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Predictors of Radiotherapy Outcomes in Breast Cancer Patients: A Logistic Regression Analysis of Clinical and Dosimetric parameters

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Abstract

This study aimed to predict radiotherapy outcome for breast cancer patients using clinical and dosimetric parameters through logistic regression analysis. The study made use of One Thousand, Four Hundred and Twenty-Two (1422) patients treated for breast cancer at the NSIA Cancer Centre, Lagos University Teaching Hospital (LUTH), Lagos State. Multivariate logistic regression analysis is performed in R Studio, with the level of significance set at $p<0.05$. The results show that among the dosimetric parameters, only V95 (volume receiving 95% of the prescribed dose) was a significant predictor ($p=0.026$) of radiotherapy outcome. Higher V95 values are associated with better outcomes. Regarding clinical parameters, cancer staging emerged as a significant predictor, with stage 3 (odds ratio=4.76, $p=0.001$) and stage 4 (odds ratio=16.17, $p<0.001$) being associated with poorer outcomes compared to stage 0. Other parameters entered into the model did not significantly predict radiotherapy outcome in this cohort of breast cancer patients. The study highlights the importance of V95 and cancer staging in predicting radiotherapy outcomes and can inform future treatment planning and patient management strategies; which vis-à-vis assist in achieving the goal three of the United Nations Sustainable Development Goals (SDG).

***Keywords**: Breast cancer, sustainable development goal, logistic regression, dosimetric parameters, radiotherapy*
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1 Introduction

Breast cancer remains one of the most prevalent cancers worldwide, accounting for a significant proportion of cancer-related morbidity and mortality among women. Radiotherapy is a cornerstone of breast cancer treatment, often used in conjunction with surgery, chemotherapy, and hormonal therapy to improve local control and survival rates (Early Breast Cancer Trialists' Collaborative

Group, 2011). Despite advances in radiotherapy techniques, predicting treatment outcomes remains challenging due to the complex interplay of various clinical and dosimetric factors.

Clinical parameters such as age, tumour grade, and cancer staging have been well-documented as critical determinants of breast cancer prognosis (Goldhirsch *et al*., 2013). Cancer staging, in particular, is a robust predictor of treatment outcomes, with advanced stages associated with poorer prognoses (Cianfrocca and Goldstein, 2004). Moreover, recent studies have highlighted the importance of dosimetric parameters—specifically, the volume of tissue receiving a particular dose of radiation (e.g., V95, V105)—in predicting radiotherapy outcomes (Clark *et al*., 2016).

Dosimetric parameters like V95 (volume receiving 95% of the prescribed dose) are particularly relevant in the context of three-dimensional conformal radiotherapy (3DCRT) and intensity-modulated radiotherapy (IMRT). These advanced techniques allow for the precise targeting of tumour tissues while sparing surrounding healthy tissues, potentially leading to better clinical outcomes (Mackie *et al*., 1999). Studies have shown that higher V95 values are associated with improved local control and survival rates, emphasising the need for accurate dosimetric planning (Ritter *et al*., 2010).

Despite these findings, there is still a need for comprehensive studies that integrate both clinical and dosimetric parameters to predict radiotherapy outcomes more effectively. Logistic regression analysis offers a robust statistical method for this purpose, allowing for the assessment of multiple predictors simultaneously and the determination of their relative importance (Hosmer *et al*., 2013).

This study aims to evaluate the predictors of radiotherapy outcomes in breast cancer patients by performing a logistic regression analysis of clinical and dosimetric parameters. By identifying significant predictors, this research seeks to enhance treatment planning and patient management strategies, ultimately improving the prognosis and quality of life for breast cancer patients.

2 Methodology

2.1 Study Design and Data Collection

This retrospective cohort study aimed to evaluate the predictors of radiotherapy outcomes in breast cancer patients by analysing clinical and dosimetric parameters. A total of 1422 breast cancer patients treated at the Nigeria Sovereign Investment Authority (NSIA) Cancer Centre, Lagos University Teaching Hospital, Lagos State, were included in the study. Clinical parameters considered included age, cancer staging, and treatment types, while dosimetric parameters included planning target volume (PTV), maximum dose (D2), dose to 98% of the volume (D98), mean dose (Dmean), volume receiving 95% of the prescribed dose (V95), homogeneity index (HI), conformity index (CI), number of fields, prescribed dose, actual delivered dose, and maximum dose.

2.2 Data Preprocessing

Data preprocessing was carried out in R Studio. This involved handling missing values through imputation, encoding categorical variables into binary indicators, and standardising continuous variables to ensure a mean of 0 and a standard deviation of 1 for easier comparison of coefficients.

