ACLTSHE-AMTS: A NEW ADAPTIVE BRAIN TUMOUR ENHANCEMENT AND SEGMENTATION APPROACHES

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by

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LIST OF ABBREVIATIONS

3D	Three-dimensional
AMTS	Adaptive Multilevel Thresholding Segmentation
ALDE	Adaptive Differential Evolution with Lévy Distribution
PSO	Particle Swarm Optimization
DE	Differential Evolution
MOGOA	Multi-objective Grasshopper Optimization Algorithm
N3	Nonparametric Nonuniformity Normalization
HE	Histogram Equalization
CLAHE	Contrast limited Adaptive Histogram Equalization
ABHE	Adaptive Bi-Histogram Equalization
ACLTSHE	Adaptive Clip Limit Tile Size Histogram Equalization
ACO	Ant Colony Optimization
AEIHE	Adaptive Entropy Index Histogram Equalization
AHE	Adaptive Histogram Equalization
AIVHE	Adaptively Increasing the Value of Histogram Equalization
AMBE	Absolute Mean Brightness Error
ATSHE	Adaptive Thresholding-Based Sub-Histogram Equalization
BBHE	Brightness Preserving Bi-Histogram Equalization
BHE	Bi-sub-imaging HE
BOHE	Block Overlapped HE
BPDHE	Brightness Preserving Dynamic Histogram Equalization
CDF	Cumulative Distribution Function
CII	Contrast Improvement Index
ccRFs	Concatenated and Connected Random Forests
CL	Clip Limit

CLR	Clip Limit Range
CLAHE	Contrast Limited Adaptive Histogram Equalization
CMBFHE	Cascaded Multistep Binomial Filtering HE
CNN	Convolutional Neural Network
CE	Cross Entropy
CSF	Cerebrospinal Fluid
CT	Computed Tomography
CRF	Conditional Random Field
DC	Differential Evolution
DSC	Dice Similarity Coefficient
DHE	Dynamic Histogram Equalization
DSIHE	Dualistic Sub-Image HE
EBBHE	Entropy-Based Bi-HE
EDSHE	Entropy-Based Dynamic Sub-HE
ET	Enhancing Tumor
EPLHE	Edge Preservation Local HE
ERHE	Exposure Region HE
ERMHE	Exposure-Region-Based Multi-H--E
ESIHE	Exposure-Based Sub-Image HE
FCM	Fuzzy C-means
FCNN	Fully Convolution Neural Network
GA	Genetic Algorithm
GLCM	Grey-Level Co-occurrence Matrix
HE	Histogram Equalization
HCNN	Heterogeneous Convolution Neural Network
HMRF	Hidden Markov Random Field
IARC	International Agency for Research on Cancer

IAECHE	Iterated Adaptive Entropy-Clip Limit Histogram Equalization
IIH	Intensity Inhomogeneity
ITRS	Information-Theoretic Rough Sets
KE	Kapur Entropy
KFECSB	Kernelized Fuzzy entropy Clustering with Baize Correction Method
LRSM	Left-Right Similarity Mask
Mean-BHEPL	Mean-Based Bi-HE Plateau Limit
Median-BHEPL	Median-Based Bi-HE Plateau Limit
MHE	Modified Histogram Equalization
MMBEBHE	Minimal Mean Brightness Error Bi-HE
MMSICHE	Median–Mean-Sub-Image Based Clipped HE
MOPSO	Multi-objective Particle Swarm Optimization
MR	Magnetic Resonance Images
OBBHE	Otsu- Based Brightness Preserving HE
OBBWTHE	Otsu-Based Bi-Weighted and Thresholded HE
PDF	Probability Density Function
POSHE	Partially Over-Loaded Sub-Imaging HE
SK-TPCNN	Small Kernel Two-Path Convolutional Neural Network
SNR	Signal-to-Noise Ratio
SRC	Sparse Representation Classification
SLIC	Simple Linear Iterative Clustering
PSNR	Peak Signal-to-Noise Ratio
PSO	Particle Swarm Optimization
QDHE	Quadrants For Dynamic Histogram Equalization
RF	Random Forest
RGB	Red, Green, Blue

RHE	Region Histogram Equalization
RLBHE	Range-Limited Bi-HE
RLWHE	Range Limited Weighted HE
RMSE	Root Mean Square Error
RMSHE	Recursive Mean Separate HE
RSIHE	Recursive Sub-Image HE
RSWHE	Recursively Separated Weighted HE
SSI	Structure Similarity Index
TS	Tile Size
TSR	Tile Sizes Ranges
WHE	Weighted HE
WMH	White Matter Hyperintensities
MOWOA	Multi-objective Whale Optimization Algorithm
WTHE	Weighted Threshold HE
WT	Whole Tumor

