CLASSIFICATION OF GLIOMA BRAIN TUMORS IN MR IMAGES USING IMAGEJ-BASED RADIOMIC ANALYSIS

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CLASSIFICATION OF GLIOMA BRAIN TUMORS IN MR IMAGES USING IMAGEJ-BASED RADIOMIC ANALYSIS

by

NURIZZATUL HADAWIYAH BINTI MOHAMED ZAFRIN

Dissertation submitted in partial fulfilment of the requirements for the degree of

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CERTIFICATE

This is to certify that the dissertation CLASSIFICATION OF GLIOMA BRAIN TUMORS IN MR IMAGES USING IMAGEJ-BASED RADIOMIC ANALYSIS is the bona fide record of research work done by Ms NURIZZATUL HADAWIYAH BINTI MOHAMED ZAFRIN during the period from October 2023 to July 2024 under my supervision. I have read this dissertation and that in my opinion it conforms to acceptable standards of scholarly presentation and is fully adequate, in scope and quality, as a dissertation to be submitted in partial fulfilment for the degree of Bachelor of Health Science (Honours) (Medical Radiation).

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TABLE OF CONTENTS

LIST OF TABLES

Page

LIST OF FIGURES

Page

LIST OF ABBREVIATIONS

AI	Artificial intelligence
BBB	Blood-brain barrier
CNN	Convoluted Neural Networks
CSF	Cerebrospinal fluid
GAD	Gadolinium
GBCA	Gadolinium based contrast agents
GBM	Glioblastoma multiforme
MRI	Magnetic resonance imaging
NAWM	Normal appearing white matter
PCE	Post-contrast enhancement
RGB	Red, green blue
ROI	Region of interest
LUT	Lookup table
T1W	T1-weighted
T2W	T2- weighted
USM	Universiti Sains Malaysia
WHO	World Health Organization

PENGELASAN TUMOR OTAK GLIOMA DALAM IMEJ MR MENGGUNAKAN ANALISIS RADIOMIK BERASASKAN IMAGEJ

ABSTRAK

Tujuan kajian ini adalah untuk mengelaskan tahap tumor glioma di otak menggunakan analisis radiomik berasaskan ImageJ. Kajian ini menggunakan pengimejan resonans magnetik (MRI) berasaskan aplikasi ImageJ (Fiji) untuk menjalankan analisis radiomik secara kuantitatif bagi menilai tumor glioma tanpa menggunakan sebarang agen kontras berasaskan gadolinium (GBCA). Glioma boleh dikategorikan dari glioma tahap rendah (LGG) (Tahap I dan II) hingga glioma tahap tinggi (HGG) (Tahap III dan IV). Penggredan tumor yang tepat adalah penting untuk menentukan kaedah rawatan yang sesuai. Ini ialah kajian retrospektif ke atas 12 imej berwajaran T2 (T2W) (n=12) ke atas pesakit yang telah di diagnosis glioma tahap satu hingga empat yang diperoleh di Jabatan Radiologi, Hospital Universiti Sains Malaysia dari Sistem Arkib dan Komunikasi Gambar (PACS). Satu potongan imej daripada siri T2W telah dipilih untuk analisis dan kesemua imej dianalisis untuk kualiti imejnya. Seterusnya, aliran kerja dan protokol untuk pemprosesan imej diterokai menggunakan ImageJ. Lesi dan tisu putih normal yang kelihatan (NAWM) telah dipilih untuk analisis histogram berdasarkan kawasan tumpuan (ROI), berikutnya, pengiraan nisbah lesi ke tisu normal (LNR) dan analisis sisihan piawai lesi (SD_L) dijalankan untuk penilaian heterogeniti dan keamatan tumor. Selain itu, penapisan nilai ambang warna secara entropi, imej jadual carian (LUT) dengan imej permukaan plot 3D, dan pengukuran sudut anjakan garis tengah otak digunakan untuk menilai ciri-ciri tumor seperti sempadan tumor, edema, dan impak tumor. Hasil kajian ini tidak menunjukkan sebarang trend bagi nilai keamatan tumor berdasarkan pengiraan

LNR, namun SD_L tumor menunjukkan trend peningkatan dari tahap glioma satu hingga empat, yang membuktikan peningkatan heterogeniti apabila tahap glioma meningkat. Sempadan tumor dapat digambarkan menggunakan imej yand ditapis nilai ambang warna secara entropi, manakala edema dapat digambarkan oleh imej LUT. Akhirnya, impak tumor dapat digambarkan dengan pengukuran sudut anjakan garis tengah otak yang menunjukkan tumor bertahap tinggi dengan nilai yang lebih jauh daripada 180.0° dan dalam imej permukaan plot 3D. Kesimpulannya, analisis radiomik berasaskan ImageJ memberikan kaedah yang mudah diakses dan ringkas untuk mengelaskan tumor glioma di otak. Kaedah radiomik ini mungkin dapat memudahkan penggredan tumor tanpa menggunakan GBCA.

