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PAPER

3D Pre-Processing Algorithm for MRI Images of Different Stages of AD

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ABSTRACT

Alzheimer's disease (AD) is a degenerative neuronal brain disorder resulting in memory loss, skills, and cognitive changes. The disorder's primary diagnostic tests are defined as total brain atrophy and hippocampal atrophy. Early diagnosis is significant, and automatic systems design is necessary for this disorder. Potential biomarkers for AD are described using a hippocampal magnetic resonance imaging volumetry system with certain limitations. For the definite identification of the hippocampus region, pre-processing of the 3D MRI images of AD is necessary. The filtering and histogram-based pre-processing techniques enhance the region of interest, which helps in effectively segmenting the biomarker, the hippocampus. The median and eight histogram clippings are defined to be 98% efficient pre-processing techniques with the comparison of image quality parameters and statistical analysis. Thus an algorithm for pre-processing of the 3D MRI images of stages of AD is designed for the further process of identification.

KEYWORDS

hippocampal atrophy, filtering, histogram, montages, sagittal plane

1 INTRODUCTION

A brain ailment called Alzheimer's disease (AD) causes a loss in cognitive abilities [1]. This neurological dysfunction becomes worse with time and affects how the brain functions. More than 30 million individuals worldwide are affected with AD, which is increasingly the leading cause of dementia in the elderly population. The prevalence of AD is often higher in populations 65 years of age or older and is significantly higher in developing nations [2]. Although there is no cure for this illness, development therapy can slow the progression of symptoms. These therapies have attracted a lot of interest, and, if early diagnosis is achievable, they have the potential to be very successful.

Alzheimer's disease condition mostly affects the learning phase of the brain, the early symptoms start with the ability to recall the just-learned information. The symptoms worsen as the disease progresses and include areas linked to behaviour,

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language, mood changes, disorientation, and motivational loss. Age and stress are always associated with this illness's basic symptoms. As the patient's health deteriorates, they become less engaged in social and emotional interactions, which gradually reduces their physiological functions. A few people experience specific brain differences before the onset of the sickness that is significantly greater than their age and educational level, but this does not impair the routine functions. However, persons found to have this mild impairment may develop other types of dementia rather than AD or MCI as such until they pass away. They might also regain normal cognitive function [3]. In the final phases of the condition, the patients are totally reliant on caregivers. Simple phrases or a single word are used to communicate, which eventually results in speech loss. Research attention has been heavily focused on factors that may speed up or slow down the conversion from MCI to dementia because several studies indicate that only some people with MCI move to full-blown dementia. The MCI was later categorized into two different types: Early MCI and Late MCI, based on the progression state of the brain.

The patient's medical history and family history are the sole basis for the diagnosis of Alzheimer's disease. This also depends on any observations made on shifts or variations in cognitive function. These cutting-edge imaging modalities, including computed tomography, magnetic resonance imaging, single photon emission tomography, and positron emission tomography, can be used to quickly analyse the pathophysiology of the disorder and its stages. For better disease diagnosis and analysis, potential biomarkers were created and specified. Various biomarkers, such as Cerebro Spinal Fluid (CSF), molecular biomarkers, and neuro-imaging biomarkers can also be used to characterize the pattern of evolution of Alzheimer's stages. Magnetic Resonance Imaging (MRI) and Positron Emission Tomography are two cutting-edge imaging modalities that are specifically used to determine these biomarkers (PET). Cognitively normal (CN) to Alzheimer's disease (AD) stages of the disease are analyzed using structural information of the brain obtained from an MRI. It is possible to image biomarkers for AD with neurodegeneration using MRI, which is non-invasive and more affordable than Positron Emission Tomography (PET) [4]. PET imaging, which defines the data on the metabolic processes correlating to radiotracers selected for the specific study, is also frequently used to diagnose AD [5].

In the proposed model, the database images of the progressive stages of Alzheimer's disease are derived for analysis and comparison of the effective preprocessing techniques after the process of orientation. The 3D MRI images obtained from the ADNI database are used for the determination of the effective filtering and histogram-based techniques for the enhancement of the region of interest, hippocampus. The hippocampus atrophy acts as a biomarker for the identification of the progressive stages of AD. Thus, the comparison of the basic pre-processing techniques is performed using the image quality parameters to analyse the efficient pre-processing technique for the identification of the hippocampus region.

2 METHODOLOGY

There are many proposed algorithms to classify the different stages of Alzheimer's disease, into Normal, Mild Cognitive Impairment (MCI) and Alzheimer's disease (AD) in the literature, and even a few approaches were made to determine the transition of stages of Alzheimer's. In the proposed model, pre-processing of the database images is performed to determine the effective region of interest, the hippocampus. Filtering techniques are implemented to remove the noises in the 3D MRI images, which is the basic step in pre-processing. The MRI brain images for processing need to be in the standard Montreal Neuro Imaging (MNI) Template for better analysis. Hence, re-orientation of the database images to the standard MNI canonical template is performed. The images acquired during analysis have a lower resolution and distortions in the form of noise. Hence the images were filtered using different filtering techniques. The pre-processing of the images mainly concentrated on the hippocampus in the temporal region of the brain. In order to enhance the hippocampus region, histogram based enhancement techniques are implemented because the individual voxels are identified and enhanced in this process. Three-dimensional analysis of the images is performed and processed for the enhancement of the region of interest. The pre-processing techniques are compared using various image quality parameters to determine the efficient technique for the enhancement of the hippocampus region.

2.1 Image acquisition

The Alzheimer's Disease Neuroimaging Initiative* (ADNI) database (http://adni.loni.usc.edu) served as the source of the image dataset used in the suggested methodology. The creation of the ADNI database is the result of the efforts of numerous research experts from various academic institutions and businesses. These data are defined by various subjects across 50 sites in North America and the United States. Every piece of information in the ADNI database is labelled as CN, EMCI, LMCI, and AD. The functional performance and cognitive information are reserved during primary screening. Therefore, an Alzheimer's disease diagnosis cannot be given. The database's three-year 3T MRI pictures are used in this investigation. T1-weighted Magnetization Prepared RApid Gradient Echo (MPRAGE) MRI on a 3-Tesla scanner is the definition of the data of each subject image. As a result, these images pulled from the database are used to compare various pre-processing methods. The database 3D MRI images as a volume and montage is described in Figure 1.

