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Examination of Treatment Outcome on Brain Tumour Using Large Sample Data of Wisconsin Diagnostic Centre

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KEYWORDS
brain tumor, treatment outcome, correlation, multinomial, logistic regression and relationship.

ABSTRACT:
This study uses a multinomial logistic regression model to examine the treatment outcome of brain tumour parameters. Wisconsin data centre is the source of the study's sample (diagnostic data). Nine variables and 2000 observations make up the data collected from Wisconsin data centre. Python programming software was employed for the analysis. The boxplot was employed to ascertain the frequency of each variable in terms of first, third and median quantile values. The correlation coefficient result was used to measure the relationship between the nine variables. The relationship between tumour grade and tumour location shows weak correlation, with values of 0.333, whereas the correlation between time to recurrence (month) and survival time is 0.42. The strong correlation between tumour grade and recurrence site for treatment is 0.99. However, other variables do not correlate effectively. Given the stages of treatment outcome, we use the treatment outcome as the independent variable to recast the relationship between the variables. The probability value was used to calculate the impact of the independent variable on the dependent variable. Treatment outcome, given a partial response on tumour grade, has no bearing on survival time (month). The other variables are impacted by the partial response to the treatment. The progressive stage treatment outcome demonstrates that while gender and survival time are unaffected by a complete response, all other factors are affected. Then we observed that on the complete response nature of the disease, there is no significant difference in treatment results across all brain tumour parameters. Treatment outcome given partial treatment has a considerable impact on the remaining variable, however, there is no significant difference between treatment outcome of gender on the effect of tumour type and survival time.

1.0

Introduction

Cells are what make up living things. Normally, the adult body only produces new cells when they are required to replace damaged or ageing ones. Young children and infants produce new cells to finish developing and those required for repairs. When aberrant or normal cells proliferate when they are not needed, a tumour forms. A mass of extra cells growing inside the brain or central spinal canal is called a brain tumour. Primary brain tumours and metastatic brain tumours are the two main types of brain tumours. Primary brain tumours originate in the brain, where they usually remain. [13]

A primary brain tumour originates in the brain. Primary brain tumours include ependymoma, medulloblastoma, glioblastoma multiforme, and astrocytoma. Benign and malignant primary brain tumours are distinguished from one another. Brain tumours that have metastasized originate from cancer that has migrated to other parts of the body. These typically develop quickly, invade, and pose a threat to human life. Brain cancer is another name for malignant brain tumours. A malignant tumour poses a serious risk to life. Nonetheless, primary brain tumours do not precisely meet the criteria for cancer because they seldom spread outside of the brain and spinal cord [6]. Cancer is a fatal illness that can strike at any point in our lives. Cancer cannot be predicted because its symptoms do not appear in the body right away. The abnormal growth of any cells or tissues within the body is what is known as cancer. These aberrant cells continue to grow, becoming bigger and bigger every day. These aberrant cells can disperse throughout the body. These cancer cells pose a serious threat to the patient's life, making them extremely deadly [6]. While there are a few methods for diagnosing brain tumours, including CT scans and EEGs, magnetic resonance imaging (MRI) is the most popular and efficient one. An MRI creates inside images of the body's organs by using radio waves and strong, efficient magnetic fields. MRI is more efficient than CT or EEG scanning because it offers more precise information about the inside organs.

Medical science has advanced significantly in the last several years thanks to artificial intelligence (AI) and deep learning. One such innovation is the medical image processing approach, which makes it easier and less time-consuming for doctors to diagnose diseases early on. Therefore, computer-aided technology is greatly needed to overcome these kinds of constraints because the medical field needs time-tested, traditional methods to identify serious illnesses like cancer, which is the top cause of patient death worldwide [4]