LIST OF APPENDICES

ACLTSHE-AMTS: KAEDAH-KAEDAH ADAPTIF BARU UNTUK PENINGKATAN DAN SEGMENTASI TUMOR OTAK

ABSTRAK

Pembahagian subkawasan tumor otak daripada imej multimodal Resonans Magnetik adalah tarikan minat terbesar untuk diagnosis tumor yang lebih baik. Ambang berbilang peringkat adalah salah satu pendekatan menonjol yang digunakan untuk pembahagian imej otak. Pada masa ini, apabila menggunakan ambang berbilang peringkat untuk pembahagian tumor otak, dua masalah penting mesti ditangani dengan teliti.. Pertama, imej otak MR yang mengalami kerumitan daripada kepekaan kepada ketidak-seragaman intensiti, kontras yang lemah dan perincian yang tersembunyi, menyebabkan kerosakan pada imej MR asal ketika diambil. Kedua, pendekatan ambang pelbagai lapis konvensional temasuk pendekatan ambang berasaskan pengoptimuman mempunyai beberapa isu utama seperti pelarasan manual ambang pelbagai lapisan, mendedikasikan kriteria ambang tunggal sebagai fungsi objektif membawa kepada kecenderungan ambang ke arah jenis imej MR tertentu, dan keperluan untuk menyesuaikan sebilangan besar parameter kawalan. Dalam tesis ini, pendekatan dua peringkat dicadangkan untuk menangani isu-isu ini. Diperingkat pertama, pendekatan terbaharu dikenali sebagai Penyamaan Histogram Klip Adaptif Had Saiz Jubin (ACLTSHE) telah dicadangkan untuk meningkatkan kontras, menyerlahkan perincian yang tersembunyi, dan mencapai taburan intensiti imej MR yang seragam. ACLTSHE mengabungkan Penyamaan Histogram Adaptif Kontras-Terhad, Algoritma Pengoptimuman Paus Pelbagai Objektif, Entropi Diskrit (DE), Nisbah Isyarat-ke-Bunyi Puncak (PSNR), dan Indeks Persamaan Struktur (SSI) untuk meningkatkan kualiti imej MR sementara mengekalkan struktur asal imej MR. Pada

peringkat kedua, pendekatan baharu yang dipanggil Pembahagian Ambang Adaptif Pelbagai Lapisan (AMTS) dicadangkan untuk pembahagian sub-rantau tumor otak tanpa seliaan daripada tisu otak biasa. Pendekatan AMTS membahagikan dan mengekstrak keseluruhan tumor, tumor teras, dan kawasan tumor yang dipertingkatkan dari imej MR otak, mengintegrasikan Algoritma Pengoptimuman Belalang Pelbagai Objektif, Entropi Kapur, Entropi Silang, dan kontur aktif setempat. Prestasi pendekatan ACLTSHE dan AMTS dinilai pada imej otak MR multimodal yang diperoleh daripada set data BRATS. ACLTSHE mampu menonjolkan butiran tempatan dan mengekalkan struktur imej MR asal tanpa amplifikasi bunyi dengan melaporkan nilai purata yang memberasangkan untuk DE, SSI, PSNR, dan Punca Min Ralat kuasa Dua (masing-masing 2.924, 0.862, 34.732 dan 2.882). AMTS digunakan untuk imej MR yang dipertingkatkan yang diperoleh daripada ACLTSHE dan mencapai skor purata dadu 0.901, 0.828, 0.843, dan 0.809 untuk membahagikan keseluruhan, teras, tidak dipertingkatkan, dan tumor yang dipertingkatkan, masing-masing. Keputusan yang dilaporkan menunjukkan bahawa pendekatan AMTS mencapai prestasi pembahagian yang memberangsangkan dan kompetitif berbanding dengan skor dadue yang dilaporkan pendekatan pembahagian tumor otak yang canggih. Secara keseluruhan, hasil pendekatan ACLTSHE dan AMTS menunjukkan potensi mereka untuk diguna pakai untuk meningkatkan dan membahagikan imej MR multimodaliti dalam aplikasi diagnosis tumor otak.

ACLTSHE-AMTS: A NEW ADAPTIVE BRAIN TUMOUR ENHANCEMENT AND SEGMENTATION APPROACHES

ABSTRACT

Brain tumor subregion segmentation from multimodal Magnetic Resonance (MR) images is of great interest for better tumor diagnosis. Multilevel thresholding is one of the prominent approaches used for brain image segmentation. Currently, when applying multilevel thresholding for brain tumor segmentation, two important problems must be carefully addressed. First, the MR brain images suffer from sensitivity to intensity inhomogeneity, poor contrast, and hidden details, which corrupt the original MR image during capturing. Second, the conventional multilevel thresholding approaches, including optimization-based thresholding approaches, have several main issues, such as manual adjustment of multilevel thresholds, dedicating single thresholding criteria as objective functions, leading to the bias of the thresholding towards a specific type of MR image, and the requirement to tune a large number of control parameters. In this thesis, a two-stage approach is proposed to address these issues. In the first stage, a new image enhancement approach called Adaptive Clip Limit Tile Size Histogram Equalization (ACLTSHE) is proposed to improve contrast, highlight the hidden details, and achieve homogenized intensity distribution of MR images. The ACLTSHE integrates Contrast-Limited Adaptive Histogram Equalization, Multi-Objective Whale Optimization Algorithm, Discrete Entropy (DE), Peak Signal-to-Noise Ratio (PSNR), and Structure Similarity Index (SSI) to improve the quality of MR images while preserving the original structure of the MR images. In the second stage, a new approach called Adaptive Multilevel Thresholding Segmentation (AMTS) is proposed for unsupervised brain tumor

subregion segmentation from normal brain tissue. The AMTS approach segments and extracts the whole tumor, core tumor, and enhanced tumor regions from the brain MR images, integrating the Multi-Objective Grasshopper Optimization algorithm, Kapur Entropy, Cross-Entropy, and Localized active contour. The performance of the ACLTSHE and AMTS approaches is evaluated on multimodal MR brain images acquired from the BRATS dataset. The ACLTSHE was capable of highlighting the local details and maintaining the structures of the original MR image without noise amplification by reporting promising average values for DE, SSI, PSNR, and Root Mean Square Error (i.e., 2.924, 0.862, 34.732 and 2.882, respectively). The AMTS achieved an average Dice score of 0.901, 0.828, 0.843, and 0.809 for segmenting the whole, core, non-enhancing, and enhancing tumor, respectively. The reported results demonstrate that the AMTS approach achieves promising and competitive segmentation performance compared to the reported Dice scores of state-of-the-art brain tumor segmentation approaches. Overall, the outcomes of the ACLTSHE and AMTS approaches indicate their potential to be adopted to enhance and segment the multimodality MR images in brain tumor diagnosis applications.