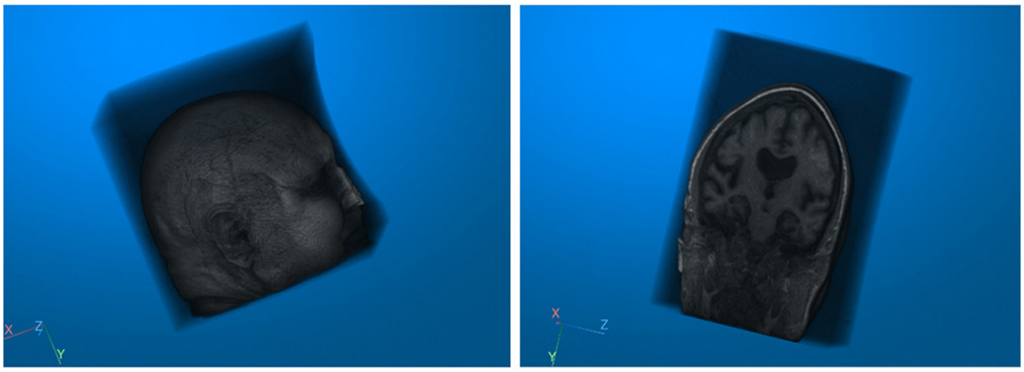


Fig. 1. Database images of 3D MRI AD as a volume

2.2 Pre-processing

In this study, pre-processing of the images started with the use of Statistical Parametric Mapping 12 (SPM 12) toolbox, where the image re-orientation was performed. Image re-orientation is the process of re-arranging the image from the database to the standard Montreal Neuro-Imaging (MNI) template. The 3052T1 is the standard brain neuro-imaging template, in which the brain images are usually processed.

The database images were re-arranged according to the voxel size to the standard one. The basic pre-processing technique implemented to analyse the images is filtering. 3D-image filtering techniques are used for the description and enhancement of the region of interest. There are different categories of basic filtering of images in spatial domain such as linear and non-linear filtering. The filtering techniques are compared using parameters like PSNR and SSIM index. After pre-processing, the enhancement of the hippocampus is required for the complete definition of the voxels of the region, hence histogram- based enhancement techniques are applied for the clear description of the atrophy in the hippocampus region based on voxels. Different histogram-based techniques are compared using parameters like F-measure and CII for the definite identification of the region of interest, the hippocampus.

2.3 Filtering

The MRI images obtained from the ADNI database are subjected to the process of reorientation and analysis with the MNI template for the configuration of the brain structure. After reorientation, different spatial filters are applied which helps in defining the exact region of interest with the specific voxel-based denoising techniques for the spatial values. Linear and non-linear filtering techniques are applied to determine the efficient filtering technique for the identification of the region of interest [6]. These are the different filters used for various MRI images for noise removal and analysis [7, 8].

- Average filter is a smoothing filter that reduces the intensity by varying (averaging) the voxels in the neighborhood.
- Despeckle filter is used for the analysis of the noises and reduces the speckle disturbances produced in the MRI images.
- Gaussian filter is a low-pass filtering technique that blurs the image and reduces each voxel based on the weighted average of high-frequency components.
- Sobel filter is a gradient operator-based filter that varies with the first derivative. The edge-based filtering detector convolutes the voxel values of the image.
- Laplacian is a spatial second-order derivate filter that highlights the intensity regions rapidly for the determination of fine edges.
- Prewitt filter is also a gradient operator-based first-order derivative filter. The approximations of derivatives are calculated in both vertical and horizontal directions of the regions to enhance the edges.
- Laplacian of Gaussian (LoG) filter is a 2D derivative filter that minimizes the noise sensitivity after smoothing. Both Laplacian and Gaussian filters are applied for the analysis of the voxels.
- Median filter is a non-linear filtering technique used to replace the voxels with median values of the neighborhood voxels. This filter is mainly used to remove salt and pepper noise.

The different filtering techniques are applied to analyze the efficient filtering technique for the removal of noises and absolute visualization of the region of interest, the hippocampus. The efficiency of the filters is determined by comparing the filtering techniques using parameters like peak signal to noise ratio (PSNR) and Structural Similarity index (SSIM) [9]. The median filter is determined to be more significant in reducing the noises and enhancing the voxels in the hippocampus region.

2.4 Histogram based enhancement technique

This proposed pre-processing method is to be performed after filtering the image enhancement to determine the hippocampus, which is a smaller region in the brain. The discrimination of the hippocampus and atrophy of the region can be obtained by enhancing the voxels of each gradient in each plane section. The histogram defines the voxel ranges in a definite manner [10]. Therefore, histogram-based enhancement techniques are implemented to structurally define the hippocampus region, which acts as a biomarker for the diagnosis of the progressive stages of Alzheimer's disease. The different histogram-based techniques are applied for the enhancement of the hippocampus region, which helps in the effective segmentation of the region of interest. Histogram clipping-based enhancement is a new method proposed with eight subdivisions for the volumetric structures of brain specifically the hippocampus.

Enhancement methods based on histograms sometimes distribute very little brightness on the input image and sometimes perform over brightness [11]. The suggested approach is presented to get around this flaw. The suggested method is generally comparable to histogram-based improvement techniques like RSIHE, ESIHE, and MMSICHE, which performs histogram clipping and image subdivision to generate the output with the enhanced region of injury. The segmented images are integrated and subtracted from the input image.

