints were disease control at 12 months. The setup-error data were collected from every setup event and were used to calculate the means and the standard deviations for errors for every patient. The resulting data were later reused in van Herk's formula to calculate the necessary PTV margins ($M = 2.5 \sum + 0.7 \sigma$) to fulfil the assumption of covering the CTV by at least 95% of the dose in 90% of the patients 6.

Statistical analysis

For each setup event, the errors were extracted and analysed individually for each direction (X, Y, Z). Afterwards, the mean and standard deviation (SD) of the recorded errors were calculated separately for each patient. Next, the overall mean ($\sum$) of systemic errors for all patients' datasets was calculated. Then, the overall SD (σ) was calculated by taking root mean square of the individual patient's SD. Finally, the CTV to PTV margin using van Herk formula ($2.5\sum + 0.7 \sigma$).

Ethical approval

The study was conduction following approval by the university hospital ethical committee and was registered in the local research committee in the Faculty of Medicine. Detailed informed consents were obtained from all participating patients in this study.

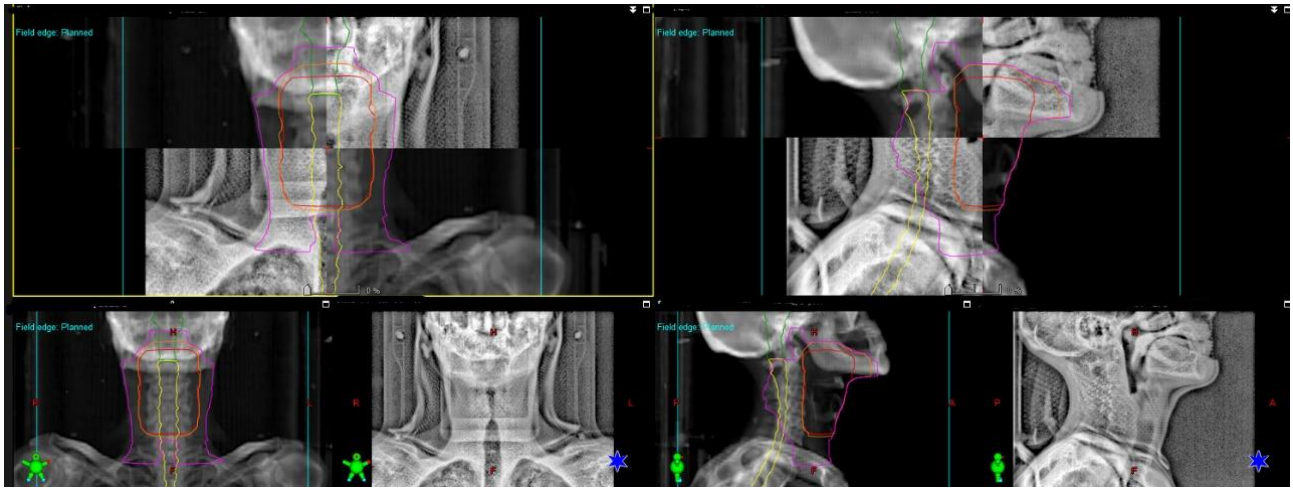

Figure 1 - AP and Lat setup image for a boy with submandibular high grade mucoepidermoid carcinoma. Red structure outlining the operative bed (60Gy) and the orange structure for high-risk nodes (56Gy). Spinal canal is outlined in yellow.