CLASSIFICATION OF GLIOMA BRAIN TUMORS IN MR IMAGES USING IMAGEJ-BASED RADIOMIC ANALYSIS

ABSTRACT

The aim of this study is to classify glioma brain tumor grades using ImageJ-based radiomic analysis. This study utilizes magnetic resonance imaging (MRI) with ImageJ (Fiji) software to perform radiomic analysis, providing a quantitative method to evaluate Glioma tumor without the use of Gadolinium based contrast agents (GBCAs). Gliomas can range from low grade gliomas (LGGs) (Grades I and II) to high grade gliomas (HGGs) (Grades III and IV) tumors. Accurate grading of tumor is vital in determination of the appropriate treatment. This is a retrospective study on 12 T2-weighted (T2W) images (n=12) of patients with pathologically diagnosed glioma of different grades retrieved at the Radiology Department, Hospital Universiti Sains Malaysia from Picture Archiving and Communications System (PACS). A single slice of T2W image is chosen for analysis and all of the images were analysed for its image quality. Then, a workflow and protocol for image processing were explored using ImageJ. The lesion and normal appearing white matter (NAWM) region of interest (ROI) were selected for histogram analysis, along with lesion to normal tissue ratio (LNR) calculations and standard deviation of lesion (SD_L) analysis for the assessment of tumor heterogeneity and intensity. Additionally, color thresholding, lookup table (LUT) images with 3D plot surface images, and midline shift angle measurements were used to assess tumor characteristics such as the margin, edema, and mass effect. The result of this study shows no specific trend for the tumor intensity based on LNR findings; however the SD_L of the tumor shows an increasing trend across the glioma grades, which proves the increasing heterogeneity as

the glioma grades increase. The margin of the tumor can be depicted by entropy thresholding, the edema is depicted by LUT images. Finally, the mass effect is depicted by the measurement of midline shift angle where higher-grade tumor depicts further deviation from 180.0° and in 3D surface plot images. In conclusion, ImageJ-based radiomic analysis provides an accessible and simple method for classifying glioma brain tumors. This approach may potentially facilitate tumor grading without the use of GBCAs.

CHAPTER 1

INTRODUCTION

1.1 Background of Study

1.1.1 Glioma Brain Tumors and Classification

According to the Global Cancer Observatory, there were an estimated 300,000 cases of brain and nervous system tumors globally in 2020 (Sailunaz et al., 2023). Brain tumors are abnormal cell growths in the brain or central spinal canal, originating from brain cells, meninges, nerves, or glands. The anatomy of a healthy brain is as shown in Figure 1.1. Brain tumors are classified as either benign (non-cancerous) or malignant (cancerous). Benign tumors have a uniform structure, while malignant tumors are heterogeneous and contain cancerous cells. Malignant brain tumors are especially dangerous as they invade neighbouring tissues and form metastases (Kumar et al., 2017). Figure 1.2 depicts a normal healthy brain, brain with benign tumor, and brain with malignant tumor in T2W MR images.

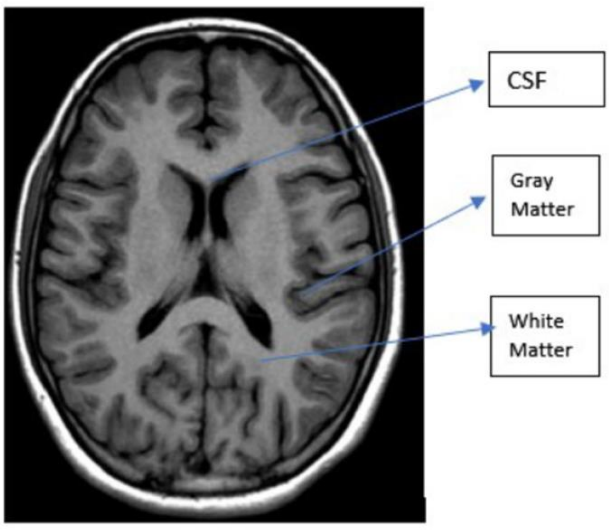

Figure 1.1 Example of healthy brain MR image anatomy (Kaifi, 2023)

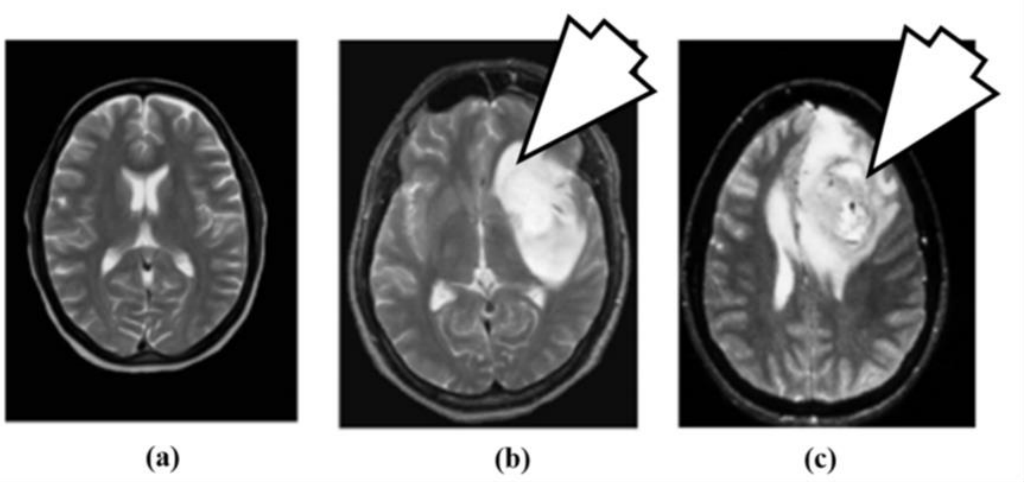

Figure 1.2 Example of T2W brain MR images (a) healthy, (b) benign tumour and (c) malignant tumor (Tandel et al., 2019)

Gliomas originate from the glial cells and are the most common brain tumors which accounts for about 78% of malignant brain tumors. They are classified based on histological traits, genetic mutations, and imaging characteristics. Gliomas range from low-grade gliomas (LGG) classified as Grade I or II, to high-grade gliomas (HGG) classified as Grade III or IV (Kaifi, 2023). Grade I gliomas grow slowly and have a good prognosis, while Grade IV gliomas are highly aggressive (Louis et al., 2016). LGGs are typically benign and can often be surgically removed, whereas HGGs are malignant and difficult to remove due to their infiltrative nature (Chatterjee et al., 2022).