- Histogram equalisation (HE) is a conventional contrast-enhancement method with a predetermined histogram by widening the dynamic range. HE offers intensity distribution and boosts contrast. One of HE's shortcomings is that it increases image brightness rather than reduce it.
- Brightness Preserving Dynamic Histogram Equalisation (BPDHE) is a dynamic histogram process that is derived based on the mean brightness values. The output image was obtained with low intensity.
- Recursive Mean Separate Histogram Equalisation (RMSHE) technique preserves brightness using bi-histogram equalization. Scaling of brightness with input and output possesses the variations with mean brightness.
- Smaller areas of an image can be analyzed using the contrast enhancement method known as Contrast Limited Adaptive Histogram Equalisation (CLAHE). By a specific or constrained distribution, the histogram of output contrast level matches the histogram of contrast photographs. The contrast spreads throughout the entire image, equating the image's intensity and making it difficult to identify the necessary location [12].
- One efficient enhancement technology that executes clipping operations is Exposure Based Sub-Image Histogram Equalisation (ESIHE). When an effective enhancement rate is attained, ESIHE separates the image into two and performs enhancement on each one separately [13]. Finally, the corrected photos are combined into one image, improving visualisation.
- Recursive Sub-Image Histogram Equalisation (RSIHE) is a technique in which the resultant image acquires the region of interest and has superior visualisation. RSIHE technique helps in energy preservation and improved contrast in the image's overall region.
- Median Mean Based Sub-Image Clipped Histogram Equalisation (MMSICHE) is a related enhancement method to ESIHE. The histogram is clipped based on the mean and median values, and the four sub-images are then enhanced. The improved analysis of the needed region of the input image is improved by the integration of the improved images into a single image. MMSICHE exhibits

effective augmentation and visualisation, but the histogram eight clipped method can be used for the grayscale variation. The suggested approach displays a precise analysis of the needed region.
- The core idea behind the proposed eight-subdivision histogram method is the clipped histogram methodology (see Figure 2). The images are clipped based on the threshold settings based on the voxels of the MRI image and the enhancement rate is examined to generate the output images in existing techniques like ESIHE and MMSICHE [14]. The suggested strategy is comparable to those in which MMSICHE and ESIHE clip the images into two and four sub-images, respectively.

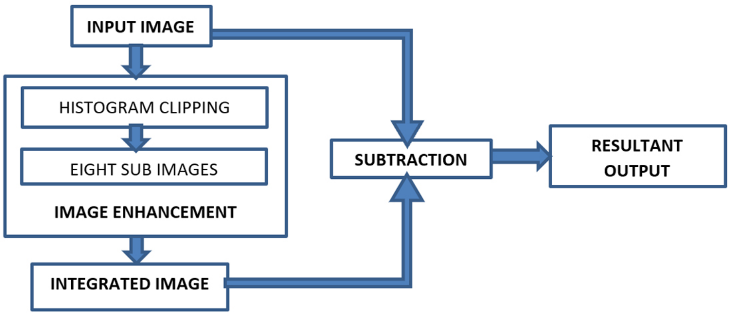


Fig. 2. Block diagram of the proposed algorithm with eight histogram clipping

The different histogram-based enhancement techniques are applied for the 3D MRI images that depend on the gray level variations in the voxels [15]. A comparison of the different histogram-based enhancement techniques is performed using quality parameters like Contrast Improvement Index (CII) and F-measure to analyse the efficient technique for enhancement of 3D MRI images of stages of AD.

2.5 Image quality parameters

The 3D MRI images of different stages of AD are analysed after pre-processing to determine the effective technique. Filtering is the first step of pre-processing in which different linear and nonlinear spatial filters are implemented. Later in the second step after filtering, histogram-based enhancement techniques are applied for the study of the voxels in the region in a precise manner that helps in proper segmentation of the image. The pre-processing techniques are compared using various image quality parameters which determine the efficiency of the techniques in three-dimensional voxels. Peak signal-to-noise ratio and similarity index are determined for the detection of effective filtering techniques. The F-measure and Contrast Improvement Index are obtained for the identification of the efficient histogram-based enhancement technique among the existing and proposed methods [16].

Peak signal to noise ratio (PSNR). Peak signal to noise ratio (PSNR) is a term used to describe the relationship between the power of the original image and the highest power of corrupted noise that might degrade the quality of the image. The PSNR is measured in logarithmic dB. In image processing, PSNR is used to gauge how well a picture has turned out, particularly after augmentation and reconstruction. The equation describes peak signal to noise ratio (1).

$$\mathrm{PSNR} = 10 \times \log\left(\frac{255^2}{MSE}\right) \tag{1}$$

The PSNR Ratio was obtained to compare the spatial filters applied to the 3D MRI images.

Structural similarity index. The Structural Similarity Index is defined to be a parameter that precisely identifies the structural resemblance of the voxel components in the output and the input images. The process is applied to differentiate the filtering techniques applied for the 3D MRI images of different stages of AD for the segregation of the region of interest, the hippocampus.

F-measure. Precision and recall are the main factors in the F-measure that describe the performance accuracy of the test. The accuracy of the exam is described by these metrics. The recall and precision values are used to define the F-measure for the enhancement approaches. F-measure is defined in the equation below (2).

$$F - measure = 2.\frac{Precision.Recall}{Precision + Recall} \quad (2)$$

Contrast improvement index. The local contrast of the output image compared to the input image is measured by the contrast improvement index (CII). The mean values of the photos are the contrast in this case. As a result of its gratifying results, CII serves as a baseline for all enhancement techniques so that the efficacy of the output image may be understood. Comparing the produced image to the methods already in use, larger CII values suggest more effectiveness. In the equation below, the contrast improvement index is expressed (3). If the CII value of the output image equals the mean value of the input image, the contrast has improved.

$$\text{CII} = \frac{\text{Contrast of the proposed image}}{\text{contrast of the input image}} \quad (3)$$

With the help of the image quality parameters, efficient pre-processing techniques are determined. The first process is filtering in which spatial filters are applied where 3D-median filters are more effective than all other filters. In the second step of enhancement of the 3D MRI image, the proposed eight-division histogram method is defined to be more efficient for the voxels enhancement in the region of interest, the hippocampus [17]. Thus, the hippocampus is marked to be definite in the output pre-processed images. Statistical analysis of the image quality parameters is performed to determine the efficient technique for pre-processing the 3D MRI images of different stages of AD.