2.3 Logistic Regression Analysis

The logistic regression equation is a family from the Generalized Linear Models (GLMs) (Agresti, 2015). These models are a flexible generalization of ordinary linear regression that allow for response variables to have error distribution models other than a normal distribution. GLMs are widely used in various fields such as statistics, biology, and economics due to their flexibility in

handling different types of response variables and their ability to model non-linear relationships. Logistic regression is a specific type of GLM used for modeling binary outcome variables. It is widely used in fields like medicine, social sciences, and machine learning for tasks such as disease prediction, risk assessment, and classification (Hosmer, *et al*., 2013). The logistic regression model can be mathematically expressed as:

$$\text{logit}(P) = \ln\left(\frac{P}{1-P}\right) = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \cdots + \beta_k X_k$$

where:

- P is the probability of the event occurring (e.g., complication from radiotherapy).
- $\ln\left(\frac{P}{1-P}\right)$ is the logit function, which is the natural logarithm of the odds.
- β_0 is the intercept term.
- $\beta_1, \beta_2, \ldots, \beta_k$ are the coefficients of the predictor variables $X_1, X_2, \ldots, X_k$.

The odds ratio for each predictor can be interpreted as the change in odds resulting from a one-unit change in the predictor variable. In this study, the logistic regression model would incorporate clinical and dosimetric parameters as predictors.

2.4 Application to This Study

Based on the variables in this study, the equation can be specifically written as:

$$\begin{aligned}\text{logit}(P) = {} & \beta_0 + \beta_{\text{Age}} \cdot \text{Age} + \beta_{\text{PTV}} \cdot \text{PTV} + \beta_{\text{D2}} \cdot \text{D2} + \beta_{\text{D98}} \cdot \text{D98} + \beta_{\text{Dmean}} \cdot \text{Dmean} + \beta_{\text{V95}} \\ & \cdot \text{V95} + \beta_{\text{HI}} \cdot \text{HI} + \beta_{\text{CI}} \cdot \text{CI} + \beta_{\text{NoFields}} \cdot \text{NoFields} + \beta_{\text{PrescribedDose}} \cdot \text{PrescribedDose} \\ & + \beta_{\text{ActualDeliveredDose}} \cdot \text{ActualDeliveredDose} + \beta_{\text{MaxDose}} \cdot \text{MaxDose} \\ & + \beta_{\text{AttachedToCourseYes}} \cdot \text{AttachedToCourseYes} + \beta_{\text{DiagnosisTypeSecondary}} \\ & \cdot \text{DiagnosisTypeSecondary} + \beta_{\text{RadiationTypeP}} \cdot \text{RadiationTypeP} + \beta_{\text{TreatmentTypeStatic}} \\ & \cdot \text{TreatmentTypeStatic} + \beta_{\text{CancerStage1}} \cdot \text{CancerStage1} + \beta_{\text{CancerStage2}} \cdot \text{CancerStage2} \\ & + \beta_{\text{CancerStage3}} \cdot \text{CancerStage3} + \beta_{\text{CancerStage4}} \cdot \text{CancerStage4}\end{aligned}$$

2.5 Model Fitting and Evaluation

The model was fitted using the generalised Linear Model (glm) function in R with a binomial family specification. The significance of each predictor was assessed using the Wald test, with a significance level set at $p < 0.05$.

3 Results

Table 1: Characteristics of the two outcome groups undergoing radiotherapy

Characteristic	Non toxic, N = 1,246	Toxic, N = 176	p-value
Attached to Course	450 (36%)	65 (37%)	0.8
Diagnosis Type			
Primary	1,241(100%)	175(99%)	0.5
Secondary	5 (0.4%)	1 (0.6%)	
Age	51 (12)	51 (12)	0.7
Tumour Stage			
0	138 (11%)	5 (2.8%)	<0.001
1	188 (15%)	2 (1.1%)	
2	451 (36%)	25 (14%)	
3	289 (23%)	47 (27%)	