CHAPTER 1

INTRODUCTION

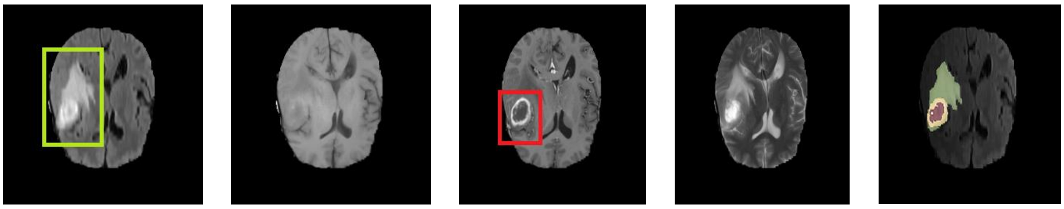
1.1 Background

According to the International Agency for Research on Cancer (IARC), the global statistics recorded up to 241,037 adult mortalities (135,843 males and 105,194 females) due to brain and tumor-related brain disease, with an estimated 296,851 new cases in adults (162,534 males and 134,317 females) (Sung et al., 2021). The alarming mortality rate has increased calls for timely diagnosis and surgical planning to treat brain tumors. In general, clinical practices, brain tumor diagnosis, and prognosis are visualized using various imaging devices, such as Magnetic Resonance (MR), Computed Tomography (CT), and Positron Emission Tomography (PET). Despite their advanced technology, most available imaging devices require manual delineation of the target tumor area on the images produced to determine the tumor characteristics, such as the location, size, type, and shape, for effective treatment planning. Consequently, the manual task is laborious and time-consuming. Hence, the medical image analysis community has focused on providing automated and rapid solutions for brain tumor delineations or segmentation using the acquired digital images.

MR imaging is preferable over CT and PET for anatomical analysis of brain tissues, given its ability to produce varying contrasting images with a greater spatial resolution that provides more details about the complexity of the brain tissues and their abnormalities. Generally, a brain tumor consists of multiple sub-regions, namely whole tumor, core tumor, and enhancing tumor. Thus, the challenge is to segment these tumor regions in a stack of MR images comprising normal brain tissues of white matter, grey matter, and cerebrospinal fluid. While numerous studies have been carried out in the field of brain tumor segmentation, researchers are still struggling to develop accurate automatic segmentation of brain tumor sub-regions. Such challenges arise due to the complex nature of MR images that frequently exhibit inhomogeneity, poor contrast, and differing image values between each MR modality.

1.2 Magnetic Resonance Imaging

Magnetic Resonance Imaging is a non-invasive medical imaging device that employs computer-produced radio waves and a strong magnetic field to generate detailed images of the target tissues in the body. Notably, MRI can distinguish between grey matter, white matter, and cerebrospinal fluid in the brain and can differentiate suspicious brain tumor regions from healthy brain tissue without emitting harmful radiation on the patients' healthy brain tissue. The brain anatomy in MR image is visualized in three different planes (views): axial, coronal, and sagittal. Practically, radiologists generate four MRI modalities for each patient, which consist of T1, T1-contrasted (T1C), T2, and Fluid Attenuation Inversion Recovery (Flair), used for brain tumor sub-region segmentation (Zhalniarovich et al., 2013), as shown in Figure. 1.1.



(a) (b) (c) (d) (e)

Figure 1.1 MR visualizations comprising (a) Flair, (b) T1, (c) T1C image, (d) T2, and (e) Segmented results.

All these four modalities show a unique signature for each normal tissue and three tumor sub-regions, namely non-enhancing tumor (shown in red), enhancing tumor (shown in yellow), and whole tumor (shown in green) in Figure 1.1(e). The details provided by each of these MR modalities are defined below:

1. In the Flair image, the whole tumor region (referring to the green box in Figure 1.1(a)) involves all three intra-tumor sub-regions, including the whole tumor region. This region, which includes the edema region, refers to the swelling surrounding the brain tissue in response to the tumor and core tumor. The whole tumor region appears in the Flair modality as a hyper-intense signal.
2. In the T1C image (Figure 1.1(c)), the core tumor region (red box) involves the non-enhancing tumor and enhancing tumor regions. The non-enhancing core tumor appears as hypo-intense (darker region inside the red box in Figure 1.1 (c)), while the enhancing tumor region appears as hyper-intensity (the brighter region inside the red box in Figure 1.1 (c)).
3. The T1 modality is typically used to identify normal brain tissues, which comprise White Matter (WM), Grey Matter (GM), and Cerebrospinal Fluid (CSF) that appear as the brighter, darker, and darkest regions, respectively, as shown in Figure 1.1 (b).
4. The T2 modality can be used to provide information for the whole tumor region.

1.3 Motivation

The segmentation of brain tumor regions from multimodality MR images is of great interest to better understand the intra-tumor heterogeneity, which is necessary for tumor diagnosis, grading, and surgical and postsurgical planning. Brain tumor segmentation approaches can be classified into three groups according to the degree of human interaction: (i) manual, (ii) semi-automatic, and (iii) fully automatic approaches. In manual brain tumor segmentation, MR images are annotated and labeled through human intervention. As a result, this approach is time-consuming and tedious for radiologists and prone to inter- and intra-rater errors. Even well-trained neurologists or surgeons could misjudge the tumor boundaries, which vary in volume, intensity, shape, and texture. To address these problems, accurate semi-automatic and automatic segmentation approaches are required to provide supporting solutions that significantly reduce the time needed to segment such insidious diseases. Semi- and fully automatic segmentation can be categorized into supervised and unsupervised approaches. The supervised method depends on ground truth samples to learn the representations of brain tumor sub-regions. However, this approach suffers from (i) large dependency on training samples, (ii) overfitting and less adaptive to unseen samples, (iii) data scarcity and imbalance, and (v) time and resource complexities. Alternatively, the unsupervised segmentation approach holds the key to overcoming the issues the supervised segmentation approach faces. The advantages of the unsupervised segmentation approaches include flexibility, adaptability, and efficiency, with the primary intention of eliminating the use of labeled data and training dataset dependency. Therefore, developing an unsupervised-based thresholding approach for segmenting brain tumor regions with better adaptability, efficiency, and flexibility in handling unbalanced data is necessary.