2.6 Statistical analysis

The image quality parameters obtained from the 3D MRI pre-processed images are analyzed using statistical techniques. The efficient algorithm can be determined using the results of the statistical analysis. Multidimensional scaling is a type of statistics technique in which the distance range plays a major role to determine the significant nature of the compared parameters. Different types of multidimensional scaling are defined for the metric and non-metric parameters [18]. The proposed methodology involves the comparison of the image quality parameters that are numeric, so metric multidimensional scaling is implemented [19]. This statistical method primarily compares the PSNR and similarity index to determine the efficient filtering technique. Later, the method also compares the F-measure and CII to define the significant histogram-based enhancement technique. The distance in the metric parameters describes the significant nature of the techniques applied for the pre-processing of 3D MRI images of progressive stages of AD. Based on the significance of the scaling distance, the proposed histogram clipping-based enhancement technique is defined to be more efficient but with respect to the filtering techniques, average, Gaussian, and median filters are defined to be significant in pre-processing of 3D MRI images. In order to analyze these filters, the Kruskal Wallis test is performed. The mean difference among the parameters is defined with a significance level to be 95% or 99%. Thus, the algorithm for preprocessing is defined for the definite description of the atrophy of the regions, which helps in the effective process of segmentation.

3 RESULTS AND DISCUSSION

In the proposed methodology, 3D MRI images of different stages of AD such as CN, EMCI, LMCI, and AD from the ADNI database for the determination of the hippocampus as the biomarker are used to determine AD and predict the progressive state of the brain towards different stages of Alzheimer's disease. Reorientation to the MNI template is performed prior to organizing the images in the standard template for further analysis and image processing techniques. The preliminary state of analysis starts with pre-processing, the images obtained are raw data. So, the first state of pre-processing is filtering in 3D [20]. 3D spatial filters, both linear and nonlinear, are used for the systematic filtering of the noises in the spatial domain for the voxel categorization in the ROI. After filtering, the images are enhanced using histogram-based techniques for enhanced voxel representation in the hippocampus region. The filtering and histogram-based enhancement techniques are compared using image quality parameters. Statistical analysis is also performed to determine the effective filtering and histogram-based enhancement technique to pre-process the 3D MRI images of different stages of AD. The reoriented full three-dimensional MRI image of AD is illustrated in Figure 3 with the cross-sectional planes of structures

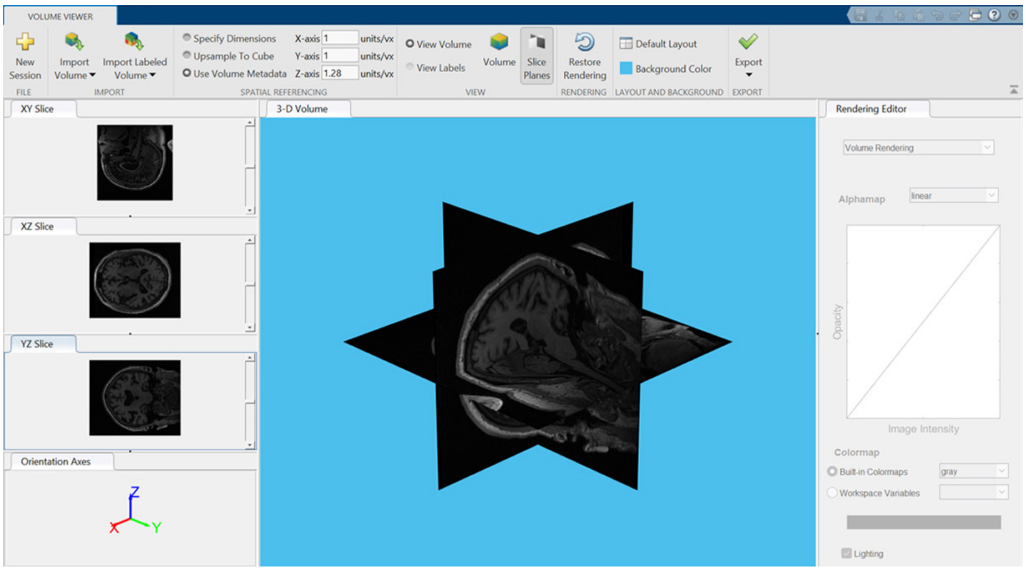


Fig. 3. Reoriented 3D MRI images plane sections of AD

After reorientation, spatial filters are applied to the 3D MRI images of different stages of AD for the reduction of noises with voxel values in spatial domain. The 3D filtered image of AD of different filtering techniques is illustrated below in Figure 4. The Figure below defines the variations in the 3D volume of the MRI images after implementation of the different filters that reduces noise parameters for significant detection of the biomarker.