Characteristic	Non toxic, N = 1,246	Toxic, N = 176	p-value
4	180 (14%)	97 (55%)	
Nominal Energy			
6000	1,150 (92%)	167 (95%)	0.2
12000	96 (7.7%)	9 (5.1%)	
Radiation Type			
Electron	156 (13%)	21 (12%)	0.8
Photon	1,090 (87%)	155(88%)	
Treatment Type			
Arc Therapy	418 (34%)	53 (30%)	0.4
Static	828 (66%)	123(70%)	
PTV	566 (123)	565 (129)	0.9
D2	45.71 (1.22)	45.73(1.19)	0.8
D98	39.03 (2.23)	38.86(2.20)	0.4
D_{mean}	43.19 (1.04)	43.25(0.98)	0.4
V_{95}	538 (104)	520 (103)	0.036
HI	0.15 (0.07)	0.16 (0.07)	0.5
CI	1.22 (0.57)	1.20 (0.58)	0.5
No of Fields	4.13 (3.10)	4.20 (3.00)	0.5
Pre Described Dose	31 (18)	30 (18)	0.6
Total Delivered Actual Dose	30 (18)	29 (18)	0.7
Maximum Dose	41 (13)	42 (13)	0.2
Number of Fracs	12 (8)	11 (8)	0.4

Table 1 presents a comparative analysis of various characteristics between two groups of patients undergoing radiation therapy, categorized as “Non-toxic” (1,246 patients) and “Toxic” (176 patients). The study found no significant differences between the two groups in terms of age, with both groups having a mean age of 51 years. Similarly, factors such as attachment to a course, diagnosis type, nominal energy used, radiation type, and treatment type showed no statistically significant variations between the non-toxic and toxic groups. However, a notable distinction emerged in the distribution of tumour stages between the two groups, with a p-value of less than 0.001 indicating strong statistical significance. The toxic group had a higher proportion of patients with advanced-stage tumours, particularly stage 4, compared to the non-toxic group. Treatment-related parameters such as Planning Target Volume (PTV), dose metrics (D2, D98, Dmean), Homogeneity Index (HI), and Conformity Index (CI) were largely similar between the two groups. However, there was a slight but statistically significant difference in V95 (volume receiving 95% of prescribed dose) between the groups, with a p-value of 0.036. Other treatment characteristics, including the number of fields, pre-described dose, total delivered actual dose, maximum dose, and number of fractions, did not show significant differences ($p>0.05$) between the toxic and non-toxic groups.

Table 2: Multivariate logistic regression predicting risk of complication from radiotherapy

Predictors	Estimate	p	Odds Ratio	95% C.I
Intercept	-1.19	0.857	0.31	0.00 - 12.25
Age	-9.06e−4	0.901	1	0.99 - 1.01
PTV	-3.13e−4	0.656	1	1.00 - 1.00
D_2	-0.06	0.567	0.95	0.79 - 1.14
D_{98}	-0.04	0.573	0.96	0.83 - 1.11
Dmean	0.09	0.291	1.09	0.93 - 1.29
V_{95}	0.00	0.026	1	1.00 - 1.00
HI	1.62	0.56	5.06	0.02 - 1171.34
CI	-0.18	0.255	0.84	0.62 - 1.14
No of Fields	0.02	0.571	1.02	0.94 - 1.11
Prescribed dose	0.02	0.48	1.02	0.97 - 1.07
Actual delivered dose	-0.01	0.674	0.99	0.95 - 1.04
Max Dose	0.00	0.956	1	0.94 - 1.06
Attached to Course				
Yes – No	-0.02	0.93	0.98	0.69 - 1.41
Diagnosis Type				-
Secondary – Primary	1.03	0.382	2.79	0.28 - 27.73
Radiation Type				-
Proton – Electron	-0.34	0.798	0.71	0.05 - 9.65
Treatment type				-
Static – Arc Therapy	-0.31	0.61	0.73	0.22 - 2.41
Cancer staging				-
1 – 0	-1.22	0.152	0.3	0.06 - 1.56
2 – 0	0.46	0.364	1.58	0.59 - 4.24
3 – 0	1.56	0.001	4.76	1.84 - 12.33
4 – 0	2.78	< .001	16.17	6.33 - 41.30

Table 2 shows the multivariate logistic regression predicting risk of complication from radiotherapy. It also shows that V95 ($p = .026$) and cancer stages 3 (OR = 4.76, 95% CI [1.84, 12.33], $p = .001$) and 4 (OR = 16.17, 95% CI [6.33, 41.30], $p < .001$) compared to stage 0 were significantly associated with increased odds of complication following radiotherapy. No other predictors reached statistical significance for predicting complication risk. The results of the logistic regression analysis indicated that among the dosimetric parameters, only V95 was a significant predictor of radiotherapy outcomes ($p=0.026$). Higher V95 values were associated with better outcomes. Regarding clinical parameters, cancer staging was a significant predictor, with stage 3 (odds ratio=4.76, $p=0.001$) and stage 4 (odds ratio=16.17, $p<0.001$) being associated with poorer outcomes compared to stage 0. Other parameters included in the model, such as age, tumor grade, Dmax, and Dmean, did not significantly predict the radiotherapy outcome in this study. The study underscores the importance of V95 and cancer staging in predicting radiotherapy outcomes, which can inform future treatment planning and patient management strategies to achieve better outcomes.

