Lung Tumor Classification on Human Chest X-Ray Using Statistical Modelling Approach

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Abstract. Lung tumor is a group of abnormal cells that are formed from the process of excessive and uncoordinated cell division in the lung or known as a neoplasia. Neoplasia refers to the growth of new cells that are different from the growth of cells around it. The tumor can be a benign tumor that does not cause cancer and malignant tumors that can cause cancer. Chest X-ray is the most technique used for detecting a lung tumor. Image processing is done by mean for distinguishing the classification lung tumor. Based on previous research the most used method is the mathematical method, but the result obtained are not maximal. Therefore, in this study we propose methods to classify lung tumor by using statistical modelling approach with logit link function based on parametric model, and nonparametric model using penalized spline estimator. Based on the proposed method, we get the classification accuracy of 80% for parametric model approach and 85% for nonparametric model approach, it means that the nonparametric model approach is better than the parametric model approach.

1. Introduction

Tumors are a group of abnormal cells that are formed as a result of excessive and uncoordinated cell division processes, known as neoplasia. Neo means new, plasia means growth or division, so neoplasia refers to new cell growth, which is different from the growth of normal surrounding cells [1]. Human organs can get cancer as well as the lungs. Lung cancer is a type of cancer that does not detect the growth of unusual cells in one or both [2]. There are two main types of primary lung cancer which are known to be the most common type, Non-small cell lung cancer (NSCLC) and the other is small cell lung cancer (SCLC). The most commonly known as lung tumors is a non-small cell lung cancer (NSCLC), as one of the original diseases that cause death to [2]. Cancer is the leading cause of death in almost all the world. From year to year the number has increased both in Japan, Europe, America and Indonesia. In Indonesia, cancer is ranked 3rd or 4th among malignancies in hospitals [3]. According to the 2012 GLOBOCAN (IARC) data, lung cancer has a high percentage of new cases in the female population, which is 13.6% and lung cancer deaths by 11.1% [4].

In the health industry, chest x-ray (CXR) is considered the most widely used technique for screening lung cancer. Generally pulmonary nodules will be seen at the time of screening, and is owned by 50% of people aged fifty years. The CXR image will display abnormal lung images in the form of round nodules and have high contrast. However, these nodules cannot be categorized as lung cancer because nodules can be caused by other lung diseases such as pneumonia or tuberculosis [5]. The difficulty of identifying and classifying nodules in the lung x-ray image has resulted in radiologists and doctors also
having an important role in diagnosing an illness, because diagnostic errors can lead to errors in providing treatment.

Research related to lung tumor detection has been carried out by several researchers, as according to [6] entitled classification of lung images with histogram feature extraction and backpropagation artificial neural networks obtained classification accuracy of 65%. Study of the identification of tumors in the tissue around the bones and lungs using segmentation based on the gray level of the image obtained classification accuracy of 40%[7]. Study of the implementation of the nearest neighbor method for classification of lung conditions from x-ray images obtained classification accuracy of 72.55%[8].

Based on the research conducted, the most widely used method is mathematical method, whereas image detection using statistical methods can provide better results, as in the study of [9] entitled detection of brain tumor with an additive nonparametric logistic regression approach based on linear local estimators with reducing dimensions of discrete wavelet transformation and principal component analysis found 100% classification accuracy for insample data and 86% for data outsample.

The data in this study are categorized into two categories namely normal lung image \( Y = 0 \) and lung tumor image \( Y = 1 \), so that the response variable on the lung tumor image data follows the Bernoulli distribution. One of the statistical methods that can be used is binary logistic regression. Logistic regression is a statistical analysis method that is used to describe relationships between variables and test hypotheses categorical response to one or more predictor variables are continuous or categorical [10]. The parametric approach assumes the predictor variable in linear binary logistic regression of its parameters, so that the model is included in the Generalized Linear Model (GLM), while nonparametric approach uses GAM (Generalized Additive Model) which is the extension of GLM that combines GLM properties with Additive Model. The use of GLM and GAM can be used in almost identical cases, but GLM emphasizes more on estimation and conclusions for its parameter model, whereas GAM emphasizes more on nonparametric data exploration [11]. The GAM regression function is generally estimated by the Local Scoring algorithm as it can accommodate nonparametric additive regression models whose distribution of response variables is included in the exponential family [12] where as Bernoulli distribution included in an exponential distribution family. Some researchers used GAM based on local polynomial modeling, kernel, and local linear to designing growth charts of children up to five years old have been done by [13 – 15]. Spline estimator has been studied by [16 – 18]. The application of the calculation of statistical approach can not be calculated by manual calculation so that Minitaban OSS-R software assistance is required. Based on the description above, in this study will be discussed about the classification of lung tumor on human chest x-ray images with wavelet discrete transformation and principle as dimension reducer based on parametrical and nonparametric approach.