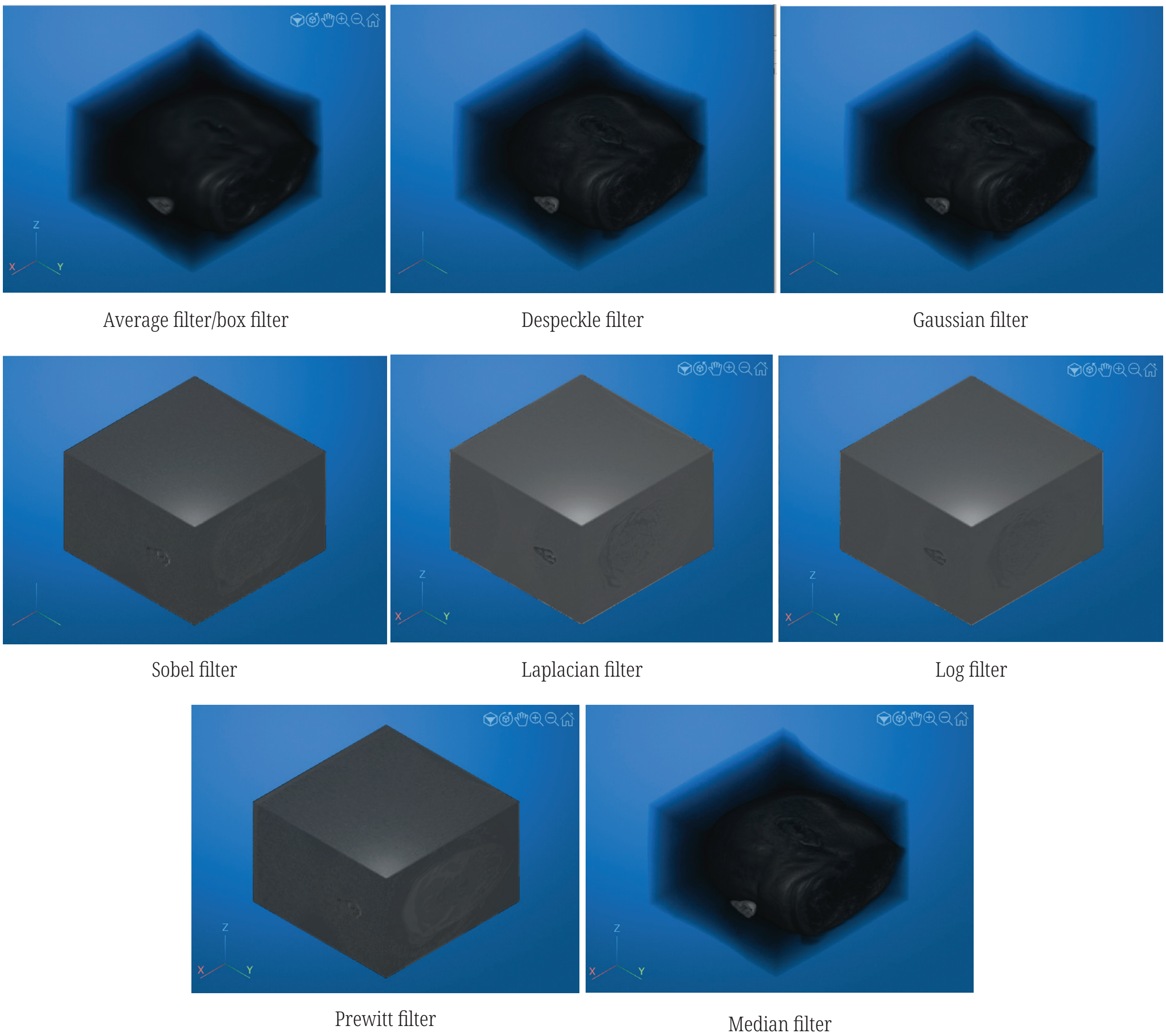


Fig. 4. 3D filtered image of different spatial filtering techniques

The filtered output images are compared using image quality parameters like peak signal-to-noise ratio and similarity index. The PSNR and similarity ratio are high for three different filters, which states is indicative of high efficiency in filtering the MRI images of stages of AD. The graphical representation of the PSNR ratio for different stages of AD compared with different filters is given below in Figure 5. The similarity index as in the graphical representation below in Figure 5 is defined to be equal to 1 for three different filters which are Average, Gaussian, and Median filters. Further statistical analysis is performed to define the efficient filtering technique.

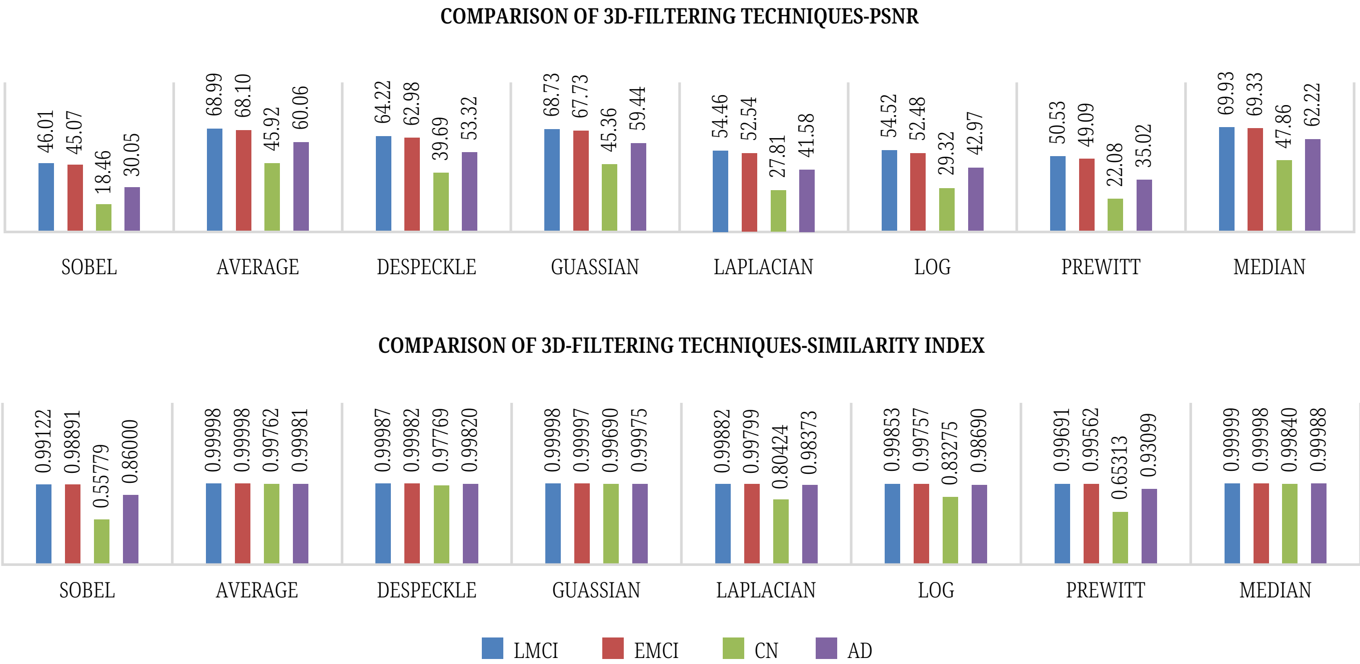


Fig. 5. Graphical representation of the 3D filtering techniques of different stages of AD

The process of enhancement is performed to visualize the voxels in the hippocampus region for the definition of the atrophy of the structure, which states the cognitive condition of the brain. The histogram-based enhancement techniques in 3D are applied to the MRI images for the voxel definition of the region of interest, the hippocampus. Different histogram-based enhancement techniques are implemented for the analysis of volumetric biomarkers in the 3D images based on the distribution of the voxels. The output images of the different 3D histogram-based enhancement techniques are illustrated in Figure 6 with volumetric variations in the MRI images.

