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Original Research Article

Early Tumour Response for Cervical Cancer Patients with Anteroposterior Separation Greater than 21cm Treated using a Four-Field Technique on Cobalt Teletherapy

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Abstract: ***Introduction*****:** Treatment of locally advanced cervical cancer requires the use of radiotherapy. The tumour response rate measured midway through radiotherapy provides valuable prognostic information. This study sought to document the dose distribution and early tumor response in patients treated with cobalt teletherapy at Cancer Diseases Hospital (CDH). The objective was to determine the effectiveness of Cobalt Teletherapy in the treatment of cervical cancer patients at CDH with an anteroposterior separation of 21 cm and above using the four-field technique. ***Methodology*****:** The study employed a cross-sectional design. Population was patient treatment files. All files fitting the criteria were included. Dose distribution and treatment response assessment data was retrieved and analysed. Descriptive and inferential statistics were run for the analysis. ***Results*****:** There was a significant association between tumour size, the level of haemoglobin, and the number of fractions received during External Beam Radiotherapy (EBRT) ($p<0.001$), before and after treatment. An increase in the number of fractions received during EBRT and an increase in the level of haemoglobin resulted in the tumour size reduction. No significant association was seen between tumour size and Anterior Posterior (AP) separation, Age, Dose to the 95% isodose line ($p>0.05$). Other factors not significantly associated with tumour size reduction include Parity HIV status, Performance status, Average radiation dose, field size, number of chemotherapy circles, chemotherapy type. ***Conclusion*****:** There is contextual evidence that tumour can reduce in size with an increase in number of fractions received during EBRT and level of haemoglobin. AP separation, Age, Parity, HIV status, Performance status, Average radiation dose, field size, number of chemotherapy circles, chemotherapy type, and Dose to the 95% isodose line did not show any effect on cervical tumour size ($p>0.05$).

Keywords: Cervical Cancer, Separation, Cobalt Teletherapy, Dose To 95% Isodose Line.

INTRODUCTION

Worldwide, cervical cancer is the fourth most frequent cancer in women, with an estimated 604,000 new cases in 2020, (Stelze *et al*., 2020). About 90% of deaths occur in low and middle-income countries (Globocan, 2022). The management of locally advanced cervical cancer requires the use of both external beam radiotherapy and brachytherapy. This is premised on an acceptable dose distribution (Faye and Alferi, 2022).

Radiation dose distribution refers to the arrangement of radiation doses in a target area during treatment using appropriate energies and techniques (Akram *et al*., 2020). Higher-energy beams (above 4 MV) offer the possibility of using a modulated dose rate, thus making it easier to conform to the tumor while sparing healthy organs at risk (Healy *et al*., 2017). The use of such beam energies are deemed appropriate for treating deep-seated tumours (anteroposterior separation greater than 21 cm) (Healy *et al*., 2017).

Radiotherapy services at the Cancer Diseases Hospital were established in 2006, by 2022 the equipment had become obsolete, the study used data for 2021 (collected during LINAC breakdowns). Patients presenting to Cancer Diseases Hospital (CDH) for cervical cancer treatment usually present with locally advanced cervical cancer (LACC) (Rongyi *et al*., 2024).

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CDH has protocols for selecting patients to be treated either with Cobalt 60 (Co60) teletherapy unit or Linear accelerator (LINAC). The protocol prescribes that cervical cancer patients with an Anteroposterior (AP) separation (the thickness of the patient's pelvis from the anterior aspect to the posterior aspect [Scott *et al*., 2021]), of 21 cm or less and a lateral separation (the pelvic thickness measured from either the left or right aspect [Scott *et al*., 2021]) of 34 cm should be planned and treated with Co60 unit. Patients with AP separation greater than 21 cm or lateral separation greater than 34 cm supposed to be treated with LINAC (beam energy greater than 4MV). However, during the breakdown of the LINAC, patients with AP separation greater than 21 cm or lateral separation greater than 34 cm are treated using the Co60 to avoid treatment breaks using the four-field technique. Deviating from standard protocol requires that efficacy of alternative protocol is justified by documenting the radiation dose distribution, analyse the dose volume histograms (DVHs) for the re-planned treatment plans, and record early tumor regression in this group of patients. Studies have demonstrated that evaluating tumour response at the time of the first brachytherapy session (during the fifth week of treatment) or after 20 Gy of EBRT (Suneja *et al*., 2017., Kang *et al*., 2020) provides useful prognostic information.