2. Research Method

This analysis steps in this research are as follows:

1. Image processing on human chest x-ray image use MATLAB with the following steps:

   - \textbf{Imread}
   - \textbf{Greyscale}
   - \textbf{Thresholding}
   - \textbf{Histogram equalization}
   - \textbf{Segmentation (32x32)}
   - \textbf{Normalization}

   \textbf{Figure 1.} Images Processing Steps using MATLAB

   Resizing size image represent as predictors/columnsmatrice and the rows are the observations.

2. Reducing dimension of image processing human chest x-ray image use Wavelet Discrete Transforms (WDT) and Principal Component Analysis (PCA) method with the following steps:

   a. The WDT method data X is nxp, requiring the number of predictor variables (p) to be expressed in \( 2^M \), with M being a positive integer. If not, then it is necessary to do data placement, so that X is nxq, with q = \( 2^M \)

   b. Transforming a \( 2^M \) sized predictor variable into an interval \([0,1)\)

   c. Calculate the WDT matrix, \( W \) the size of qxq, where the column elements are values of \( \phi(t) \) and \( \psi(j, k) (t) \) for various \( t \in [0,1) \)
d. Transform variables to get the D wavelet coefficient,
e. Dimension reduction is done by taking \( m < q \) from the wavelet coefficients to obtain \( D_{nxm}^{*} = X_{nqx}W_{qxm}^T \) by giving a zero value in the column \((m + 1)\) up to \( q \) from the matrix \( W^T \).
f. Calculate the correlation matrix from \( D_{nxm}^{*} \) to see its colinearity.
g. Determine the variable \( Z \) as a result of standardization of variable \( D^{*} \).
h. Determine the \( Z^T Z \) covariance matrix.
i. Determine eigenvalues.
j. Determine the value of the eigenvector \( v_j \) of each eigenvalue \( \lambda_j \).
k. Determine the main component of \( w_i \) through the eigenvalue selection procedure \( \lambda_j, w_j = v_1Z_1 + v_2Z_2 + v_3Z_3 + \ldots + v_mZ_m \).
l. Determine the number of selected main components \( (k) \) based on cumulative variance proportions.

3. Making the classification of lung tumor and normal lung from the result of dimension reduction data with parametric logistic regression approach based on these following steps:
a. Estimate binary logistic regression with logit link function.
b. Estimate probability value on each observation with formula \( \pi_i = \frac{\exp(X_i\beta)}{1+\exp(X_i\beta)} \).
c. Classifying \( \pi_i \) value based on cut off value for 0.5.
d. Estimate the accuracy classification based on APPER.

4. Making the classification of tumor and normal lung from the result of dimension reduction data with nonparametric logistic regression approach using OSS-R based on these following steps:

A. The \( f_j \) estimate for each predictor
   - The \( f_j \) akan function is estimated based on the penalized spline estimator with the following steps:
     a. Determine the order of the polynomial \( m_j \), the number of knots \( k_j \), and the smoothing parameter \( \lambda_j \) optimal.
     b. Define the matrix \( (X_j) \) by entering the optimal polynomial knots and order points.
     c. Define the estimation value \( \hat{\beta}_j \) by entering the optimal smoothing parameter value.
     d. Calculate the estimated model \( \hat{f}_j(X_j) \).

B. Iteration of local scoring and backfitting algorithms to obtain an additive model based on the penalized spline estimator with the following steps:
   a. Define the response variable \( k_j \), and the predictor variable \( (X_j) \).
   b. Determines the initial value to be used in the 0 iteration \((h = 0)\) with steps:
      i. Specify \( \hat{f}_j^{(0)}(X_{ij}) \) for \( j = 1,2, \ldots, p \) and \( i = 1,2, \ldots, n \) based on the steps specified.
      ii. Determine the adjusted dependent variable vector \( z_i^{(0)}, \mu_i^{(0)} \) and \( \eta_i^{(0)} \).
      iii. Specify matrix \( W_i^{(0)} \).
   c. Use local scoring algorithm for \((h = 0,1,2, \ldots)\) with steps:
      i. Determine partial residual \( R_j^{(h+1)} \).
      ii. Specify smoothing function \( f_j^{(h+1)} \).
      iii. Determine the value \( RSS^{(h+1)} \).
      iv. Narrate steps a through c until an RSS value that satisfies the convergence value is obtained \( |RSS^{(h+1)} - RSS^{(h)}| < \varepsilon \).
      v. Determine the vector dependent dependent \( z_i^{(h+1)}, \mu_i^{(h+1)} \) and \( \eta_i^{(h+1)} \).
      vi. Determine the matrix \( W_i^{(h+1)} \).
      vii. Calculate Avg (Dev).
viii. Narrate steps (i) to (vi) until the Avg value (Dev) is obtained which meets the convergent criteria, namely $|\text{Avg}(\text{Dev})^{(h+1)} - \text{Avg}(\text{Dev})^{(h)}| < \epsilon$