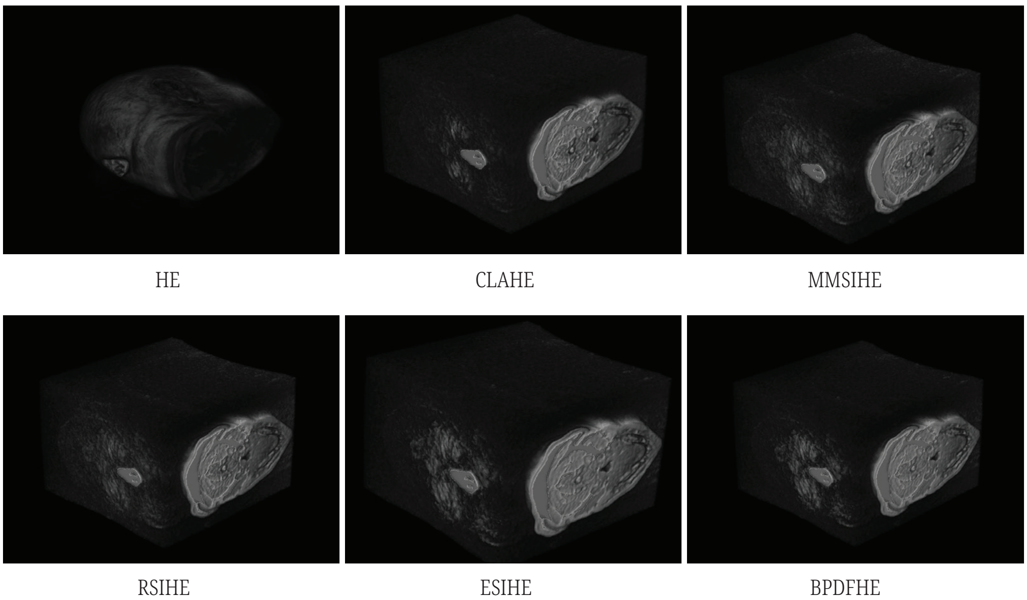
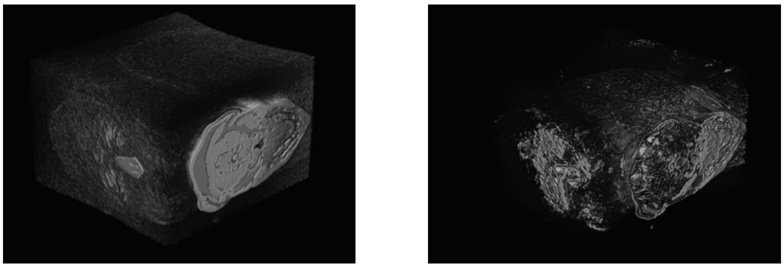


Fig. 6. *(Continued)*



RMSHE PROPOSED HISTOGRAM CLIPPING

Fig. 6. Resultant images of different histogram based enhancement techniques

The histogram-based enhancement techniques are compared using image quality parameters like contrast improvement index (CII) and F-measure [21, 22]. The CII is defined to be more definite for the proposed histogram eight clipping-based enhancement technique. The F-measure defines the proposed eight clipping histogram bases technique to be appropriate with the probability values to be near one [23]. The graphical representation of CII and F-measure for the histogram-based techniques are compared for different stages of AD in Figure 7.