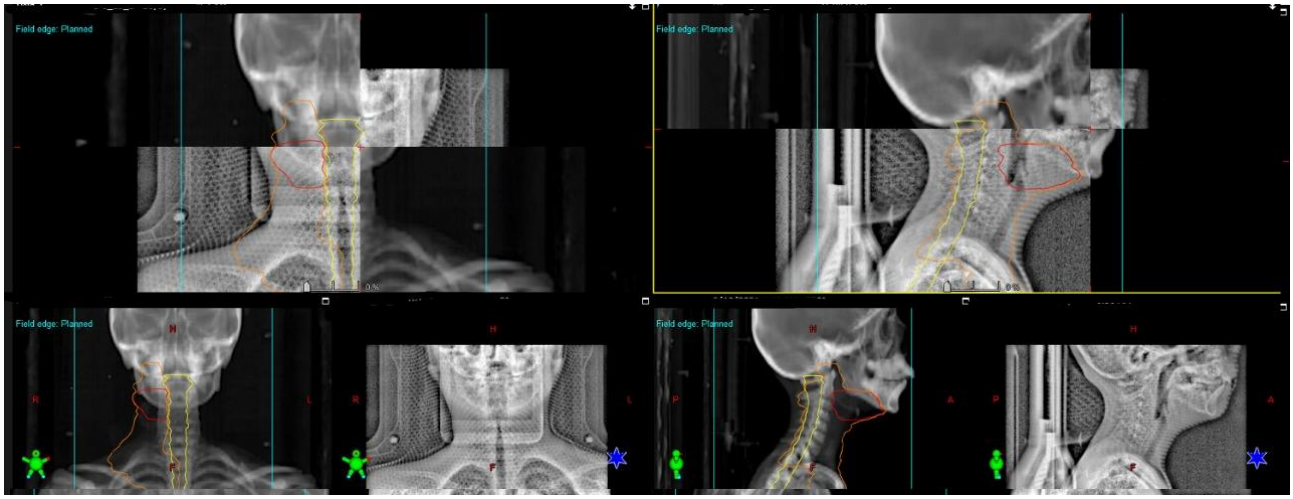

Figure 2 - AP and Lat setup image for a lady with advanced irresectable oral cavity cancer. The GTVp, PTV70Gy and PTV 56Gy were outlined as blue, red and orange, respectively. Notice the tongue bite fixaor system (Klarity BiteLok® for fixating the tongue downward).

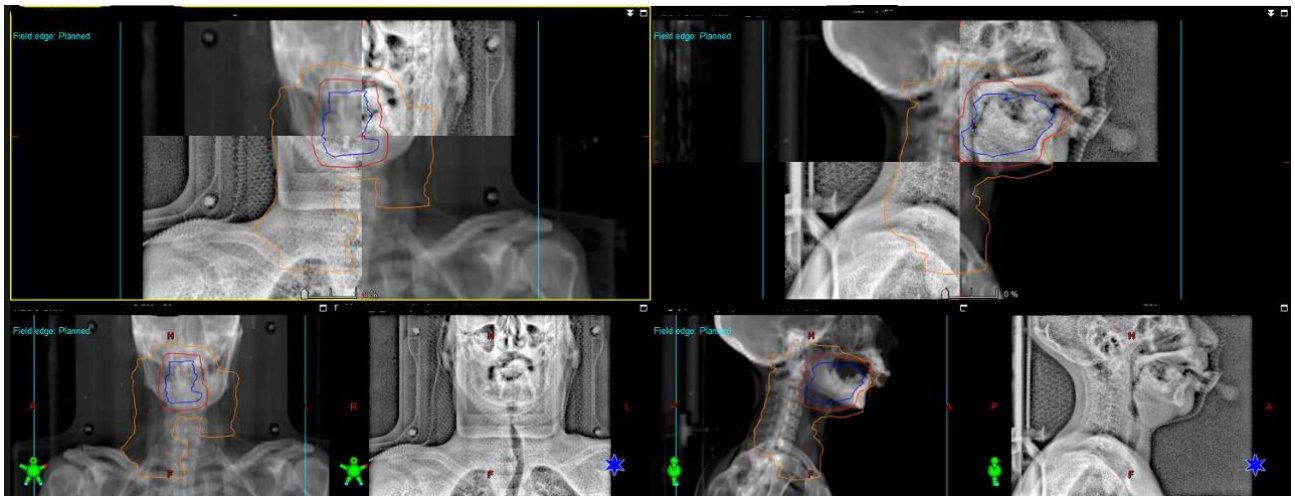

Figure 3 – AP and Lat setup image for a gentleman with advanced glottic and supraglottic disease. The PTV 70Gy, PTV 63Gy and PTV 56Gy were outlined in red, orange and magenta, respectively. The spinal canal was outlined in yellow.

Results:

A total of 55 patients were included in this study, with 678 setup events and 1356 setup images. Twenty-eight (50.9%) patients had positioning errors within 2 mm within the first two weeks of therapy and underwent reduced setup frequency over the next five weeks of treatment. Fourteen (25.5%) patients experienced setup errors 4 mm or more within the first two weeks of treatment, and increasing setup events were necessary. The remaining 13 patients had an average setup error of 3 mm and stayed on the biweekly verification setup schedule. No correlation was found between the disease site and the need to increase the frequency of setup events (chi-square P = 0.41, Table 01). Based on van Herk's formula, the PTV margins were 3.5, 4.6, 3.8 mm for vertical, lateral and longitudinal axes, respectively.