5. Calculate the value of cut of probability
6. Define the initial incidence of tumor and normal lung and classify the estimation of $\mu_i$ value
7. Calculate the accuracy classification
8. Compare the accuracy classification between parametric approach and nonparametric approach.

3. Result and Analysis

3.1. Image Processing

The initial steps before classifying lung tumor on human chest x-ray image is to perform image processing steps. The purpose of image processing is to improve the image quality for the retrieval of existing information in the image can be processed to the next stage. Stages of image processing in this study is done by using MATLAB software with several stages, starting from reading process of chest x-ray image data file, greyscale process, thresholding process, histogram equalization process, segmentation process and normalization process. The pictures are shown below:

![Figure 2. Images Processing Steps](image)

3.2. Reducing Dimensions of Images Processing Result with Discrete Wavelet Transform (DWT) and Principal Component Analysis (PCA) Method

Dimensions reducing is necessary because the results obtained in image processing have very high dimensions and do not meet the criteria of the data to be analyzed by statistical approach that requires the condition of number of observations more than number of predictors. These criteria must be met so that the estimation and inference process can be applied. Dimension reducing method which is used in this study is discrete wavelet transform (DWT) and principal component analysis (PCA). Discrete wavelet transform (DWT) is a dimensional reduction method that is computationally easy and simple in its application, and is able to handle data that has high dimensions. The discrete wavelet transform (DWT) method still allows multicollinearity in modeling, a method that can be used as a solution to overcome this problem is using the principal component analysis (PCA).

In this study, data obtained by image processing data has number of predictor variable for 1024. The number reduction predictor variable for 1024. Dimension reduction with discrete wavelet transforms produces a matrix $D^{*}50x20$ and if the correlation matrix is calculated, it turns out that between wavelet coefficients are still highly correlated, this can be overcome with principal component analysis (PCA). From the PCA 4 components were selected because the total variance that can be explained by the 4 main components is 96.55%.

3.3. Identify Lung Tumor by Using GLM and GAM Approaches

Reducing dimensions by using DWT and PCA produces predictor variables as many as 4 with many observations of 40 which later will be modeled to determine the classification of tumor and normal lung in the image. The steps are based on parametric approach with link function logit that is parameter model estimation, simultaneous or individual significance tests, and calculation of classification accuracy in each observation. Estimated model parameters generated can be seen on Table 1 as follows:
Table 1. Parameter Model Estimation for GLM

| Predictor | Coef  | SE Coef | Chi-Square | P     |
|-----------|-------|---------|------------|-------|
| Constant  | 0.256 | 0.413   | 16.59      | 0.002 |
| X1        | 1.81  | 1.09    | 3.45       | 0.063 |
| X2        | 6.23  | 3.70    | 3.35       | 0.067 |
| X3        | 9.21  | 4.52    | 5.08       | 0.024 |
| X4        | 12.40 | 5.53    | 6.37       | 0.012 |

Calculation of classification accuracy is done by calculating probability value using \( \pi \). In this study, each observation has a probability value so that it will be discussed on the 10th observation alone. 10th observation by definition cyst image \( y = 1 \) has estimated probability as follows:

\[
\pi_{10} = \frac{e^{(0.256 + (1.81x_{10} - 0.121991) - (6.23x_{20} + 0.063441) + (9.21x_{30} - 0.06721) + (12.4x_{40} + 0.096061))}}}{1 + e^{(0.256 + (1.81x_{10} - 0.121991) - (6.23x_{20} + 0.063441) + (9.21x_{30} - 0.06721) + (12.4x_{40} + 0.096061))}}
\]

\[
\pi_{10} = \frac{\hat{f}(X_{10} - 0.1012826)}{1 + e^{(0.256 + (1.81x_{10} - 0.121991) - (6.23x_{20} + 0.063441) + (9.21x_{30} - 0.06721) + (12.4x_{40} + 0.096061))}} = 0.809107
\]

Obtained \( \pi_{10} \) value then classified based on cut off value of 0.5, because \( \pi_{10} \) value is 0.809107 more than 0.5 so 10th observation classified as lung tumor image \( (y = 1) \). If probability value \( \pi \) less than 0.5 then it classified as normal lung image \( (y = 0) \).