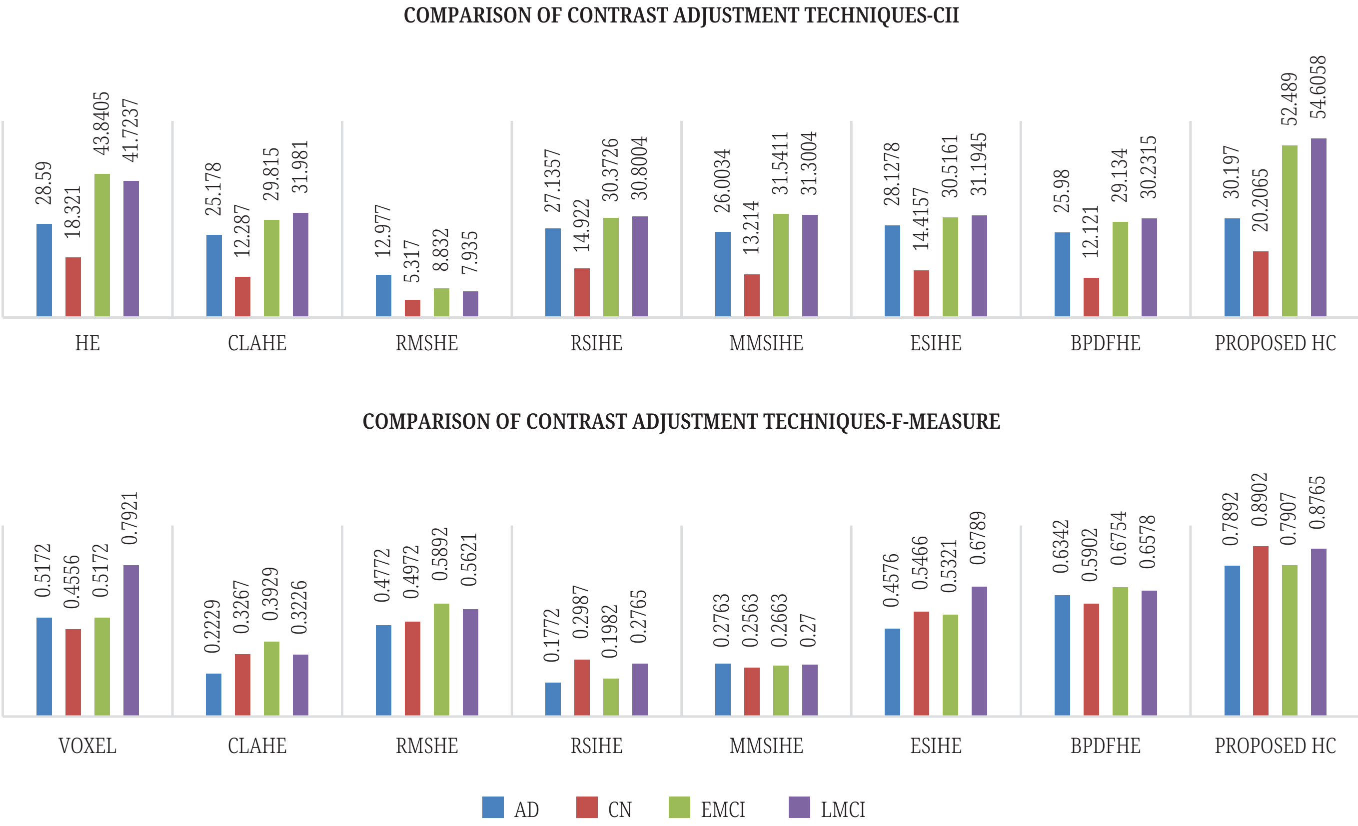


Fig. 7. Comparison of the histogram-based enhancement technique for different stages of AD

The pre-processing step involves filtering and histogram-based enhancement technique for the analysis of the region of interest, the hippocampus. The hippocampus region is determined to detect the progressive stages of AD defining the cognitive state of the brain. This also helps in predicting the stages of Alzheimer's Disease. The resultant preprocessed images as a montage and in full dimensional view respectively is given below in Figure 8.

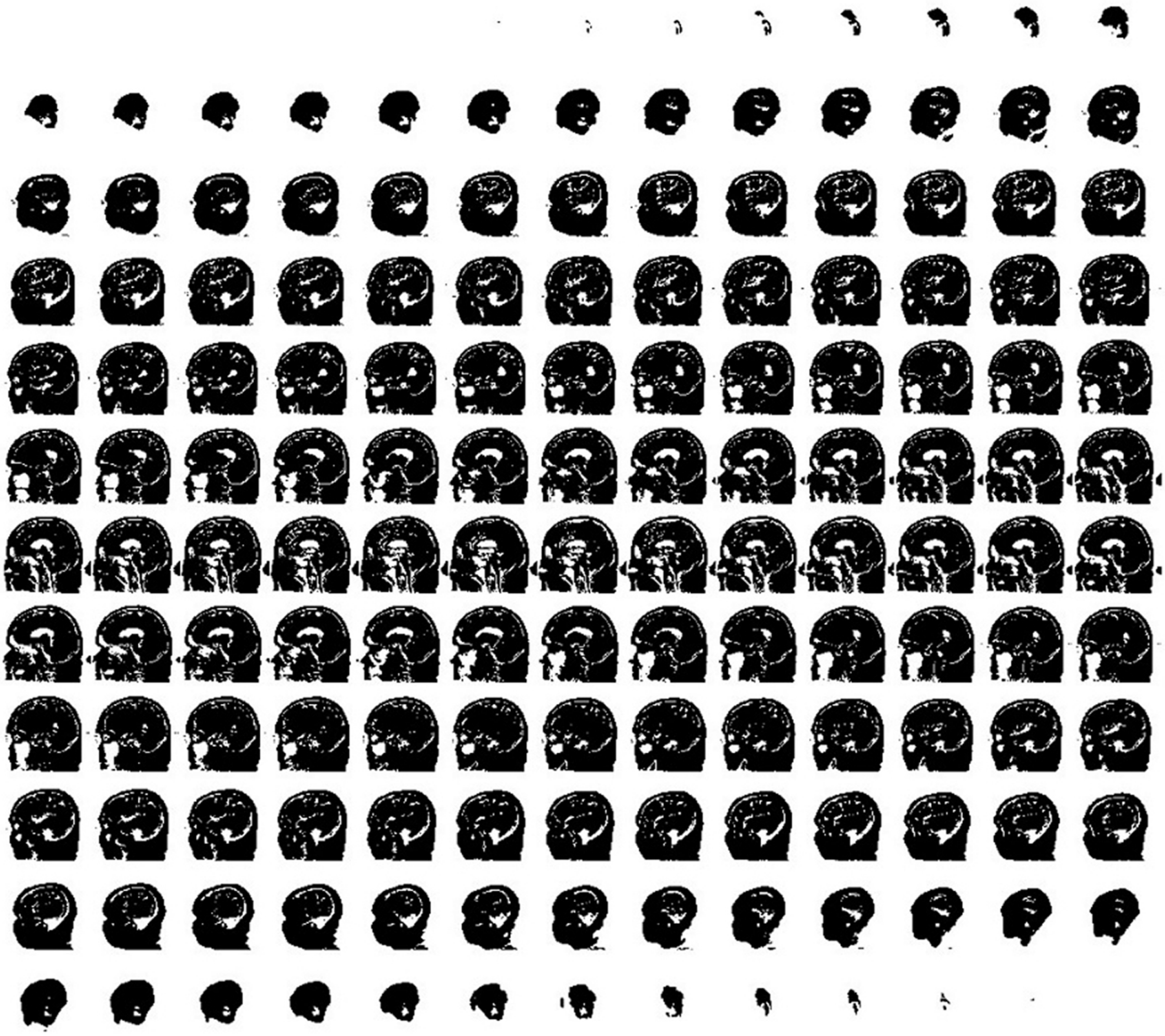


Fig. 8. Resultant image after pre-processing as a montage

Statistical analysis using multidimensional scaling is performed for the description of the effective filtering and histogram-based enhancement technique for pre-processing the 3D MRI images [24]. Variations in the distance range of the metric parameters define the significance of the various pre-processing techniques applied and compared separately with specific image quality parameters. The scaling results of the different filtering techniques are illustrated below in Figure 9. With the results of scaling, the comparison of the filtering techniques is identified to be significant for three efficient filters. In order to determine the efficient filter, the Kruskal-Wallis test is performed to illustrate the significant range of the three filters. The median filter was determined to be more efficient among the filtering techniques applied for the 3D MRI images of AD. By comparing the means of the filters, the median filter is defined to be more efficient. Kruskal Wallis test results for the parameters are illustrated in Figures 10a and 10b. The P value was defined to be near 0.001, stating the variation of mean values among the three filters with the help of the image parameters like PSNR and similarity index.