1.4 Problem statement

In recent years, multilevel thresholding approaches have been widely reported in the literature for brain MR image segmentation (Dhal et al., 2020). However, these approaches still suffer from some challenges. These challenges can be classified into two main categories: (i) high sensitivity to poor MR image quality and intensity inhomogeneity and (ii) the subjective effect of manually setting the values of segmentation thresholds. The first challenge is the poor image quality of the MR images, which suffer from intensity inhomogeneity, poor contrast, and hidden details. These issues narrow the intensity distribution among the brain tumor regions and normal brain tissue, which often corrupts the original structure of the MR image (Shijin Kumar & Dharun, 2016, leading to over- or under-brightness and vague boundaries. The accuracy of manual and automated segmentation approaches is reduced due to the problems mentioned above (Despotović et al., 2015). Two image enhancement methods proposed by (Sled et al., 1998; Tustison et al., 2010) are commonly used to improve the quality of brain MR images. However, The resultant MR images persistently exhibit spatial variations in illumination, poor quality, and low contrast. The current methods cannot increase the richness of information and highlight the tumoral tissue's local details. Additionally, these methods cannot enhance the visual aspect or maintain a uniform intensity distribution among various subjects within a particular region, even with images from the same MR modality (Pereira et al., 2016). Based on the limitations in the current enhancement methods, the Contrast Limited Adaptive Histogram Equalisation (CLAHE) method proposed by (Zuiderveld, 1994) is frequently employed to achieve uniform intensity distribution and improve the contrast of the MR images (Jintasuttisak & Intajag, 2014; Yoshimi et al., 2023). The CLAHE method includes two primary parameters, namely the Tile Size (TS) and Clip

Limit (CL), which are used to adjust image qualities. The CLAHE is a subjective task and heavily relies on the user's prior knowledge to manually set the CLAHE parameters (TS and CL). As such, poor image quality and noise amplification may be obtained when improper TS and CL parameters are chosen. In addition, setting standard values of the TS and CL can be incompatible and non-adaptable with specific image characteristics, generating unnatural appearance and over or under-enhancement.

Accordingly, researchers have proposed various optimization algorithms, such as Particle Swarm Optimisation (PSO) and CLAHE (Mohan & Mahesh, 2013), Firefly and CLAHE (H. Singh et al., 2018), modified PSO and CLAHE (Aurangzeb et al., 2021), Quantum Arithmetic Optimization Algorithm and CLAHE (Pashaei & Pashaei, 2023) and Sparrow Search Algorithm and CLAHE (Fan et al., 2023) to select the optimal parameter values for the CLAHE heuristically. However, these approaches suffer from the following drawbacks: (i) Various parameters need to be tuned, which is time-consuming, subjective, error-prone, and highly affects the performance of the optimization algorithms. (ii) These algorithms dedicate a single objective to partially exploring the search space. Thus, other important features of the enhancement solutions could not be considered. Optimizing a single objective function, such as the Peak Signal-to-Noise Ratio (PSNR) or Discrete Entropy (DE), results in a biased enhancement task toward the optimized objective in the resulting image. The enhanced image is produced according to the selected criteria and disregards other crucial image quality factors, which may decrease the overall quality of the resulting image. (iii) The objective functions of these approaches are non-Pareto in nature, as they are formulated similarly to single objective functions through the multiplication or aggregation methods using positive weights. The major disadvantages of this approach are the need to apply the optimization algorithm multiple times to obtain multiple optimal solutions, the requirement to consult the experts to determine the optimal weights, and the lack of information sharing between the resultant solutions during optimization. Additionally, these approaches using uniformly distributed weights for objective functions do not result in a uniformly distributed set of Pareto optimal solutions. Choosing the right optimization algorithm for the problem of selecting the optimal CL value depends on the problem's characteristics and the optimization objectives. Searching for an optimal single CL value from the CL range is considered a convex or single-modal objective function, meaning there are single peaks or valleys in the search space. Convex objective functions are characterized by their linearity. (iv) Selecting the optimum CL value from a wide range of decimal numbers, where the search space is too broad, leads to slow convergence and local optimum. This problem usually occurs when the search agents are randomly placed in a wide search space to be explored exhaustively.

The second challenge lies in image segmentation using a multilevel thresholding approach to segment the brain tumor regions using image information, such as intensity and does not rely on prior information from the training dataset. The thresholding methods are considered subjective to user experience and t hus prone to errors and time-consuming since the computation of multiple thresholds must be repeated manually until desired segmented images are obtained (Chouksey et al., 2020). Due to these limitations, researchers have directed towards adopting various optimization algorithms, such as PSO (Kaur et al., 2016; M. Sharif et al., 2020), Crow Search Algorithm (CSA) (Oliva et al., 2017), Electromagnetism phenomenon optimization algorithm (EMO) (Sandhya et al., 2017), Ant Colony Optimization algorithm (ACO) (Khorram & Yazdi, 2019), Differential Evolution (DE) (Tarkhaneh

& Shen, 2019), Success-History based Adaptive DE (SHADE) (Oliva et al., 2021), Social Spider Optimization (Ghafourian et al., 2023) Fractional-Order Darwinian PSO (Hamdaoui & Sakly, 2023), Reptile Search Algorithm and the Runge Kutta Algorithm (Emam et al., 2023), and a Salp Swarm Algorithm (Halawani, 2023) to select the optimum multiple thresholds. These algorithms have been adapted to solve multilevel thresholding problems heuristically as optimization problems. However, the optimization-based thresholding approaches still suffer from two specific drawbacks. (i) Only one criterion (Kapur's entropy or cross-entropy) is used as the objective function to guide the search for optimal solutions. This could lead to obtaining the optimum solutions according to the selected criterion but not the global best according to a set of segmentation attributes. Thus, these methods fail to provide a generic segmentation approach considering the varying image characteristics generally seen among MR images. Moreover, using Kapur's entropy or cross-entropy as a single objective function could cause the segmentation task to become biased toward specific MRI characteristics. (ii) A large number of control parameters needs to be fine-tuned, which is time-consuming and highly affects the performance of the optimization algorithm (Upadhyay & Chhabra, 2020). (iii) The objective function for multilevel thresholding is considered non-convex or multi-modal, meaning multiple solutions exist in the search space. In multimodal optimization, sharing knowledge or information among agents is vital to effectively explore and converge multiple solutions or modes.