Because of its enhanced soft tissue contrast, magnetic resonance imaging (MRI) has emerged as the gold standard for non-invasive brain tumour diagnosis in recent years [6]. Eighty per cent of all malignant brain tumours derived from glial cells in the central nervous system are gliomas. The World Health Organisation (WHO) divided gliomas into two general categories based on their aggressiveness and infiltrative character. Low-grade gliomas (LGG) include glioblastoma multiform (GBM) or low-grade and intermediate-grade gliomas (WHO grades II and III) as well as high-grade gliomas (HGG) (WHO grade IV) [14]. While the majority of LGG tumours develop more slowly than HGG tumours and respond well to treatment, a subset of LGG tumours can cause GBM if they are not detected early and are not treated. Given that, an early and accurate determination of the tumour grade can result in a favourable prognosis, appropriate treatment planning (including surgery, radiation, and chemotherapy individually or in combination) becomes important in both scenarios [13]. In this study we are going to examine the effect of treatment outcome of factors affecting brain tumour given the stages of treatment outcome.

2.0 MATERIALS AND METHODS

This section will begin with a quick explanation of the data presentation and move on to overview of regression models. The

2.1 General linear regression model

Regression models come in a wide range of forms (basic, linear, non-linear logistic, etc.), and the use of each model is contingent upon the problem under investigation. When the answer variable (Y)is dependent on a group of explanatory variables ($X_1, X_2, X_3 \dots\dots\dots X_m$)multiple regression models are employed. Because economic and social phenomena are often complicated, it takes more than one explanatory variable to fully understand and analyse them.[1] The linear regression model is defined by a dependent variable (Y) explained through a set of multiple explanatory variables (X_J) and it is based on the assumption that there is a linear relationship between the explained variable (Y_I) and the explanatory variables ($X_1, X_2, X_3 \dots\dots\dots X_m$). Random error ($\varepsilon_I$) is associated with each of the Observations (Y_I), (i = 1,2, …, n), as a linear function in the explanatory set.

$$Y_i = \beta_0 + \beta_1 X_{1i} + \beta_2 X_{2i} + \beta_3 X_{3i} \dots\dots\dots \beta_m X_j m + \varepsilon_i \quad (1)$$

and: i = 1,2, … , n , j = 0,1,2, … , m ,X_0 = 1. β_0, β_1, …, β_m: Represent the parameters of the [3] regression. ε_i Represents random errors. The model can be written briefly as follows:

$$Y_i = \sum_{j=0}^{m} \beta_j X_{ij} + \varepsilon_i \quad (2)$$

Using the matrix form, the above equation can be formalized as follows:

$$\begin{bmatrix} Y_1 \\ Y_2 \\ \cdot \\ \cdot \\ \cdot \\ Y_n \end{bmatrix} = \begin{bmatrix} 1 & X_{11} & X_{12} & \cdot & \cdot & X_{1m} \\ 1 & X_{21} & X_{22} & \cdot & \cdot & X_{2m} \\ \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ \cdot & \cdot & \cdot & \cdot & \cdot & \cdot \\ 1 & X_{n1} & X_{n2} & \cdot & \cdot & X_{nm} \end{bmatrix} \begin{bmatrix} \beta_1 \\ \beta_2 \\ \cdot \\ \cdot \\ \cdot \\ \beta_n \end{bmatrix} + \begin{bmatrix} \varepsilon_1 \\ \varepsilon_2 \\ \cdot \\ \cdot \\ \cdot \\ \varepsilon_n \end{bmatrix} \quad (3)$$

2.2 Non-Linear Regression Models

The regression model studies the relationship between the variable of the interest y and one or more explanatory variables $X^{(j)}$

The general models

$$Y_i = h\left(X_1^{(1)}, X_{2,}^{(2)} X_3^{(3)} \dots\dots\dots X_i^{(m)} : \emptyset_1, \emptyset_2, \dots\dots\dots \emptyset_p\right) + \varepsilon_t \quad (4)$$

Here, h is an appropriate function that depends on the explanatory variable and parameter that [11]. we want to

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summarize with vector $\underline{X}=\left\{X_1^{(1)}, X_{2,}^{(2)} X_3^{(3)} \ldots \ldots \ldots . X_i^{(m)}\right\}^T$ and $\underline{\emptyset}=\left\{\emptyset_1, \emptyset_2, \ldots \ldots . . \emptyset_p\right\}^T$. The unstructured deviations from the function h are described via the random errors ε_t. The normal distribution is assumed for the distribution of this random error, so $\varepsilon_t \sim$ N $(0,\sigma^2)$ independent.