The next step is to determine the probability value at each observation by using the nonparametric regression model approach based on penalized spline estimator. We obtain optimum lambda for each predictor as given in Table 2.

Table 2. Optimum Lambda Value for each Predictor Variable

| No | Predictor variable | Orde | Number of knot | Knot Point | Minimum GCV | Optimum Lamda |
|----|-------------------|------|----------------|------------|-------------|---------------|
| 1  | \( X_1 \)         | 1    | 1              | -0.1012826 | 0.2592283   | 0.3           |
| 2  | \( X_2 \)         | 1    | 1              | -0.02813263 | 0.2509593  | 100           |
| 3  | \( X_3 \)         | 1    | 1              | -0.01800934 | 0.2562773  | 100           |
| 4  | \( X_4 \)         | 1    | 2              | -0.03769803 | 0.2402308  | 100           |

Based on the result of local scoring algorithm iteration, the estimated parameter values are as follows:

\[
\hat{\beta}_1 = [-2.289376 \ 1.321686 \ 0.797374]^T
\]

\[
\hat{\beta}_2 = [0.7471454897 \ 6.0980695296 \ 0.0009127548]^T
\]

\[
\hat{\beta}_3 = [0.7624393118 \ 9.3705596681 \ -0.0001958976]^T
\]

\[
\hat{\beta}_4 = [0.8697156 \ 12.40311 \ 0.0006904491 \ 0.001083890]^T
\]

The form of penalized spline estimator for the initial value of \( \hat{f}(X_{ji}) \) function for each predictor in each observation is as follows:

a. \( \hat{f}_1(X_{1i}) = -2.289376 + 1.321686X_1 + 0.797374(X_1 + (0.1012826))_+ \)

with terms:

\[
\hat{f}_1(X_{1i}) = \begin{cases} 
-2.289376 + 1.321686X_1 & X_1 < -0.1012826 \\
-2.208616 + 2.11906X_1 & X_1 \geq -0.1012826 
\end{cases}
\]

b. \( \hat{f}_2(X_{2i}) = 0.7471454897 + 6.0980695296X_2 + 0.0009127548(X_2 + (0.02813263))_+ \)

with terms:

\[
\hat{f}_2(X_{2i}) = \begin{cases} 
0.7471454897 + 6.0980695296X_2 & X_2 < -0.02813263 \\
0.74717167 + 6.098982284X_2 & X_2 \geq -0.02813263 
\end{cases}
\]

c. \( \hat{f}_3(X_{3i}) = 0.7624393118 + 9.3705596681X_3 - 0.0001958976(X_3 + (0.01800934))_+ \)

with terms:
\[ f_3(X_{3i}) = \begin{cases} 
0.7624393118 + 9.3705596681X_3 & ; X_3 < -0.01800934 \\
0.762435783 + 9.370363771X_3 & ; X_3 \geq -0.01800934 
\end{cases} \]

d. \[ f_4(X_{4i}) = 0.8697156 + 12.40311X_4 + 0.0006904491(X_4 + (0.03769803))_+ \\
+ 0.001083890(X_4 - (0.02535196))_+ \]

with terms :

\[ f_4(X_{4i}) = \begin{cases} 
0.8697156 + 12.40311X_4 & ; X_4 < -0.03769803 \\
0.869741628 + 12.40380048X_4 & ; -0.03769803 \leq X_4 < 0.02535196 \\
0.869714149 + 12.40488437X_4 & ; X_4 \geq 0.02535196 
\end{cases} \]

Based on the optimum lambda values and the obtained order in Table 2, we determine the initial value \( f_j(X_{ji}) \) for every predictor by using the penalized spline estimator. In this study, every observation has an initial value and the expected value. So, for example, we will discuss for the 10th observation only. The 10th observation by defining lung tumor image (Y=1) has initial values estimate as follow :

a. The first predictor variable at 10th observation is equal to 0.121991. This value is include in criteria \( X_1 \geq -0.1012826 \), so the function used for \( (X_{1,10}) \) is

\[ f_1(X_{1,10}) = -2.208616 + 2.11906X_1 ; \] \( X_1 \geq -0.1012826 \)
\[ f_1(X_{1,10}) = -2.208616 + 2.11906(0,121991) \]
\[ = -1.950 \]