1.1.2 The Role of MR Imaging in Brain Tumor Assessment

Magnetic resonance (MR) imaging is the primary diagnostic tool for brain tumors due to its superior soft tissue contrast compared to other imaging methods. T1-weighted (T1W) and T2-weighted (T2W) images, along with contrast-enhanced sequences, are used to visualize tumor anatomy, morphology, and location (Chatterjee et al., 2022).

Typically, images are acquired in three basic planes, which include the axial, sagittal, and coronal planes, to thoroughly visualize the brain's anatomy. Tumor grading and classification involve both non-invasive imaging and invasive biopsies, combining visual interpretation by oncologists and pathological analysis. Figure 1.3 shows all the basic MRI planes; axial view, sagittal view, and coronal view used in standard brain protocol.

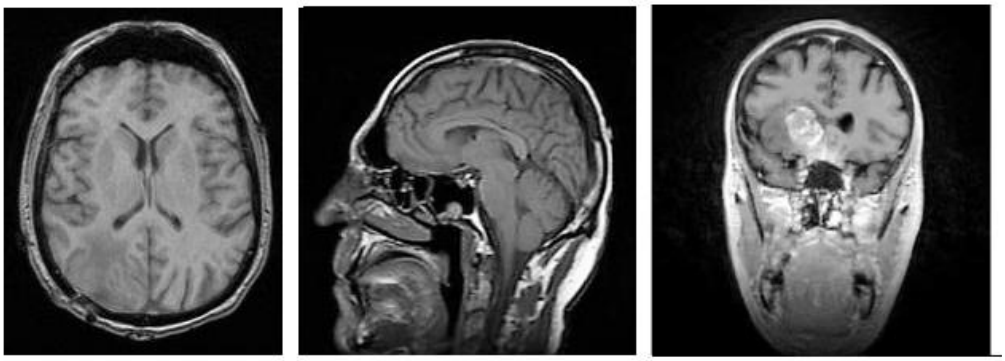

Figure 1.3 Basic MRI planes (Tandel et al., 2019)

1.1.3 Radiomic Approach in Brain Tumor Assessment

Radiomic analysis involves extracting and analysing quantitative features from images, which enables the detection of additional imaging traits not visible to the naked eye (Hassani et al., 2019). Typically, in medical image analysis, quantitative approach acts as complementary tool to qualitative assessments, offering a more comprehensive understanding and interpretation of certain situations. These methods involve a diverse range of software platforms such as MATLAB, Python, and ImageJ (Fiji), each offering unique functionalities tailored to specific analytical tasks.

ImageJ (Fiji) is a Java-based image processing tool that is available on the public domain which runs on operating software. It has a simple interface, user-friendly, and can perform a wide range of imaging manipulations (Abramoff et al., 2004). It provides an alternative, and affordable way of robust image analysis with wide range of capabilities including image segmentation, colorimetric detection, and color thresholding with various color spaces (Woolf et al., 2021). It provides a versatile framework for image analysis, enabling researchers to develop and apply a variety of plugins tailored to specific imaging tasks. ImageJ (Fiji) also integrates various plugins and facilitates easier installation and usage of these extensions, significantly enhancing its functionality and usability for complex image analysis tasks (Schneider, 2012). The typical ImageJ (Fiji) interface is as shown in Figure 1.4.

Researchers can use this software to perform tasks such as image segmentation, feature extraction, and data visualization. The platform's extensibility and robust plugin architecture make it particularly well-suited for handling various high-dimensional data which is typical in radiomic studies (Hassani et al., 2019). Additionally, with this

software, feature selection and extraction can be done followed by classification whereby related datasets can be classified together according to shared features. Consequently, this technique may allow for computer-aided diagnostic (CAD) technology for radiologists that use computer visualization for the analysis of radiological and pathological images.

Thus, in this study, radiomic analysis with the integration of ImageJ (Fiji) software can be developed in quantifying the hidden features and characteristics of the MR images.

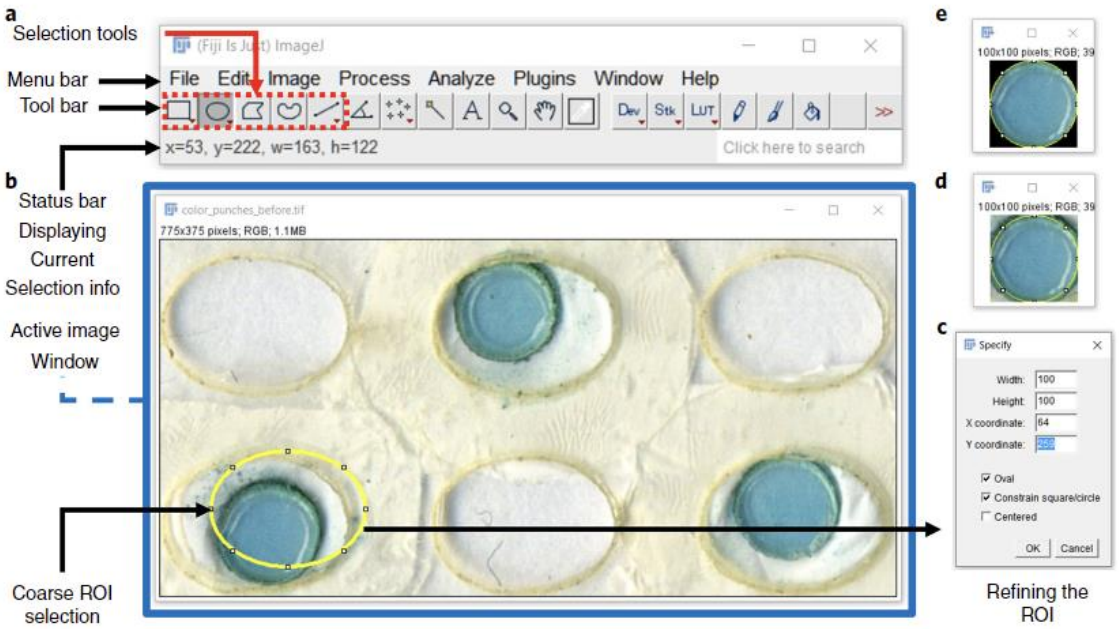

Figure 1.4 Overview of ImageJ (Fiji) interface (Woolf et al.,2021)

1.2 Problem Statement

Usually, a normal MRI scan is performed to detect brain tumours. Contrast enhanced MRI using Gadolinium-based contrast agent (GBCAs) are performed to further investigate whether the tumours are benign or malignant. This dynamic contrast-enhanced MRI study provides detection of tumours from other pathological processes and distinguishes information on tissue perfusion, vasculature, capillary permeability, and interstitial space volume (Zhang et al., 2020).