2.3 Multinomial logistic regression model

Nonetheless, a lot of discrete response variables (such as political opinion, candidate supported in an election, favoured means of transportation, etc.) include three or more categories. Numerous research and experiments in a wide range of various fields contain multi-category response variables. When studying a multiple answer, it's crucial to determine if the response is nominal or ordinal, assuming that the response variable Y>2 categories. Certain models are exclusively suitable for ordinal responses, whereas other models can be applied to both nominal and ordinal responses. We can use a log-linear model with a multiway contingency table if the response variable is polytomous and all possible predictors are discrete. [2]

This information, however, comes from a medical study looking into the long-term impact of brain tumours on diagnostics. Both grouped and ungrouped data comprise the response variable. We shall take into consideration a multinomial logistic regression model for the investigation because the data set is categorised and ungrouped.

Let i be a response for i row $Y_i=(Y_1, Yi_1, Y_{i2} \ldots \ldots \ldots . . Y_{i1})$

Is assumed to have multinomial distribution with an index

$$n_i = \sum_{j=1}^{r} y_{ij} \tag{6}$$

With parameter ,$\pi_i = (\pi_{ii}\pi_{i2}, \pi_{i3} \ldots \ldots \ldots \pi_{ir})$

When the response is categorised as $1, 2 \ldots \ldots r$ are un-order.[8]

A set of $r-1$ baseline-category logit taking j^* as the baseline category that is

$$\log\left(\frac{\pi_{ij}}{\pi_{ij}}\right) = X_i^T \beta_j \tag{7}$$

$j \neq j^*$

If X_i has length p then this model has $(r-1) \times p$ free parameter which we can arrange as a matrix of vector if $j^* = r$[9]

$$\beta_i = (\beta_1, \beta_2, \beta_3 \ldots \ldots \ldots \beta_{r-1}) \tag{8}$$

$$vec(\beta) = \begin{bmatrix} \beta_1 \\ \beta_2 \\ . \\ . \\ \beta_{r-1} \end{bmatrix} \tag{9}$$

$$\pi_{ij} = \frac{\exp(X_i^T \beta_j)}{1+\sum_{k \neq j^*}^{r} \exp(X_i^T \beta_j)} \tag{10}$$

If $j \neq j^*$

$$\pi_{ij^*} = \frac{1}{1+\sum_{k \neq j^*}^{r} \exp(X_i^T \beta_j)} \tag{11}$$

GOODNESS OF FIT

If the estimated expected counts

$\mu_{ij} = n_i \pi_{ij}$ is large enough that we can test the fit of our model versus a saturated model that estimates π_i independently for $i = 1,2, \ldots N$

$$G^2 = 2\sum_{k=1}^{N} y_{ji} log \frac{y_{ij}}{\mu_{ij}} \tag{12}$$

The saturated model has $N(r-i)$ free parameters [7]

and the current model has $p(r-1)$ where is the length of X_i so the degrees of freedom are $df = (N-P)(r-1)$

(13)

3.0 RESULTS AND DISCUSSION

The study uses Wisconsin's Diagnostic Centre brain tumour data to determine how treatment outcomes affect several brain tumour parameters, including age, type, and grade. Within the Wisconsin dataset, every one of the 2000 rows and 9 columns has its unique ID. The modelling technique uses the impact of the treatment result stages on the brain tumour parameter.

3.1 Box plot

The box plot showed in figure 1; The first age quartile is 52 years old, meaning that 20% of those diagnosed with brain tumours are younger than 52 years old. The third

age quartile is 62 years old, meaning that 20% of the population is older than 62 years old. Based on the box plot observation, we found that 60% of the population is between the ages of 52 and 62. Given that the median age is 55, half of the population is likely younger than the other half.