The objective of this study therefore was to determine the effectiveness of Co60 Teletherapy treatment in managing cervical cancer patients at CDH with AP separation of 21 cm or lateral separation of 34 cm or more using the four-field technique.

METHODOLOGY

Study Design

This study utilised a quantitative cross-sectional study. Retrospective patient's information from files and radiotherapy treatment planning data was employed to investigate that effectiveness of Co60 teletherapy treatment.

Study Site

The study was conducted at CDH, Lusaka, Zambia. This setting was selected because at the time of data collection, it was the only hospital in Zambia with a radiotherapy department.

Population and Sampling

The study population included all patient data files for cervical cancer patients treated with radiotherapy at CDH whose radiotherapy planning data was on the radiotherapy treatment planning system (TPS). A census approach was utilised because of the limited population size (N=74). The study eligibility criteria were all cervical cancer treatment plans and patient case files with radical intent, prescribed with 50Gy in 25 fractions and four field techniques, separation of AP 21cm lateral 34cm and above, patients who had received weekly chemotherapy, histology of squamous cell carcinoma and Stage IB3-IVA and case files with CT image data. CT image data was used for treatment planning. The exclusion criteria were patient data files for patients with parallel opposed beam arrangement (AP Posteroanterior [PA]) techniques, extended fields (para-aortic fields), and history of total abdominal hysterectomy (TAH).

Data Collection Process

Treatment plans that fitted the inclusion criteria were identified from the patient treatment registers for 2021. This was followed by identifying the treatment plans from the TPS. The isodose distribution and the Dose Volume Histogram (DVH) were then analysed. From the DVH, the following were recorded: minimum and maximum dose to the Planning Target Volume (PTV), mean dose to the PTV, and dose to the 95% isodose. Additional information from the patient files includes anthropological measurements (AP and lateral separations), field size, and Dosimetric parameters.

Patient files were reviewed to document the tumours size at two (2) time points (At start of EBRT and at first brachytherapy application [usually at four to five weeks post start of EBRT]). A comparison of these tumour sizes and calculation of the percentage reduction was then performed. This was calculated by dividing the tumor size after treatment (T2) by the tumour size before treatment (T1), then multiplying by 100% and subtracting the result from 100% ([T2/T1 X 100%]-100%).

Data Management and Analysis

Data was transferred from the hardcopy collection tools, cleaned and stored in an Excel sheet. Continuous data was analysed for normality using the Shapiro-Wilk test (with significance set at 0.05). Measures of central tendency and dispersion were used to summarise the continuous data. Categorical data was summarised as frequencies and percentages. To assess if there was any significant difference among the independent variables, a bivariate analysis using Spearman's correlation was performed. Furthermore, to establish the relationship between dependent and independent variables, a linear regression was performed. Statistical analysis was performed using GraphPad Prism version 8.0.1(244) and Stata version 16.0.

Ethical Considerations

Ethical approval was obtained from the University of Zambia Ethics Committee, UNZABREC (REF: 4176- 2023), and the National Health Research Authority (NHRA) (NHRAR-R-353/08/05/2023). Authority was further sought from CDH, ethics committee (RER: MH/CDH/101/14/1).

RESULTS

In this study the demographic characteristics of the participants from the patient files are summarised in

table 1. The continuous data was not normally distributed (p values were all less than 0.05). The median age was 54 years (IQR 43-61). The youngest participant was 28 years old while the oldest was 77 years. The median parity was 4, IQR 3-5. Most of the cervical cancer patients were HIV positive 40 (53%). Most of the patients had performance status of Eastern Cooperative Oncology Group 1, (ECOG) (N=72; 94.7%).

Table 1: Demographic Characteristics

Age		**Median 54 (IQR, 43-61)**
Parity		**Median 4 (IQR, 3-5)**
HIV Status	**Positive**	**40 (53%)**
	Negative	**35 (46%)**
Performance Status	**ECOG 1**	**72 (94.7%)**
	ECOG 2	**2 (5.3%)**

Anthropological and Dosimetry Measurements

The median AP separation was 21, IQR 19.56 – 23.14). The median dose to 95% isodose line was 47.26, IQR. The other anthropological and Dosimetry Measurements are shown in table 2 below.