However, the Gadolinium-based contrast agents (GBCAs) which are administered in dynamic contrast-enhanced MRI can impose risk to patients such as diverse minor side effects including dizziness, nausea, itching and are unsuitable for patients with renal insufficiency. Besides, patients with significant renal issues are more susceptible to gadolinium poisoning and nephrogenic systemic fibrosis (Asadollahzade et al., 2022).

Radiomic approach provides quantitative information through various methods of image extraction and analysis. In this study, we apply ImageJ-based radiomic analysis to develop a technique to be used in classification of glioma brain tumour grades using the available methods. We explore the possibility to differentiate the glioma grades without any use of GBCAs.

1.3 Research Aim and Objectives

1.3.1 General Objective

The aim of the study is to classify glioma brain tumor grades using ImageJ-based radiomic analysis.

1.3.2 Specific Objectives

1. To analyse the intensity and the homogeneity of the tumor and normal appearing white matter (NAWM) tissues surrounding the tumor according to glioma brain tumor grades using ImageJ-based histogram.
2. To analyse the margin (edge) and edema (fluid leakage) surrounding the tumour based on threshold and lookup table (LUT) images.
3. To analyse the mass effect of the tumor based on 3D surface plot images and midline shift angle measurements.

1.4 Significance of Study

This research proposes the classification of glioma brain tumor grades by using radiomic analysis using a freely available software called ImageJ. This study will help in determining a potential method to analyse and characterize the type of brain tumours based on MR images. In which the methodology of this study is able to be implemented by anyone universally, regardless of their economical disposition, as the ImageJ software is freely available on the public domain for download. ImageJ is user-friendly and is able to provide a wide range of image powerful manipulation capabilities without financial costs. Moreover, it provides a recognition of patterns and further understanding of the texture and contrast of the tumours as compared to the normal tissue.

CHAPTER 2

LITERATURE REVIEW

2.1 Brain Tumors

Brain tumors are unexpected growth of brain cells arising from the surrounding cells of the brain which include the central spinal canal, meninges, nerves, or glands. Brain tumors, though relatively rare, have significant clinical implications due to their high morbidity and mortality rates. According to Kaifi (2023), brain tumors account for approximately 1.4% of all new cancer cases annually in the United States of America. There are an estimated of 23,820 new cases of primary brain tumors diagnosed each year.

2.1.1 Glioma Brain Tumors

The World Health Organization (WHO) categorized brain tumors into 120 kinds based on the origin and behaviour of the cell. In brief, gliomas can be classified from Grade I (least malignant) to Grade IV (most malignant).

For example, pilocytic astrocytoma falls under Grade I, while diffuse astrocytomas, oligodendrogliomas, and oligoastrocytomas fall under Grade II. Grade III tumors include anaplastic astrocytoma and anaplastic oligodendrogliomas. All glioblastomas, which are highly malignant and infiltrative, are classified as Grade IV (Chatterjee et al., 2022). Table 2.1 demonstrates all the gliomas and their classifications under the WHO grading system.

Table 2.1 Classification of glioma brain tumors (Adapted from Perry & Wesseling, 2016)

WHO Grade	**Diffuse glioma**			**Other astrocytic tumor**
	Astrocytic	Mixed	Oligodendroglial	
I				Pilocytic astrocytoma subependymal giant cell astrocytoma
II	Low grade diffuse astrocytoma	Low grade Oligoastrocytoma	Low grade Oligodendroglioma	Pleiomorphic Xanthoastrocytoma
III	Anaplastic astrocytoma	Anaplastic Oligoastrocytoma	Anaplastic Oligodendroglioma	Anaplastic Pleiomorphic Xanthoastrocytoma
IV	Glioblastoma			

2.2 Brain MRI

Instrumentation of a standard clinical brain MRI protocol is comprised of various components designed to optimize image quality and diagnostic accuracy. The core element is a high-field magnet, typically 1.5 Tesla or 3.0 Tesla, which provides a strong and stable magnetic field central for aligning hydrogen protons in the brain.

For brain MRI, a radiofrequency (RF) head coil is used to transmit RF pulses and receive the resulting signals. Gradient coils produce varying magnetic fields that enable the spatial encoding of MR signals, which provides detailed three-dimensional imaging. The patient lies on a table that slides into the magnet gantry bore, while an advanced computer system controls the MRI machine, processes signals, and reconstructs the images.

The standard brain MRI protocol sequences include T1W, T2W and FLAIR images to highlight different tissue properties and abnormalities. GBCAs are often used to enhance the visibility of certain tissues or abnormalities, and are employed with T1W sequence images (Kaifi, 2023).

2.2.1 General Protocol

The conventional evaluation using clinical radiology is done by acquiring multiple MRI sequences such as T1W, T2W and FLAIR with and without the use of Gadolinium contrast followed by visual assessment of the radiologist. Figure 2.1 shows the examples of typical MRI sequences such as FLAIR, T1W and T2W images. Furthermore, added MRI techniques such as diffusion-weighted imaging (DWI), MR spectroscopy (MRS), and perfusion-weighted imaging (PWI) are also utilized in grading of tumors.