The first survival time quartile is 25, meaning that 10% of the population does not have a brain tumour. The third survival time quartile is 40, meaning that 10% of the population does not respond to treatment. Based on our analysis of the box plot, we found that 80% of people in the population who are between the ages of 25 and 40 had a good chance of surviving with therapy. According to the media's 30 levels of therapy, 30% of people will not survive, while the remaining population will.

However, from figure 2 indicate the plot of correlation matrix; With the correlation value of 0.99, there is a strong association between the tumour grade and the place of recurrence for therapy. The correlation coefficient of 0.42 indicates a medium association between the time to recurrence (month) and survival time. Tumour grade and tumour site had a weak link, with values of 0.333. Other variables, however, do not correlate effective. [5]

3.2 Model fitting and explanation.

The four stages of treatment partial response, complete response, advancing disease, and stable disease are used as the conditions for parameter estimate in the multivariate logistic regression model of brain tumour parameters. The treatment result is used as the independent variable.

3.3 Model estimation of partial response

3.3.1 Model estimation for treatment outcome for the partial response given other parameter.

$$log\left[\frac{pro(Y_i=1/X_{i1}.........X_{8i})}{pro(Y_i=4/X_{i1}.........X_{8i})}\right]=c_{10}+c_{11}X_{1i}+c_{12}X_{12}+c_{13}X_{13}+c_{14}X_{14}+c_{15}X_{15}+c_{16}X_{16}+c_{17}X_{17}+c_{18}X_{18}$$

Where

c_{10}= constants of the model

X_{1i}= Age

X_{2i}= gender

X_{3i}= Tumor Type

X_{4i}= Tumor Grade

X_{5i} = Treatment

X_{6i}= Time to Recurrence (months)

X_{7i}= Recurrence site

X_{8i}= Survival Time (month)

$$log\left[\frac{o(Y_i=partial/X_{i1}.........X_{8i})}{pro(Y_i=4/X_{i1}.........X_{8i})}\right]=-0.4-0.28X_{11}+-0.2X_{12}+0.17X_{13}+0.09X_{14}+-0.2X_{15}+0.4X_{16}+-0.45X_{17}+-0.05X_{18}$$

From the results above, we observed that treatment outcomes provided on partial response of tumour grade, and survival time (month) were not significantly difference, given that their P-values (0.543 and 0.316) are higher than 0.05. This indicate that tumour grade and survival time are unaffected by treatment outcomes with partial responses, but that of the age, gender, tumor type, treatment, time to recurrence (months), and recurrence site variables were affected because their probability is less than (0.05).[10]

3.3.2 Model estimation for treatment outcome for the progressive response given other parameter

$$log\left[\frac{pro(Y_i=2/X_{i2}.........X_{8i})}{pro(Y_i=4/X_{i2}.........X_{8i})}\right]=c_{20}+c_{21}X_{1i}+c_{22}X_{2i}+c_{23}X_{2i}+c_{24}X_{2i}+c_{25}X_{2i}+c_{26}X_{2i}+c_{27}X_{2i}+c_{28}X_{2i}$$

$$log\left[\frac{o(Y_i=complete/X_{i1}.........X_{8i})}{pro(Y_i=4/X_{i1}.........X_{8i})}\right]=-0.89-0.33X_{21}+0.169X_{22}+0.76X_{23}+0.98X_{24}-0.59X_{25}+1.23X_{26}-0.62X_{27}-0.134X_{28}$$

From the results of the progressive response on the treatment outcome, we observed that there is no statistical significant difference in gender or survival Time (month). The results show, that their P-values are 0.188 and 0.06 are higher than 0.05. That means that if the treatment outcome is given a progressive response, it should not base gender or survival time. However, we can accept that, the progressive response is significant difference with the following; age, tumor type, tumor grade, treatment, time to recurrence (months), and the recurrence site.