Based on the two main issues stated earlier, three main research questions are addressed in this thesis concerning brain image enhancement and segmentation, as follows:

i. *How can a suitable optimization algorithm be adopted to obtain the optimum CLAHE parameters for MR image enhancement and optimum multiple thresholding values for MR image segmentation?*

ii. *How can the best feasible range of the candidate solutions vector be obtained to provide the most relevant or promising parts of the search space for CLAHE parameters?*

iii. *How can the multi-objective functions be modeled to guide the search for optimal solutions to produce general enhancement and thresholding approaches applicable to different MRI modalities?*

1.5 Research Objectives

The work in this study intends to answer the research questions via the collective use of new adaptive and automated enhancement and thresholding approaches for segmenting brain tumor regions from MR images. Thus, new alternatives are proposed to address the gaps in the CLAHE method for MR image enhancement and thresholding for image MR image segmentation by incorporating the optimization algorithms. The main objectives of this thesis are established as follows:

1. To formulate a new adaptive and automatic hybridized enhancement approach by integrating the Multi-objective Whale Optimization Algorithm, Discrete Entropy (DE), Peak Signal-to-Noise Ratio (PSNR), and Structure Similarity Index (SSI) to improve the quality of MR images while maintaining the original structure of the MR images.

2. To improve the initial candidate solutions of CLAHE-based image enhancement automatically and adaptively by evaluating partial solutions or branches of the search space prior to optimizing the

CLAHE parameters to overcome stagnation into local optima and expedite the convergence rate.

3. To formulate a new multilevel thresholding-based approach by integrating the Multi-objective Grasshopper Optimization Algorithm (MOGOA), Kapur's entropy, cross-entropy, and localized active contour to segment the brain tumor sub-regions.

1.6 Contribution of the Study

The established sub-objectives in this study draw attention to three significant contributions, as follows:

1. Propose a new adaptive version of the Histogram Equalization approach by integrating the MOWOA and new multi-objective function to provide an automated and adaptive parameter setting to the conventional CLAHE to enhance the brain MR images. The proposed enhancement approach improves the information richness and highlights the weak and blurred boundaries of the brain tumor regions, reduces the effect of noise and intensity inhomogeneity, and preserves the structure of MR images.
    - Propose a new multi-objective function comprising triple image quality measurements, including DE to highlight local details, PSNR to avoid noise amplification, and SSI to maintain the original structure of the MR images to guide the MOWOA for selecting the optimum pair of candidate CL and TS values used to produce good results. Instead of optimizing a single objective function, the proposed multi-objective function aims to obtain compromise solutions that maximize

DE, PSNR, and SSI to provide a compromise solution between highlighting local details, preventing noise amplification, and preserving local structure in the output image.

- Adapting the MOWOA to the image enhancement problem by selecting the optimal CL value for the CLAHE method. The search operators of MOWOA, such as the encircling prey and spiral updating mechanisms, allow whales to move efficiently toward the optimal solution in convex landscapes. These operators are well-suited to handling the linearity of convex functions, making MOWOA highly effective in handling the convex nature of optimizing CL value.

2. Proposing a new heuristic-based domain knowledge method to improve the quality of the initial candidate solutions of the CLAHE parameters heuristically to obtain feasible ranges of CL and TS extracted locally from each slice.

3. Proposing a new adaptive multilevel thresholding segmentation approach to segment brain tumor regions from brain MR brain images. The proposed approach considers the optimal selection of threshold values as an optimization task and uses MOGOA to select the candidate solutions (i.e., thresholds) that maximize Kapur's entropy and minimize cross-entropy as contradictory objective functions utilizing the local spatial MRI characteristics.

- Adapting the MOGOA to select the optimum threshold values for brain tumor segmentation problems. The MOGOA uses movement strategies, such as attraction and repulsion, to update the positions of search agents. Based on these strategies, grasshoppers are typically attracted to the best solution while avoiding overcrowding around it, making it highly effective in handling the multi-modal nature of optimizing multilevel thresholding problems. Additionally, the MOGOA leverages the concept of sharing information among individuals in a swarm. By exchanging information, the search agents of MOGOA collectively contribute to identifying and converging to different modes in the objective function landscape simultaneously, facilitating the identification of optimal threshold values at multiple levels.

- Formulating a new multi-objective function comprising two contradictory objectives to ensure that each threshold value would be simultaneously evaluated according to the maximum Kapur’s entropy and minimum cross-entropy so that a set of diverse but complementary solutions are achieved instead of optimizing a single solution. Using two types of thresholding criteria reduces the bias of the thresholding approach toward particular kinds of MR images.

1.7 Scope of the Study

This thesis focuses on developing a two-stage approach for brain tumor sub-region segmentation. The first stage intends to enhance the brain MR images to improve the contrast and highlight the tumor regions’ boundaries through optimization. The second stage proposes an adaptive segmentation of the brain tumor regions from the enhanced brain MRI results. The scope of this study is restricted to specific constraints as follows:

- The radiologists selected the Flair MRI modality to delineate the edema region of brain tumors. Accordingly, this study is applied to segment the edema region of brain tumors from Flair MR images.

- The radiologists selected the T1C modality to delineate the core, non-enhancing, and enhancing tumor regions. Accordingly, this study is applied to segment the core, non-enhancing, and enhancing regions of brain tumors from T1C MRI results.