b. The second predictor variable at 10th observation is equal to 0.063441. This value is include in criteria \( X_2 \geq -0.02813263 \), so the function used for \( (X_{2,10}) \) is

\[ f_2(X_{2,10}) = 0.74717167 + 6.098982284X_2 ; \] \( X_2 \geq -0.02813263 \)
\[ f_2(X_{2,10}) = 0.74717167 + 6.098982284(0.063441) \]
\[ = 1.134102235 \]

c. The third predictor variable at 17th observation is equal to -0.06721. This value is include in criteria \( X_3 \leq -0.01800934 \), so the function used for \( (X_{3,10}) \) is

\[ f_3(X_{3,10}) = 0.7624393118 + 9.3705596681X_3 ; \] \( X_3 \leq -0.01800934 \)
\[ f_3(X_{3,10}) = 0.7624393118 + 9.3705596681(-0.06721) \]
\[ = 0.132643996 \]

d. The fourth predictor variable at 10th observation is equal to 0.096061. This value is include in criteria \( X_4 \geq 0.02535196 \), so the function used for \( (X_{4,10}) \) is

\[ f_4(X_{4,10}) = 0.869714149 + 12.40488437X_4 ; \] \( X_4 \geq 0.02535196 \)
\[ f_4(X_{4,10}) = 0.869714149 + 12.404888437(0.096061) \]
\[ = 2.061339746 \]

In full, the penalized spline estimator of 10th observation is :

\[ \eta_{10} = \sum_{j=1}^{4} f_j(X_{j,10}) \]
\[ = -1.950 + 1.134102235 + 0.132643996 + 2.061339746 \]
\[ = 1.378085977 \]

Next, by using nonparametric logistic regression we get the following estimated values :

\[ \hat{\mu}_{10} = \frac{\exp(1.378085977)}{1 + \exp(1.378085977)} = 0.798 \]

Obtained \( \hat{\mu}_{10} \) value then classified as category \( y = 1 \) for lung tumor and \( y = 0 \) for normal lung. This is done by determining the threshold value is used as a comparison or cut off in the classification of normal lung and lung tumors contained in Table 3 as follows :
| No. | Threshold | Accuracy |
|-----|-----------|----------|
| 1.  | 0.04      | 50       |
| 2.  | 0.06      | 52.5     |
| 3.  | 0.08      | 50       |
| 4.  | 0.1       | 52.5     |
| 5.  | 0.11      | 55       |
| 6.  | 0.15      | 57.5     |
| 7.  | 0.16      | 55       |
| 8.  | 0.17      | 57.5     |
| 9.  | 0.19      | 60       |
| 10. | 0.21      | 62.5     |
| 11. | 0.23      | 67.5     |

Threshold that will be used as a reference for cut-off category 0 or category 1 is determined by looking at the highest classification accuracy score and highest threshold value which has the highest classification accuracy, so that the selected threshold value obtained previously has value 0.60. If expected $\hat{\mu}_i$ value more than threshold value so it classified as lung tumors image $y = 1$, vice versa. The classification result based on value $\hat{f}_i$ in the observation which have been analyzes using parametric and nonparametric regression models approaches are given in Table 4.

| Observation | Lung Tumor | Normal | Total |
|-------------|------------|--------|-------|
| Lung Tumor  | 16         | 4      | 20    |
| Normal      | 4          | 16     | 20    |
| Total       | 20         | 20     | 40    |

Next, we calculate the probability of errors by APPER calculation based on parametric and nonparametric regression models approaches.

$$APPER = \frac{4 + 4}{16 + 4 + 4 + 16} \times 100\% = 20\%$$

$$APPER = \frac{4 + 2}{16 + 4 + 4 + 18} \times 100\% = 15\%$$

Based on APPER values, we obtain the classification accuracy values of lung tumor are 80% for parametric regression model approach and 85% for nonparametric regression model approach. It means that nonparametric regression model approach based on penalized spline is better than parametric regression model approach based on logit link function for determining classification accuracy values of lung tumor on human chest x-ray image.

The Press’Q is compared with $\chi^2_{0.05,1} = 3.841$. Because of the Press’Q = 19.6 is greater than $\chi^2_{0.05,1} = 3.841$, so the nonparametric regression model approach based on penalized spline estimator is significantly appropriate for identify lung tumor oh human chest x-ray images.
4. Conclusion
The classification accuracy normal lung and lung tumor by using penalized spline estimator show high accuracy than by using nearest model implementation[8]. The accuracy classification for lung tumor is 85%. So we can conclude if the classification using penalized spline estimator is good to classify lung tumor on human chest x-ray.

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