3.3.3 Model estimation for treatment outcome for complete response given other parameter.

$$log\left[\frac{pro(Y_i=3/X_{i3}.........X_{8i})}{pro(Y_i=4/X_{i3}.........X_{8i})}\right]c_{30}+c_{31}X_{3i}+c_{32}X_{3i}+c_{33}X_{3i}+c_{34}X_{3i}+c_{35}X_{3i}+c_{36}X_{3i}+c_{37}X_{3i}+c_{38}X_{3i}$$

$log\left[\frac{o(Y_i=progressive/X_{i1}.........X_{8i})}{pro(Y_i=4/X_{i1}.........X_{8i})}\right]$=-11447+65.6$X_{31}$+151.9$X_{32}$+231.26$X_{33}$+323.628$X_{34}-16.86X_{35}$+228.283$X_{36}-399.37X_{37}-23647X_{38}$

The results showed that there is no significant effect between treatment outcomes given complete response on all the factors namely; age, gender, tumor type, tumor grade, treatment, time to recurrence (months), recurrence site and the survival time (months). Since their P- value is greater than 0.05. This should that the treatment outcome does not give complete response base on the above mentioned factors.

3.3.4 Model estimation for treatment outcome for gender given other parameters.

$log\left[\frac{pro(Y_i=4/X_{i4}.........X_{8i})}{pro(Y_i=4/X_{i4}.........X_{8i})}\right]=c_{40}+c_4X_{4i}+c_{42}X_{4i}+c_{43}X_{4i}+c_{44}X_{4i}+c_{45}X_{4i}+c_{46}X_{4i}+c_{47}X_{4i}$

Here, we consider the following parameters as follows;

Where

c_{10}= constants of the model

X_{41}= Age

X_{42}= Tumor Type

X_{43}= Tumor Grade

X_{44} = Treatment

X_{45}= Time to Recurrence (months)

X_{46}= Recurrence site

X_{47}= Survival Time (month)

$log\left[\frac{o(Y_i=stable/X_{i1}.........X_{8i})}{pro(Y_i=4/X_{i1}.........X_{8i})}\right]$=-0.014-0.4$X_{41}-0.037X_{42}-0.19X_{43}-0.17X_{44}-0.0077X_{45}-0.214X_{46}-0.17X_{47}$

There is no significant different on gender between treatment outcomes of tumor type and time to recurrence (months). Since their P-value are (0.521 and 0.202) which is greater than 0.05. This shows that the treatment outcome on gender does not affect tumor grade and time to recurrence.

5.0 Conclusion

This study assessed the correlation between the diagnostic data of brain tumour characteristics in Wisconsin. We adopt the method of multinomial logistics regression with the help of python programming software to obtain the results. Nine variables and two thousand (2000) observations make up the data set. The box-plot was employed to ascertain the frequency of each variable. We determine the first, third, and median quantiles by critically analysing the time box plot of all the variables. The correlations plot was used to measure the relationship between the nine variables. The relationship shows that the correlation relationship between tumour grade and tumour location is weak, with values of 0.333, whereas the correlation between time to recurrence (month) and survival time is 0.42. The plot shows that, the strongest correlation is between tumour grade and recurrence site for treatment at 0.99.

Other variables, however, do not correlate effectively. On examine the stages of the treatment outcome (partial response, progressive diseases, complete response, and gender), we take the treatment outcome as the independent variable to recast the relationship between the variables. The effect of the independent variable on the dependent variable was measured using the probability value in Table 4.1. Treatment outcome, given a partial response on tumour grade, has no bearing on survival time (month). These mean that the treatment outcome that results in a partial response should influence the remaining variables but not the tumour grade or survival time. From the results of progressive diseases, we observed that the treatment outcome has no significant difference to gender or survival time (month). This indicate that while survival time and gender are unaffected by treatment outcomes when progressive response is provided, while other outcomes are affected. The results from the complete response nature of the disease, indicates that there is no statistical significant difference in treatment results across all brain tumour parameters. These ensure that, in the case of a complete response condition, treatment outcomes do not impact every variable in the model. Regarding tumour kind, there is no discernible relationship between treatment outcomes and gender during illness.

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Table.