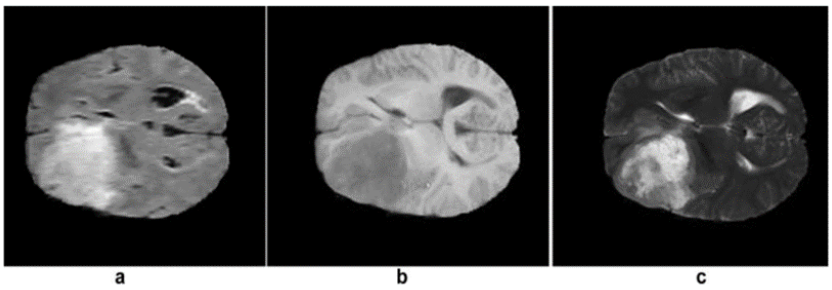

Figure 2.1 Examples of different of MRI sequences; (a) FLAIR, (b) T1W, and (c) T2W images (Kaifi, 2023)

The grey level intensity values depend on cell density, causing the intensity of tumorous tissues in brain MRI images to vary. On T1W images, tumors generally appear with low or medium grey intensity, while on T2W images, they typically exhibit bright intensity. The characteristics of different MRI sequences are detailed in the Table 2.1.

Table 2.2 Characteristics of brain tissue in different MR image sequences (Kaifi, 2023)

	T1	T2	Flair
White Matter	Bright	Dark	Dark
Gray Matter	Gray	Dark	Dark
CSF	Dark	Bright	Dark
Tumor	Dark	Bright	Bright

2.3 Classification of glioma brain tumour in MR images

2.3.1 Radiological Characteristics

The radiological characteristics of the glioma brain tumor can be summarized by observing four different features of the tumor which is the homogeneity and the intensity of the tumor, the margin which is denoted by the edge of the tumor, the peritumoral edema surrounding the tumor and the mass effect measured by the midline shift of the brain (Radiologyassistant.nl.,2008). The difference observed between LGGs and HGGs are as shown in Table 2.3.

2.3.1(a) Homogeneity and Intensity of Tumor

In T2W and FLAIR images, gliomas are to appear hyperintense, whilst in 92% of T1W images they appear as hypointense. Additionally, HGG demonstrated heterogeneous contrast enhancement with other characteristics such as bleeding, necrosis, and edema (Haydar et al., 2022). LGG tumors generally show homogeneous signal intensity and less contrast enhancement (Essig et al., 2006).

2.3.1(b) Margin/ edge

According to Radiologyassistant.nl (2008), high-grade gliomas (HGGs) demonstrate irregular edges in MR images. The aggressive infiltration of tumor cells into adjacent brain parenchyma contributes to this irregular appearance.

Low-grade gliomas (LGGs) (Grade I and II), on the other hand, tend to have more defined and smoother margins compared to high-grade gliomas. The tumor edges are often clearer and more demarcated, suggesting slower growth and less invasive nature of LGGs (Essig et al., 2006). Additionally, LGGs usually present with well-defined edges

due to the lack of edema and necrosis seen in HGGs. The tumor boundaries are more distinct, making it easier to differentiate the tumor from surrounding brain tissue in MR images.

2.3.1(c) Peritumoral edema

Peritumoral edema is routinely determined using MR images to visualize the proper development of brain lesions, T2W images are used to represent peritumoral edema as high intensity areas due to increased water content, while T1W PCE images detect only the tumor mass. The peritumoral edema is the most frequently observed in HGGs (Haydar et al., 2022).

The region of peritumoral edema is associated with the disruption of the blood brain barrier (BBB) integrity. The BBB is usually leaks at about the centre of well-vascularized, actively proliferating edge of lesion adjacent to the tumour area. Thus, there is a correlation between the degree of enhancement and the volume of the peritumoral edema (Essig et al., 2006). Figure 2.2 demonstrates the difference in visualisation of HGG with peritumoral edema in T1W PCE, T2W and FLAIR images.

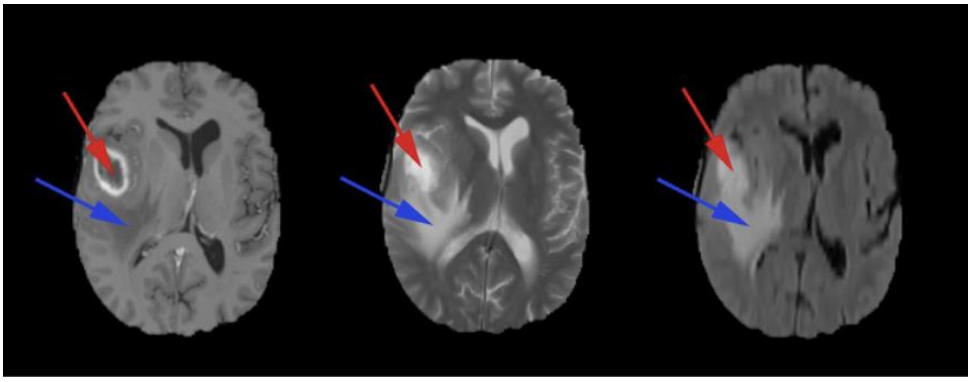

Figure 2.2 High grade glioma (HGG) on T1W PCE, T2W, and FLAIR image (Red arrow) with peritumoral edema (Blue arrow) (Left to right) (Chatterjee et al., 2022)

2.3.1(d) Mass effect

The mechanical interaction of the growing tumor and the surrounding tissue is called the mass effect. Midline shift is one of the mass effects caused by shifting of the brain structures in the presence of tumor (Lipková et al., 2022). In the presence of a tumor, the fluid build-up around the tumour core causes swelling which increases the intracranial pressure (ICP) of the brain which then leads to an imbalance of pressure to the left and the right hemisphere of the brain, which results in deformity to the midline.