1.8 Organization of the Thesis

This thesis is organized into six main chapters. Following the introduction in this chapter, Chapter 2 provides a critical review of various brain tumor segmentation methods and image enhancement approaches. The literature review discusses the strengths and limitations of each considered method. Chapter 3 provides an overview of the two methodologies adopted in this thesis to enhance the information richness of MRI slices and segment the brain tumor regions from the enhanced slices. Furthermore, this chapter briefly describes the brain tumor dataset and quality factors used to assess the quantitative performance of the proposed approach. Chapter 4 explains the first stage of this study, which involves the MRI enhancement approach via optimization algorithms and a thorough description of the proposed methodology. The results are compared and evaluated qualitatively and quantitatively against state-of-the-art image enhancement techniques. Chapter 5 describes the second stage of this study, which outlines the development of an adaptive multilevel thresholding approach for segmenting brain tumor regions from enhanced MRI using an optimization algorithm. This chapter also discusses the segmentation results qualitatively and quantitatively, as well as compares them against state-of-the-art brain tumor segmentation approaches to highlight the effectiveness of the proposed method. Finally, Chapter 6 summarizes the methodology used in this study and concludes the findings. The potential directions for future work are also presented.

CHAPTER 2

LITERATURE REVIEW

2.1 Introduction

This chapter mainly provides an overview of the adopted stages for brain image segmentation from MR images. These stages include (i) image enhancement methods and (ii) MR brain image segmentation methods. The structure of this chapter is organized as follows: Section 2.2 describes the categories of image enhancement methods that are well renowned in the literature. This is followed by a literature review on the state-of-the-art segmentation methods proposed for brain segmentation in MRI, as described in section 2.3. In both Sections 2.2 and 2,3, common issues related to image enhancement and segmentation methods are analyzed in detail. Finally, this chapter summarizes the segmentation methods, highlights their advantages and disadvantages, and analyzes the research gap. The discussion on research gaps and weaknesses concludes the direction of the work presented in this thesis.

2.2 Image enhancement approaches

The image enhancement approaches aim to achieve two main objectives: (i) to produce enhanced MR images that can be used for manual brain image analysis; Physicians prefer manual annotation on well-contrasted medical images, thus highlighting the available essential details of the target tissue. (ii) to obtain well-contrasted medical images that can be used in subsequent tasks of computerized vision analysis, such as segmentation, feature extraction, and classification. It has been proved that the effectiveness of the automated and semi-automated segmentation methods depends on some ideal characteristics of brain images (Li et al., 2014). The ideal characteristic supposes the particular tissue should always have similar intensity within its region in a single image and does not exhibit inhomogeneous intensity despite variability in the location in the image. This characteristic is desired to improve the performance of fully and semi-automated analysis methods such as segmentation and classification (Xu et al., 2013). Nevertheless, this ideal assumption never occurs in reality due to the existence of noises and unwanted artifacts, which can considerably affect the homogeneity of MR image intensity. Manual, semi-automated, and fully automated segmentation methods can greatly degrade accuracy due to various noise and unwanted artifacts in the MR images. The intensity variations induced by these artifacts result in inaccurate segmentation and classification results. This issue is more observed in multimodality MR image segmentation because these modalities provide complementary information about brain tumor regions by generating different types of contrast images of the same patient from different directions (sagittal coronal and axial) and time (slice sequence). The MR images often suffer from intensity inhomogeneity and over or under-brightness issues. For this reason, image enhancement methods are highly recommended to reduce unwanted noise and maintain a uniform intensity distribution for better qualitative and quantitative assessment of MRI volumes.

Thus far, various research methods have been proposed to correct the intensity distribution of MR images and increase information richness. These methods are mainly categorized into prospective and retrospective (Vovk et al., 2007). These methods are proposed based on the assumption that inhomogeneity and unwanted artifacts smoothly vary the multiplicative field with an additive noise as expressed using Equation (2.1).

$$R(x,y) = I(x,y)B(x,y) + n(x,y) \quad 2.1$$

Where *x and y represent the index of an image pixel,*his noise is called scanner noise and follows the Gaussian distribution (Sijbers et al., 1998). Another noise representation is known as the additive model. This model assumes that the noise originated from the inhomogeneity of tissue $B(x,y)$ and may contain a higher signal-to-noise ratio (SNR) (Prima et al., 2001). It is defined as follows:

$$R(x,y) = (I(x,y) + n(x,y))B(x,y) \quad 2.2$$

The third assumption model for the noise and inhomogeneity field is a logarithmic additive (Van Leemput et al., 1999), which assumes the noise and the inhomogeneity field n can be corrected by calculating the log-transformed intensities, where the multiplicative bias field becomes additive.

$$logR(x,y) = logI(x,y) + logB(x,y) + n(x,y) \quad 2.3$$

The methods that work under prospective methods include mathematical models used to calibrate MR machines (Mcveigh et al., 1986), newly designed medical imaging sequences (Wicks et al., 1993), and shimming techniques (Weili Lin, 2005). These methods aim to improve and calibrate the MRI acquisition process and correct the inhomogeneity field produced by MRI hardware imperfections. Nevertheless, these methods cannot completely rectify the bias field because of the following: (i) they are required to rescan, and (ii) They cannot enhance all parts of an image at the same time. Meanwhile, the retrospective approaches can effectively remove patient-specific intensity inhomogeneity as well as the inhomogeneity of information introduced by the MRI scanners, which directly deal with the inhomogeneity of MR slices. These methods perform correction tasks based on the intensities of images and the prior information about the imaged target tissue. The retrospective methods for inhomogeneity field correction can be further classified into (i) surface fitting-based methods, (ii) filtering-based methods, (ii) segmentation-based methods, and (iv) histogram-based methods (Vovk et al., 2007).