Table 1: Parameter Estimation of Brain Tumor

Treatment Outcome							
	parameter	**coef**	**std err**	**z**	**P>|z|**	**0.025**	**0.975**
partial response	Age	-0.2803	0.077	-3.624	0.000**	-0.432	-0.129
	Gender	-1.2882	0.085	-15.205	0.000**	-1.454	-1.122
	Tumor Type	0.1708	0.079	2.154	0.031**	0.015	0.326
	Tumor Grade	0.0891	0.089	1.002	0.316	-0.085	0.263
	Treatment	-0.2061	0.071	-2.891	0.004**	-0.346	-0.066
	Time to Recurrence (months)	0.4220	0.083	5.092	0.000**	0.260	0.584
	Recurrence Site	-0.4483	0.077	-5.791	0.000**	-0.600	-0.297
	Survival Time (months)	-0.0519	0.085	-0.608	0.543	-0.219	0.115
	const	-0.4006	0.083	-4.843	0.000**	-0.563	-0.238
Treatment Outcome							

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	Parameter	coef	std err	z	P>|z	[0.025	0.975]
progressive response	Age	-0.3291	0.083	-3.962	0.000**	-0.492	-0.166
	Gender	0.1694	0.092	1.836	0.066	-0.011	0.350
	Tumor Type	0.7553	0.095	7.950	0.000**	0.569	0.941
	Tumor Grade	0.9861	0.095	10.408	0.000**	0.800	1.172
	Treatment	-0.5933	0.098	-6.046	0.000**	-0.786	-0.401
	Time to Recurrence (months)	1.2347	0.106	11.656	0.000**	1.027	1.442
	Recurrence Site	0.6178	0.099	6.259	0.000**	0.424	0.811
	Survival Time (months)	0.1343	0.102	1.318	0.188	-0.065	0.334
	const	-0.9867	0.103	-9.577	0.000**	-1.189	-0.785
Treatment Outcome (progressive disease)							
	parameter	coef	std err	z	P>|z|	[0.025	0.975]
complete disease	Age	65.63	303.45	0.216	0.829	-529.12	660.39
	Gender	151.95	733.48	0.207	0.836	-1285.64	1589.54
	Tumor Type	231.26	1085.85	0.213	0.831	-1896.96	2359.49
	Tumor Grade	323.62	1415.03	0.229	0.819	-2449.78	3097.03
	Treatment	-16.86	170.639	-0.099	0.921	-351.31	317.57
	Time to Recurrence (months)	228.28	992.3	0.230	0.818	-1716.64	2173.21
	Recurrence Site	-399.37	1742.43	-0.22	0.819	-3814.476	3015.72
	Survival Time (months)	-236.47	1033.19	-0.22	0.819	-2261.494	1788.55
	const	-1144.74	4897.79	-0.234	0.815	-1.07e+04	8454.74
Treatment Outcome							
	parameter	coef	std err	Z	P>|z|	[0.025	0.975]
Gender	Age	-0.408	0.057	-7.175	0.000**	-0.520	-0.297
	Tumor Type	-0.037	0.058	-0.642	0.521	-0.152	0.077
	Tumor Grade	-0.190	0.061	-3.128	0.002**	-0.310	-0.071
	Treatment	-0.170	0.057	-3.006	0.003**	-0.282	-0.059
	Time to Recurrence (months)	-0.077	0.061	-1.276	0.202	-0.197	0.042
	Recurrence Site	-0.214	0.059	-3.645	0.000**	-0.329	-0.099
	Survival Time (months)	-0.17	0.065	-2.617	0.009**	-0.297	0.043
	const	-0.014	0.055	-0.269	0.788	-0.122	0.092