The brain midline is observed clearly in the middle slice of the CT brain image. The midline is portrayed as a curve connecting the centres of attachment of the falx. Figure 2.3 represents the middle brain CT image its anatomical markers. Clinically, in the middle axial slice of a radiological image portraying the frontal horn and third ventricle are used as the marker of the brain midline shift (Liu et al., 2014). The midline is an imagined line separating the brain into left and right hemispheres. The ideal midline of a healthy brain is a straight line. Figure 2.4 shows the difference between an ideal, straight midline and a curved midline of the brain.

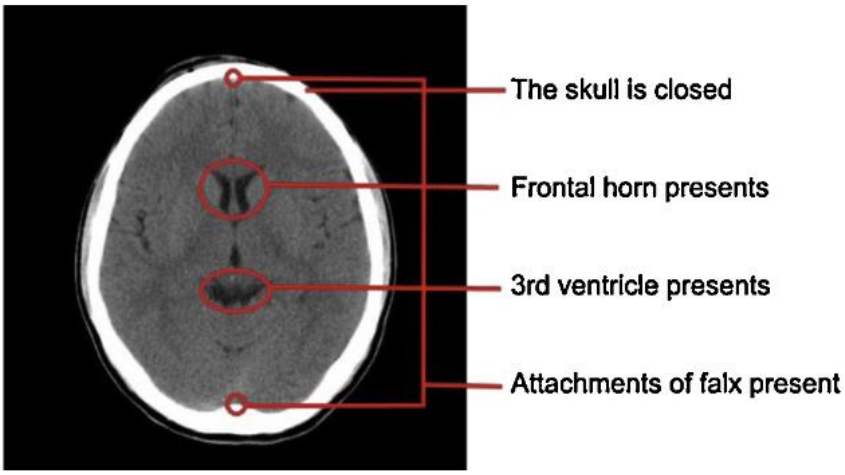

Figure 2.3 The middle brain CT image and the anatomical markers (Liu et al., 2014)

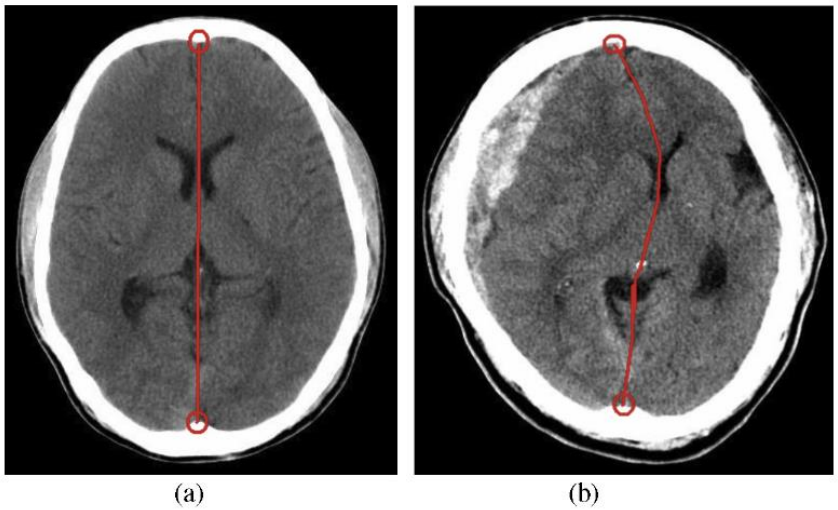

Figure 2.4 (a) Straight midline, (b) Curved midline of the brain (Liu et al., 2014)

Table 2.3 Clinical radiology characteristics of glioma grades (Adapted from Radiologyassistant.nl.,2008 and Haydar et al., 2022)

Characteristic	Low grade (Grade I and II)	High grade (Grade III and IV)
Enhancement	Hyperintense Homogenous enhancement seen in the solid component of Pilocytic astrocytoma	Hyperintense and heterogenous Patchy enhancement can be seen due to bleeding, necrosis, and edema. In GBM, areas of hyperintensity are seen combined with regions of necrosis and haemorrhage. GBM can also have a low signal intensity as they seldom are dense and have a low water content and hypercellular causing high nuclear-cytoplasmic ratio.
Margins/ edge	Usually have well-defined margins	Poor and ill-defined margin of the lesion edge. Is less distinctive and poorly demarcated compared to LGG
Edema	Minimal or no surrounding edema is usually present.	Tumors can disrupt the normal integrity of the BBB, leading to fluid leakage into the surrounding brain tissue. This is associated with increased presence of peritumoral edema.
Mass effect	Less pronounced to no significant midline shift and herniation	Significant pressure is exerted onto surrounding tissues causing midline shift and herniating.

2.4 Radiomics

Radiomics can be defined as a method that involves the extraction of a large number of quantitative features from medical images using data characterization algorithms based on physical properties of the object of interest. These features encompass various aspects of the images, such as the shape, texture, attenuation, and intensity, which are converted into comprehensive datasets.

MRI feature extraction can be used for diagnostic grading and prognosis of gliomas, providing a more powerful diagnostic tool (Chen et al., 2022). This aligns with the radiomic approach, which leverages advanced image processing techniques to extract quantitative features from medical images, facilitating a more comprehensive analysis of tumor characteristics. Figure 2.5 shows an example of ImageJ radiomics workflow while Figure 2.6 shows an example of image analysis workflow that includes input, output, and visualization.