Radiotherapy field-boarder relapse was observed in two patients with a 12-month geometrical miss related-failure rate of 3.6% (Fig 4). In contrast, 13 patients suffered from persistent disease at 12 months with a 12-month control rate of 74.5%. The local control rate was 69.2%, 76%, 76.9% for patients with increased, reduced and biweekly setup events, respectively (Fig 5).

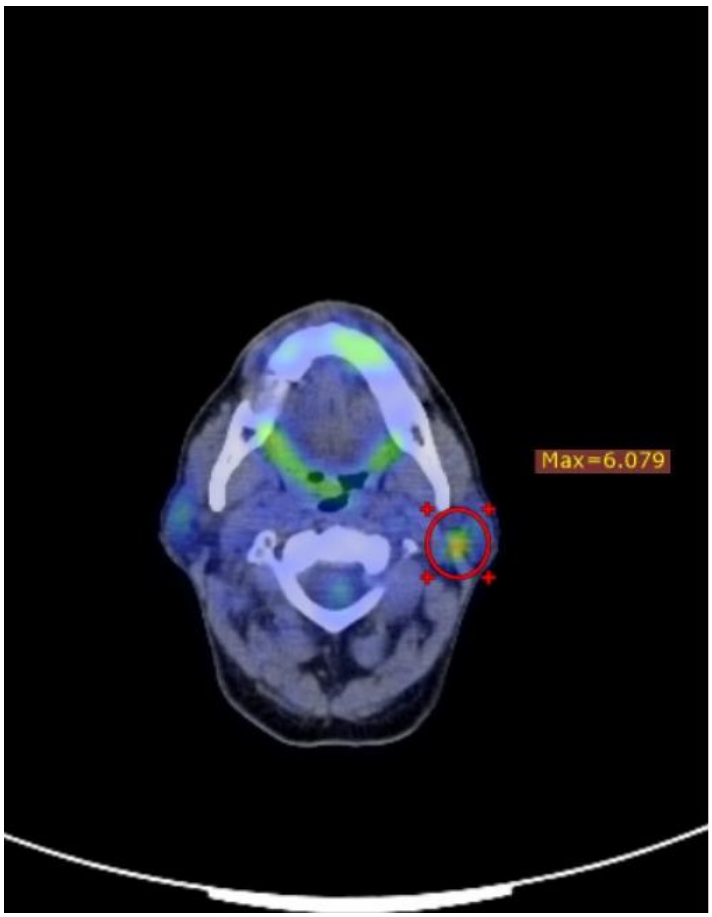

Figure 4 – Positive chemoradiation PET CT showing a positive node at outer boarder of left level II representing a geometrical miss at radiotherapy field boarder. Patient was salvaged by lymph node dissection and after 6 months FU, he is free of disease.