Table 2: Anthropological and Dosimetry Measurements

Measurement		
Category	**Specific**	**Median (IQR)**
Anthropological	Anterior-posterior separation (cm)	21 (19.56-23.14)
	Lateral separation (cm)	27.52 (30.89 -35.61)
	Area (AP x Lateral separation [cm^2])	711 (616.8-825)
	Field size area (cm^2)	475 (430.7 -525)
	Lateral field size (cm^2)	422.5 (368-417)
Dosimetry	Dose to 95% isodose line (Gy)	47.26 (46.26 – 47.89)
	Mean Dose (Gy)	50 (49 -50)

Comparison of Tumor Size before and After Treatment

There was a significant difference between the tumour size before treatment (T1) (Median 19 cm, IQR 3- 48) and tumour size after treatment (T2) (Median 4cm, IQR 0-30), p< 0.0001.

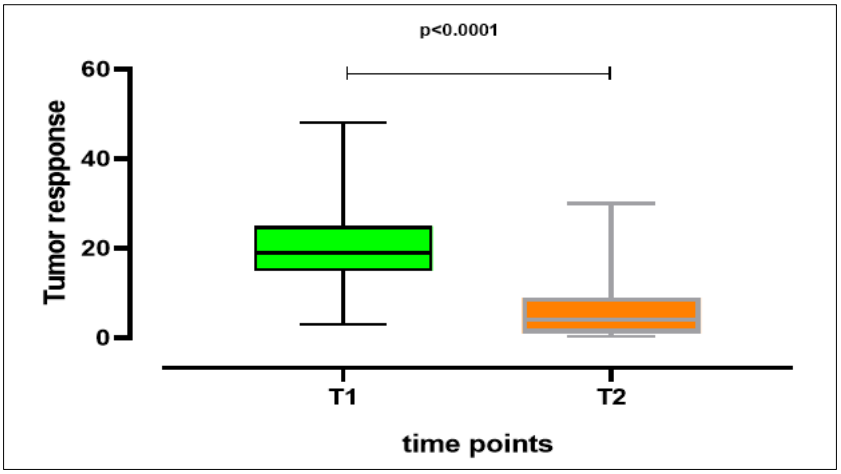

Figure 1: Comparison of tumour size before (T1) and after treatment (T2)

Relationship between Percentage Reduction in Tumour size and Age, HIV Status, Tumour Stage, Fractions, Heamoglobin, AP x Lateral Separation, Field size Area, Dose to the 95% Isodose Line and Mean Dose

A relationship between Percentage Reduction in tumour size and Age, stage, HIV status, Fractions, Heamoglobin, AP x lateral separation, Field size Area, Dose to the 95% isodose line and the mean dose are shown in table 3. There was a significant association between the percentage reduction in tumor size and the level of heamoglobin after radiotherapy (t=3.44, p=0.001), and the number of fractions received during radiotherapy (t=2.23, p=0.0029). An increase of one-unit change in heamoglobin resulted in a 4. 63g/l change in reduction of tumor size, holding other variables constant**.** An increase of one unit in the number of fractions received (treatment sessions) by the tumor also resulted

in 3.064 cm of tumor size reduction, holding other variables constant.

Table 3: Relationship between Percentage reduction in tumour size and Age, HIV status, Tumour stage, Fractions, Heamoglobin, AP x Lateral separation, Field size Area, Dose to the 95% isodose line and Mean dose

Model	Coefficient	P-value	95.0% Confidence Interval
Age	.2908198	0.081	-.0651735
Stage	4.814453	0.311	-14.5338
HIV status	5.758665	0.239	-4.666541
Fractions	1.373048	**0.029**	.3212763
Heamoglobin	1.346452	**0.001**	1.940252
AP X LAT	.0184182	0.779	-.0316065
Field size Area	.000055	0.142	-.0001918
Dose 95%	2.130634	0.791	-.0741639
Mean Dose	.054325	0.529	-3690024
(Constant)	103.3084	0.413	-291.5361