4 Discussion

The findings from this study provide insightful information into the predictors of radiotherapy outcomes in breast cancer patients, focusing on both clinical and dosimetric parameters.

4.1 Tumour Stage

One of the most significant findings of this study was the strong association between tumour stage and the occurrence of toxicity. Higher tumour stages (stage 3 and stage 4) were significantly associated with an increased risk of toxicity ($p < 0.001$). This is consistent with existing literature, which has repeatedly shown that advanced tumour stages are linked to poorer outcomes and higher complication rates due to the more aggressive nature of the disease and the increased intensity of required treatments (Edge and Compton, 2010; Matsen and Neumayer, 2013).

4.2 V95

The study also identified V95 (the volume of tissue receiving 95% of the prescribed dose) as a significant predictor of toxicity, with lower V95 values being associated with increased toxicity ($p = 0.036$). This finding again is in agreement with previous study indicating that adequate dose coverage (high V95 values) is crucial for effective tumour control and minimising complications (Bentzen, 2006). Ensuring a high V95 value can reduce the likelihood of residual tumour cells, thereby lowering the risk of recurrence and associated toxicities.

4.3 Other Dosimetric Parameters

Interestingly, other dosimetric parameters such as D2, D98, Dmean, HI, and CI did not show significant differences between the non-toxic and toxic groups. This might suggest that while these parameters are important for overall treatment planning, they may not be as critical in predicting acute toxicity as V95. Previous studies have suggested that while these parameters are important for understanding overall dose distribution and potential hotspots, their impact on toxicity can vary depending on individual patient anatomy and tumour characteristics (Emami *et al.*, 1991; Marks *et al.*, 2010).

4.4 Age and Diagnosis Type

Age and diagnosis type were not significantly associated with toxicity in this study. The mean age of patients in both groups was identical (51 years), and the p-value of 0.7 indicates no significant difference. This is somewhat surprising, as older age is often considered a risk factor for increased treatment-related complications (Sineshaw *et al.*, 2014). The lack of significance between age and toxicity in this study could be due to the specific cohort characteristics or the comprehensive supportive care provided, which may mitigate age-related risks.

4.5 Nominal Energy and Radiation Type

The nominal energy levels used (6000 vs. 12000) and the type of radiation (electron vs. photon) did not show significant differences between the non-toxic and toxic groups ($p = 0.2$ and $p = 0.8$, respectively). This suggests that within the ranges and types of radiation used in this study, these factors did not play a major role in predicting toxicity. Previous study has shown that while higher energy levels and different types of radiation can impact treatment effectiveness and side effects, the specific context and patient selection criteria play a crucial role in these outcomes (Livi *et al.*, 2015).

4.6 Treatment Type

The treatment type (arc therapy vs. static) also did not show a significant difference between the groups ($p = 0.4$). This is in agreement with some studies that suggest both methods can be equally effective and safe when appropriately planned and executed (Fiorino *et al*., 2012).

5 Conclusion

This study's findings provide valuable insights into the predictors of radiotherapy toxicity in breast cancer patients. The significant association of higher tumor stages and lower V95 values with increased toxicity underscores the need for precise treatment planning and dose coverage. These insights contribute to the ongoing efforts to optimize radiotherapy protocols and improve patient outcomes, ultimately supporting the broader goals of public health and sustainable development.

5.1 Recommendations

To improve radiotherapy outcomes for breast cancer patients and align with the United Nations Sustainable Development Goals (SDGs), the following recommendations are made:

1. Optimise Dosimetric Planning: - Utilise advanced radiotherapy techniques such as intensity-modulated radiotherapy (IMRT) and image-guided radiotherapy (IGRT) to ensure accurate dose distribution and achieve higher V95 values, supporting SDG Three (SDG3) by enhancing treatment quality and effectiveness.
2. Develop Stage-Specific Treatment Plans: - Tailor radiotherapy protocols based on cancer stage, providing less aggressive treatment for early stages and more intensive treatment for advanced stages.
3. Promote Multidisciplinary Care:- Establish collaborative teams of radiologists, medical physicists, oncologists, dosimetrists, and other healthcare professionals to develop and review treatment plans collectively. This comprehensive approach supports SDG 3 by ensuring coordinated, holistic care for better patient outcomes.

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