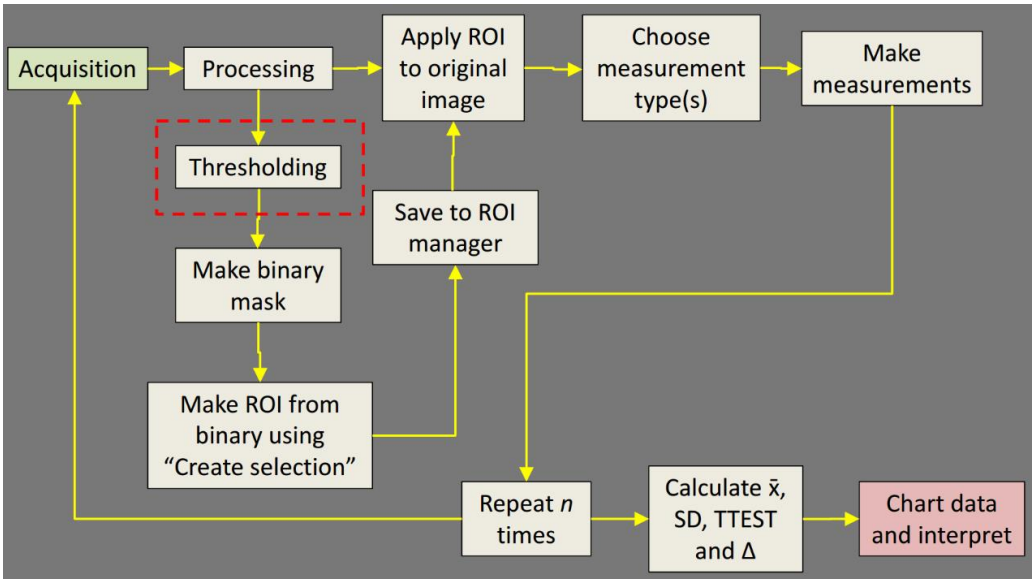

Figure 2.5 Example of ImageJ radiomics workflow (Willett & Johnson, n.d.)

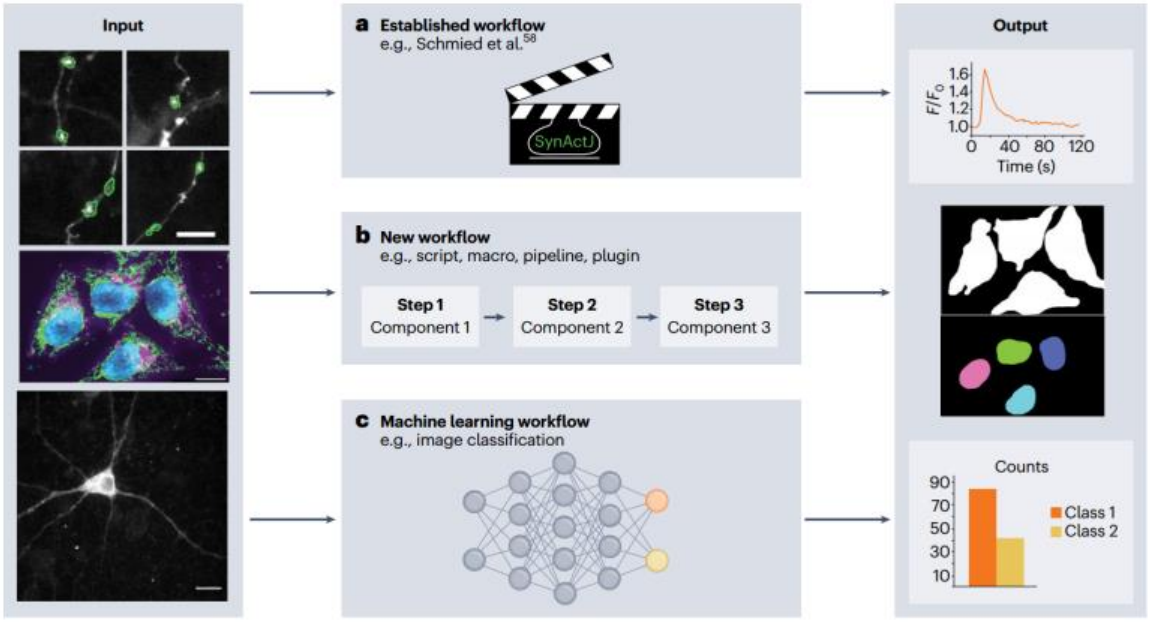

Figure 2.6 An example of image analysis workflow that includes input, output, and visualization (Schmied et al., 2024)

2.4.1 ImageJ (Fiji)

ImageJ is a freely available Java-based image processing program, that was developed at the National Institutes of Health (NIH) in collaboration with the Laboratory for Optical and Computational Instrumentation. ImageJ offers various tools that can be used to achieve objective, colorimetric detection and subsequently robust data analysis by exploiting a range of image manipulation techniques, including region of interest (ROI) selection, color thresholding and image masking via independent manipulation of color channels. ImageJ delivers a simplistic and user-friendly approach, providing users who have low experience and expertise in image processing or computer programming with the ability to access and curate an objective, colorimetric data (Woolf et al., 2021).

ImageJ, particularly with its latest extended Fiji distribution, plays a significant role in the radiomic process. It provides versatile tools for image preprocessing, segmentation, and feature extraction, which is crucial for detailed radiomic analysis

(Abramoff et al., 2004). By using ImageJ (Fiji), researchers can methodically analyse tumor heterogeneity and other imaging biomarkers, improving diagnostic accuracy and treatment planning (Woolf et al., 2021).

2.4.2 ImageJ based radiomic analysis

2.4.2(a) Histogram analysis

ImageJ (Fiji) supports the processing and analysis of RGB (Red, green, blue) images, which are composed of three color channels which are red, green, and blue. RGB colour space is a widely used model where each component can range from 0 to 255 in 8-bit colour depth (2^8 = 256) which results in over 16 million possible colour combinations.