DISCUSSION

In this study the demographic characteristics included age, parity status, and HIV status. ECOG 1, though not a risk factor for cervical cancer, in this study, it has been classified as such. This is because, it evaluates the patients' functional status. The risk of cervical cancer has been shown to increase with an increase in patients age, parity, HIV positive patients with lower immunities (Coghill *et al*., 2013). In this study, age of patients at diagnosis was comparable with global trends which place the average age at presentation to be 53 years (Globocan 2022). This is also in keeping with trends in sub-Saharan countries where the average age at presentation of cervical cancer is 53.4 years (Mazvita *et al*., 2020). HIV among cervical cancer patients affects outcomes and may be poorer for women with HIV (Coghill *et al*., 2013). This study found that most of the patients were HIV positive (40; 53%) compared to those who were HIV negative (35; 46.6%). This is also in-keeping with, both global and regional trends. About 5.8% of all new cervical cancer cases worldwide in the year 2018 were diagnosed in women infected with HIV (Stelle *et al*., 2020). This is equivalent to 33,000 new cases per year, 85% of which occurred in women in sub-Saharan Africa (Stelle *et al*., 2020).

To evaluate cervical tumour response, there is need to examine how certain radiotherapy treatment factors influence this response. In this study, some of the radiotherapy treatment response factors include hypoxia and fractionation of radiotherapy. Hypoxia impacts the parameters governing the radiotherapy tumour response (Rakotomalala *et al*., 2021). This is an important predictor of poor clinical outcome to radiotherapy treatment. It indicates that a patient needs to have a high heamoglobin level for tumour response to be effective (Claire *et al*., 2024). The correlation between haemoglobin and tumour response is biologically driven by the oxygen enhancement ratio (OER) where oxygen causes radiation – induced DNA damage making oxygenated tumors more sensitive to therapy (Huang *et al*., 2024). This study's Median heamoglobin was 10.5g/l, IQR 2 – 14.8 g/l, p=0.001. Further, tumour response (percentage reduction) was statistically significant, p=0.001. The preceding finding is consistent with Telerovic *et al*., 2021.

Fractionation in the context of radiation therapy is the process of dividing a dose of radiation into multiple "fractions" (Chmiel *et al*., 2025). This practice seeks to maximize the destruction of malignant cells while minimising damage to healthy tissues (Chmiel *et al*., 2025). Tumour regression is expected after receiving some fractions from the prescribed radiation dose. A study by Parthasarathy *et al*., 2019 indicated that 50% cervical regression occurred at 27Gy at about 18 days of radiotherapy treatment. Awusi *et al*., 2021 also reported similar findings to the findings of this study and the preceding study.

Other factors that can influence cervical tumour size include anthropological and dosimetry measurements (Scott *et al*., 2021). In this study, the anthropological and dosimetry measurements of concern were the patient AP separation and the mean dose and dose to the 95% isodose. Regrettably, in this study, AP separation and the mean dose and dose to the 95% isodose did not show any influence on cervical tumour size.

The measurements for patient separation influence treatment techniques and outcomes. Studies indicate that AP separation greater than 18cm can utilise Co60 using the four-field box (Scott *et al.,* 2021). In this study, the AP separation used was 21cm using four field technique ensured adequate dose coverage according to the prescribed dose. This agrees with the findings of a study by Mutrikah *et al*., 2017.

The mean dose (D mean) is identified as a reasonable predictor for risk of toxic effects in some normal organs (Lawrence and Stefan 2022). The International Commission for radiological units (Fletcher 2014) defines maximum target dose, minimum target dose, mean target dose, median target dose, modal

target dose, and hot spot, regarding the treatment planning process and the recommended dose to be reported at a prescribed point. In this study, the median dose is reported contrary to the mean dose reported by other studies. However, the findings were comparable (Mutrikah *et al*., 2017; Dutta *et al*., 2020).

Although Mutrikah *et al*., 2017 compared treatment delivery techniques (four field technique and APPA technique), the dose to the 95% isodose finding of their study was comparable to the findings of this study which just employed four field technique). For dose coverage, Mutrikah *et al*., 2017 reported the conformity index to show dose coverage, while this study did not. This study's conformity index was reviewed in the treatment planning system and approved by the multi-disciplinary team (Radiation oncologist, Medical Physicist, and radiation therapists) before treatment to ensure the planning objective of 95% isodose receiving at least 95% of the prescribed dose was achieved.

CONCLUSION

This study has shown contextual evidence that cervical tumour size can reduce with increasing the number of fractions received during EBRT and level of haemoglobin. AP separation, Age, Parity, HIV status, Performance status, Average radiation dose, field size, number of chemotherapy cycles, chemotherapy type, and Dose to the 95% isodose line did not show any influence on cervical tumour size reduction.

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