2.2.1 Surface-based methods

Surface-based methods perform correction based on polynomial or spline functions to model the bias field and extract a set of image features representing inhomogeneity information from the MR images. The extracted features are fitted into a parametric surface to represent the inhomogeneity field. Despite using the polynomial or spline function in the fitting process, the effectiveness of these methods heavily depends on the selected set of image features. The surface-based methods can be further categorized into intensity-based and gradient-based methods depending on the various image feature sets used in the surface fitting process. Intensity-based methods assume that tissue intensities do not vary unless bias field artifacts corrupt them. These artifacts could be estimated by calculating the intensity variation inside the same region type of tissues (Vemuri et al., 2005; Zhuge et al., 2002).

On the other hand, the gradient-based methods assume the noises and intensity inhomogeneity artifacts also alter the local gradient. Therefore, the local average of intensity gradients has been selected as an inhomogeneity elimination feature (Meyer et al., 1995). The main drawbacks of surface fitting methods are the requirement for clear region separation, large homogeneous areas, and longer processing time.

2.2.2 Filtering-based Methods

Filtering-based methods consider the intensity inhomogeneity and noise as low-frequency artifacts that can be eliminated from the high-frequency regions of images using filtering methods. These methods are computationally inexpensive and have been widely adopted for both noise and inhomogeneity field removal in MRI studies, such as the Weiner filter (Pitchai et al., 2021), anisotropic Diffusion filter (Khalil et al., 2020), Median filter (Nyo et al., 2022; Sheela & Suganthi, 2022) Gaussian filters (Halawani, 2023). However, filtering-based methods reduce noise but suffer drawbacks: (i) They could not assure homogenized intensity distribution in the resulting images. (ii) the conventional filtering methods can mistakenly remove useful low-frequency intensities of tissue that closely resemble the inhomogeneity field. (iii) filtering methods may distort homogeneous tissues near the edges due to filtering artifacts produced by high contrast structures characterized at low frequencies.

2.2.3 Segmentation-based methods

The group of segmentation-based methods combines segmentation and inhomogeneity correction processes into a unified procedure to obtain better results for each step simultaneously. The methods produced better results by mutually iterating between segmentation and inhomogeneity correction (Ahmed et al., 2002; Bansal et al., 2004; Pham & Prince, 1999). However, these algorithms are still sensitive to parameter initialization. These methods utilized metaheuristic approaches to improve segmentation results and perform automatic and adaptive parameter initialization, thus addressing the inhomogeneity artifacts (Maulik, 2009; C. Yang et al., 2015; Z. Yang et al., 2016). However, the effectiveness of these methods is still limited because of the need to design effective fitness functions and subjective tuning of parameters.

2.2.4 Histogram-based methods

Histogram-based methods search for the inhomogeneity field spatially in the pixel intensity using an image histogram to redistribute (maximizing, minimizing, and histogram matching) the high-frequency bins of the tissue intensity (Shekari & Rostamian, 2023) (Vovk et al., 2007). Many of these techniques require proper initialization and prior knowledge about the intensity distribution of the image. Various techniques have been implemented under histogram-based intensity correction, such as the Nonparametric Nonuniformity Normalization (N3) technique (Sled et al., 1998). N3 is one of the well-known inhomogeneity correction techniques used in medical MR images. N3 iteratively smoothed the input image histogram by increasing the high-frequency bins. The method experimentally starts to find the intensity distribution of tissue using an image histogram. The affected image histogram was then deconvolved in the log intensity domain to remove inhomogeneity. By using linear interpolation, the produced histogram is utilized to correct the image intensity in each pixel. B-spline smoothed the residual field (the difference between corrected and original intensities), which yields the bias field (Tustison et al., 2010) proposed the N4 method, which improves the iterative schema of the N3 method. The Insight Registration and Segmentation toolkit (ITK) software has applied the N4 method. N3 and N4 approaches require extraction of foreground regions, and effectiveness might depend on the accurate removal of background regions, initialization of histogram range of inhomogeneity field, and spline distance. In addition, these methods could not improve the visibility of the regions in the brain. In order to make the intensity distribution and contrast of MR images more uniform across acquisition and subjects, the Histogram Equalization approaches are commonly used to achieve uniform intensity distribution and improve the contrast of the MRI image. The Histogram Equalization approach (HE) operates directly on the intensity of image histograms so that the pixels of the specific intensity level of images are redistributed spatially over the whole range of the grey levels to achieve homogeneous intensity distribution to the enhanced image. First, the Histogram Equalization approach calculates each grey-level bin's Probability Density Function (PDF). Secondly, the Cumulative Density Function (CDF) is then calculated. Eventually, the approach computed the transfer function to achieve the intensities redistribution of the image and produce the resultant image. Four derived groups from the Conventional Histogram Equalization (CHE) approach were developed to improve its performance and overcome its limitations. The four CHE-derived groups are Region Histogram Equalization (RHE), Image Division, Modified Histogram Equalization (MHE), and Metaheuristic-based Histogram Equalization. A descriptive diagram of the CHE and its sub-class methods is illustrated in Figure 2.1.