Histograms in ImageJ (Fiji) can be used to analyse the distribution of colors or grayscale of an image. The histogram depicts the distribution of pixel intensities where the range depends on bit-depth (8-bit = 255, 12-bit = 4095, 16-bit = 65,535). A color histogram computes the frequency of each color and displays these counts as bars or lines, creating a visual representation of color composition. In ImageJ, color histograms can be produced for each RGB channel, enabling users to analyse and compare the intensity frequencies of colors within an image (Woolf et al.,2021). An example of a greyscale histogram is as shown in Figure 2.7.

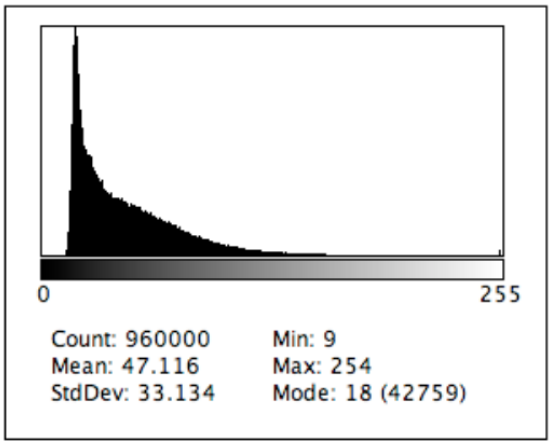

Figure 2.7 Example of greyscale histogram (Woolf et al.,2021)

2.4.2(b) Color thresholding

On the other hand, color thresholding is an essential method for segmenting images by isolating objects of interest from the background based on their color. Using ImageJ (Fiji), users can perform color thresholding by manually adjusting thresholds for each RGB channel individually. The thresholding approach is a straightforward and effective way to separate the required region. Based on picture intensity, threshold values are chosen using histogram analysis. The ImageJ-generated histograms provide a pathway to more objective segmentation, providing that choosing threshold values is not completely random or arbitrary. Figure 2.8 demonstrates the color thresholding window of an image. This capability enhances the precision of segmentation tasks, making it easier to analyse images accurately (Woolf et al.,2021).

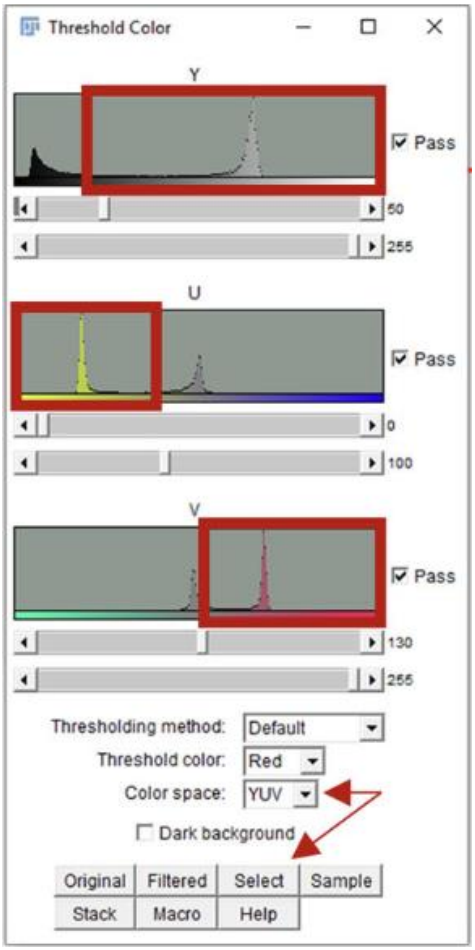

Figure 2.8 Color thresholding an image (Woolf et al.,2021)

2.4.2(c) LUT images

Lookup table (LUT) images are used in various fields of imaging and data visualization to map and manipulate the colors of an image based on its intensity values. LUTs can be used to enhance the contrast of an image, enhancing certain features. For instance, modifying the LUT can help in emphasizing the boundaries of structures in medical images. Additionally, applying a LUT can map grayscale values to colors, making it easier to differentiate between different intensity levels. This is also particularly useful in medical imaging where subtle differences in intensity can suggest important information (Schneider, 2012).

2.4.2(d) 3D Surface plot

3D surface plot in ImageJ is typically used to analyse various types of data where visualizing intensity, elevation, or where the depth in three dimensions is beneficial. The 3D surface plot image produces maps of regions of high and low expressions by extracting quantitative data such as volume, surface area, and feature dimensions. This provides a visual gradient and transition in intensity which can indicate different tissue properties or biological states (Schneider, 2012).

2.5 Review of previous studies related to brain tumor analysis

In the recent past, there are various other studies conducted on classification of brain tumours of different types, based on multiple methods, which includes convoluted neural networks (CNN), machine learning, spatiospatial models, and multi-level thresholding.

2.5.1 Lesion-to-normal ratio (LNR) calculation

In a study conducted by Taib et al. (2020), a method of calculating the lesion-to-normal tissue ratio (LNR) to analyse the severity of a Leukoaraiosis spot, a type of brain lesion is introduced. The LNR parameter of this study is measured using the parameter called mean diffusivity (MD) and is calculated using the following formula,

$$LNR = \frac{MD_N - MD_L}{MD_N} \quad 2.2$$

Whereby, MD is the mean diffusivity, MD_N stands for the mean diffusivity of the normal tissue and MD_L is of the lesion. The MD is one of the quantitative parameters of diffusion tensor imaging (DTI) that is able to provide recognition between normal and pathological tissues on a molecular level. Additionally, MD is able to provide information about the mean displacement of water diffusion in white matter tissues in the brain MR image. As well, it is found that LNR increases correlation accuracy by including the mean diffusivity (MD) of a normal tissue in classification of tissue damage severity (Taib et al., 2020).

Consequently, in this study, the use of this formulae is explored to be utilised in classification of the grades of glioma brain tumours by integrating the use of ImageJ.