Footnote: **= significant at 5%

Figures

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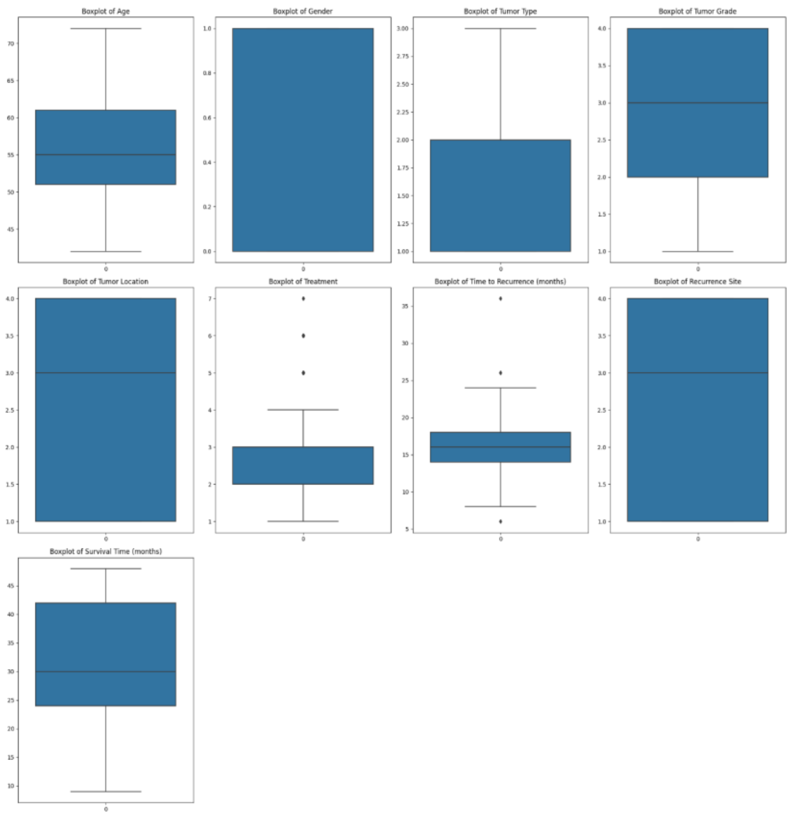

Figure 1: Box-plot of brain tumour

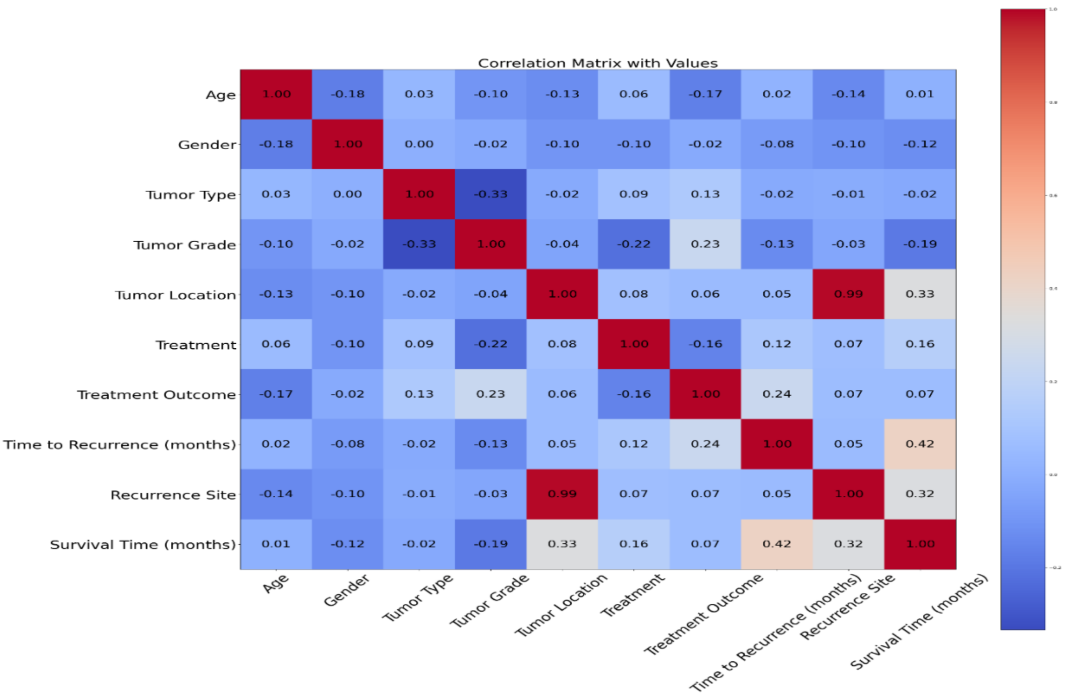

Figure 2: correlation Matrix Brain tumour