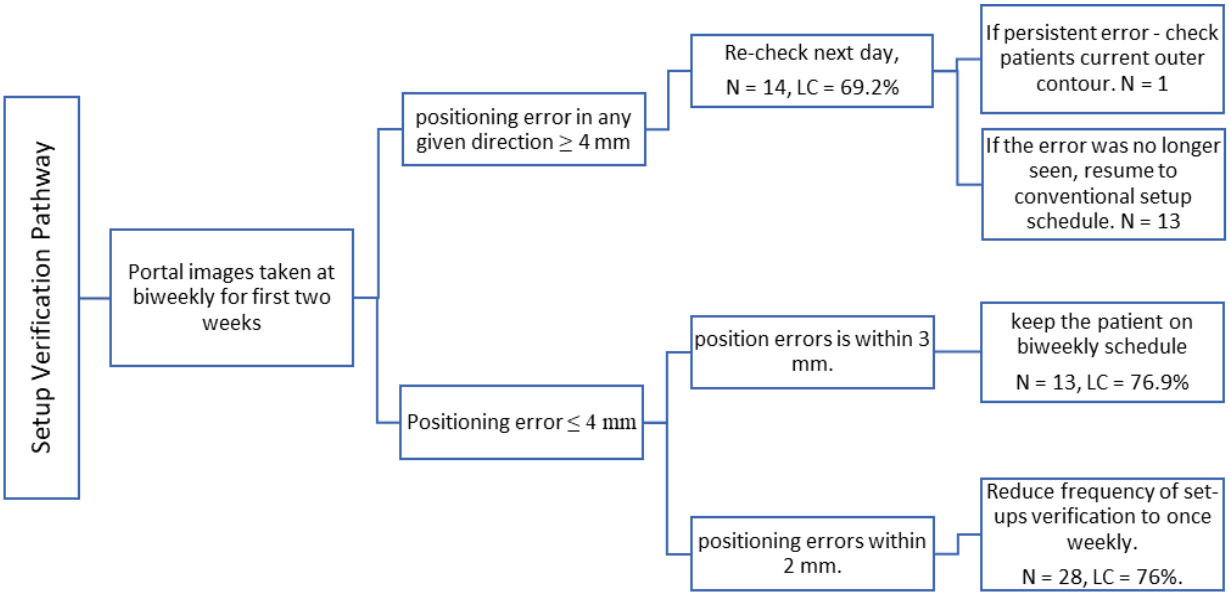

Figure 5 – Flow chart of adaptive setup verification based on initial error seen in first weeks of therapy along with related local control rates.

Table 1 – Disease site * Verification schedule Freq Crosstabulation

			Verification schedule Freq			
			Increased	Reduced	Standard	Total
Tumor	Larynx	41.8%	5	12	6	23
	Hypopharynx	3.6%	2	0	0	2
	PNS	7.1%	0	2	1	3
	Oral Cavity	18.18%	3	6	1	10
	Nasopharynx	21.8%	2	6	4	12
	Oropharynx	3.6%	0	1	1	2
	Occult nodes	1.8%	1	0	0	1
	Salivary Glands	3.6%	1	1	0	2
Total			14	28	13	55

Discussion:

Intensity-modulated radiation therapy facilitated the delivery of high dose radiation to the tumour and reduced collateral damage to the organ at risk. Several studies pointed to the benefit of improving long-term xerostomia and swallowing with IMRT/VMAT compared to 3D conformal radiotherapy [7]. However, IMRT harbours a significant risk of geometrical miss, especially at the field edge [8.] Monte Carlo simulation for the impact of the geometrical miss on dose coverage and tumour control probability founds that magnitude of impact aggravates extensively with the complexity of the techniques, such as VMAT [2]. Therefore, modern practice depends on advanced setup verifications such as KV CBCT, especially in head and neck cancer [5].

Unfortunately, access to sophisticated linear accelerators with elite verification systems is not always possible. For example, a recent survey by International

Atomic Energy Agency found that there were only 430 megavoltage accelerators in the African continent with megavoltage units per million as low as 0.02 [9]. In addition, the scarcity of the service and lack of financial resources forced oncology departments in emerging healthcare systems to relay to low-line linear accelerators that do not pose the functionality of CBCT verification, as seen in the majority of linear accelerators in Egypt [10]. Moreover, the acquisition of CBCT is time-consuming and routine use is not always suitable to busy departments, especially in countries with limited resources and a low number of megavoltage units per million [11].

This prospective study aims to provide a small prospective phase 2 cohort of 55 patients with different head and neck cancer. We tested adaptive verification of protocol that depended on the Megavoltage portal image. Each patient was individually assessed and had a more personalised setup verification protocol. Suppose the seen setup error was ≤ 2 mm, we initiate a more reduced frequent verification, one setup event every week using MV portal image. If the setup errors exceeded 4 mm, the frequencies of setup events were increased to adapt for the increased error. Otherwise, the patients continued the biweekly verifications till the end of the radiotherapy course. In this study, roughly half of the patients had acceptable errors within the 2 mm tolerance and experienced a reduced frequency of setup events. The adaptive setup verification was associated with an acceptable local control rate of 74.5% at 12 months for the entire population. The rates were similar between the increased, reduced, and same frequency arms (69.2%, 76%, 76.9%, respectively), comparable to the published loco-regional control rate in head and neck cancer [12].

Conclusion:

Adaptive MV portal imaging using EPID is an effective way to evaluate setup errors and head and neck cancer patients and is suitable for departments with busy schedules or without access to sophisticated verification equipment resources.

List of abbreviations

VMAT, volumetric modulated arc therapy.
IMRT, intensity-modulated radiation therapy.
CBCT, Cone beam computed tomograph.
MV, Mega-Voltage.
GTV, gross tumour volume.
PTV, planned tumour volume.
CTV, clinical target volume.
3D, three-dimensional.
EPID, electronic portal imaging device.

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