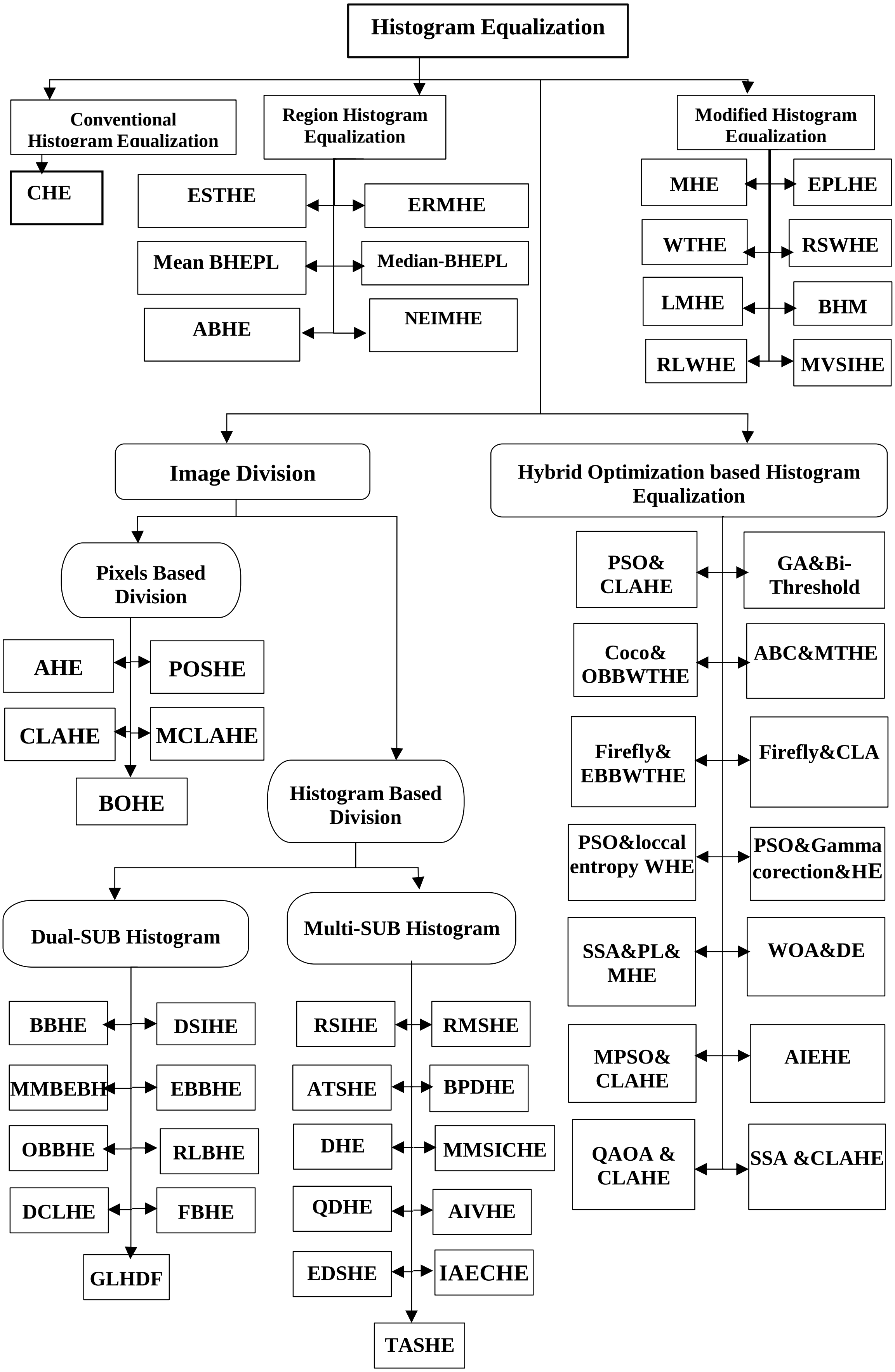


Figure 2.1 Histogram equalization and its sub-classes.

2.2.4(a) Region Histogram Equalization

Region histogram equalization is the first class derived from HE, which splits the histogram into regions. This approach improves image brightness based on formulated regions and produces enhanced images, such as the global histograms category. Some approaches are purposely designed under this sub-class to preserve image brightness in non-homogenous intensity images, such as exposure-based sub-image HE (ESIHE) (K. Singh & Kapoor, 2014a), Exposure Region-based Multi-HE (ERMHE) (Tan & Isa, 2019), Median and Mean bi-HE plateau limit (Mean-BHEPL & Median-BHEPL) (Tang & Mat Isa, 2016), and adaptive bi-HE (ABHE) (Tang & Mat Isa, 2016). By applying the exposure threshold, the ESIHE approach splits the image's histogram into two areas, and both sub-histograms will be clipped using the grey level's mean value. Then, CHE is applied for sub-histograms. The ESIHE method offers good preservation of local details and contrast enhancement but does not perform properly with samples containing multi-exposure areas (i.e., normal, under, and overexposure). Both ABHE and BHEPL approaches are proposed to overcome the limitation of ESIHE by working with overexposure and underexposure regions (too dark or too bright regions). However, they do not perform well with images that have normal exposure areas. The ERMHE approach tackles the problem of multi-exposure regions. Although the approach offers high-quality brightness and lower noise in resulting images, one exposure area can be greater than the other(s). This issue can cause the problem of dominant high frequency over frequencies of lower intensity, thus causing loss of information in some parts.

2.2.4(b) Image Division

Image division is the second sub-class derived from CHE. The image division approach was developed to address the limitations of CHE by modifying and improving the information richness of non-overlapping contextual grey-level regions derived from the image while retaining information by filtering through all image pixels. The division in this sub-class is classified by pixels and histogram-based divisions. The pixel division relies on cutting the image into small tiles. For example, an image with 100 × 100 pixels can be divided into ten tiles. The size of each tile is 10 × 10 pixels. The division of the histogram depends on a specific value computed from the image's histogram to divide it into sub-histograms.

2.2.4(b)(i) Pixels-based division

Pixels-based division techniques improve small grey-level regions and retain image details by mapping the limited scope of pixels of an image to the entire visualization range. It is designed to address the low contrast issues in the HE class by splitting the input image into a block of pixels (e.g., 6 × 6) called contextual regions. Some approaches proposed in this class include Adaptive Histogram Equalization (AHE) (Zimmerman et al., 1988), partially overloaded sub-image HE (POSHE) (J. Y. Kim et al., 2001), and Contrast-Limited Adaptive HE (CLAHE) (Zuiderveld, 1994). These methods address the intensity inhomogeneity drawback of CHE by operating on small blocks of pixels to produce a resulting image with uniform intensity instead of operating on whole image pixels. But these techniques amplify the resulting images' noise and consume long-running time. (J. Y. Kim et al., 2001; S. Mirjalili et al., 2017) The approaches of CLAHE and POSHE also suffer from unnatural appearances in the resultant images (Zimmerman et al., 1988).