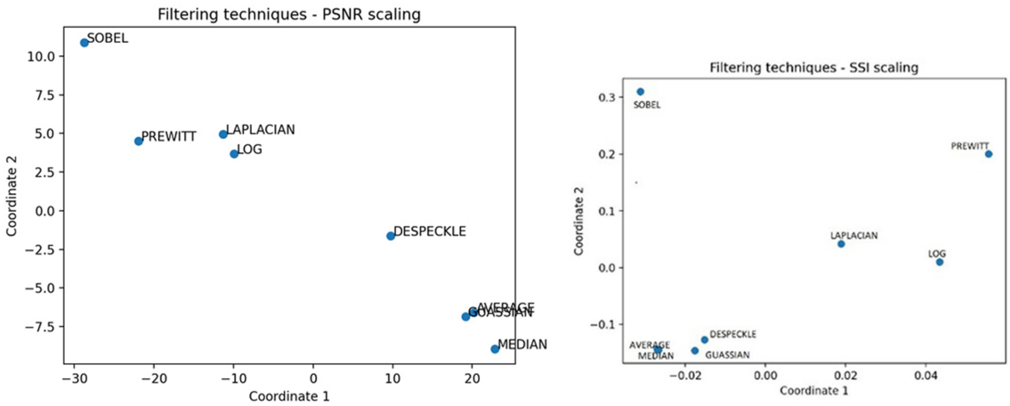


Fig. 9. Multidimensional scaling of the parameters of 3D filtering techniques

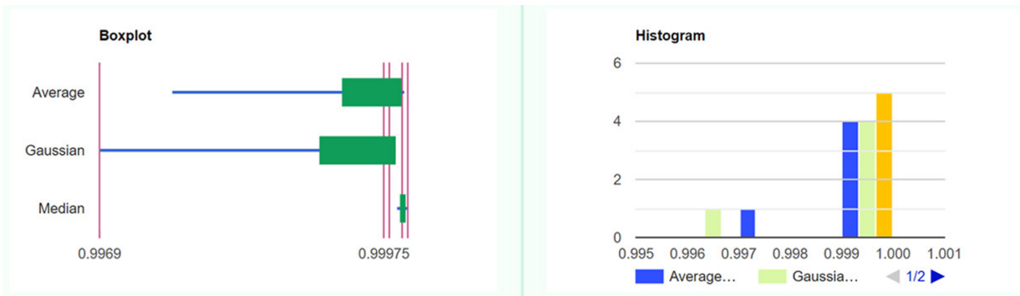


Fig. 10a. Graphical description of the variations among the mean similarity index values of the filters

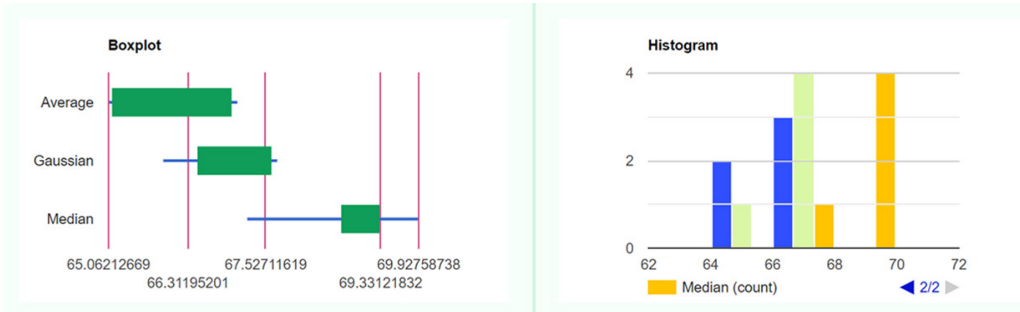


Fig. 10b. Graphical description of the variations among the mean PSNR values of the filters

As the next step of pre-processing, enhancement is performed with histogram-based techniques. The techniques of histogram clipping are analysed using the statistical method called multidimensional scaling. The scaling of the techniques defines a drastic range with respect to the significant level. The variations and significance mean the difference among the histogram-based enhancement techniques illustrate that the proposed histogram eight clipping is the efficient technique. The multidimensional scaling applied for both the image quality parameters like CII and F-measure is described below in Figure 11.

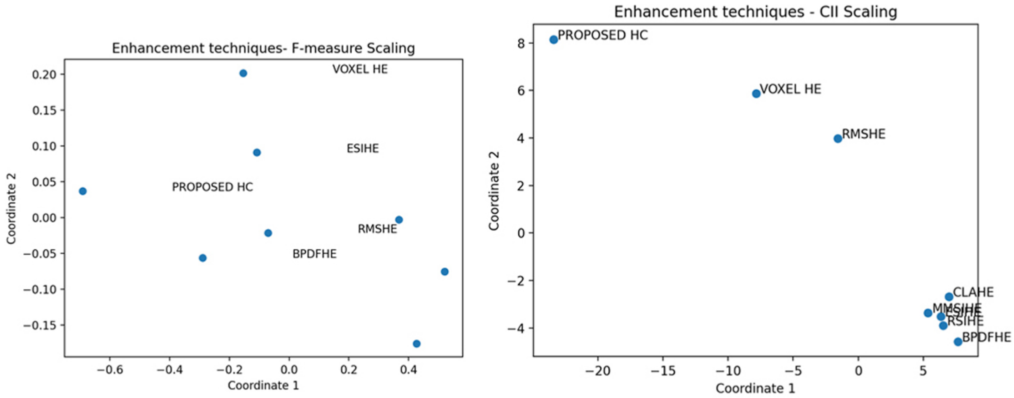


Fig. 11. Multidimensional scaling of the parameters of 3D histogram-based enhancement techniques

Thus, the algorithm for pre-processing the 3D MRI images of different stages of AD is performed with the help of a median filter and eight clipping histogram-based enhancement techniques. This algorithm defines the voxel space of the region of interest, the hippocampus.

The algorithm defined for the pre-processing of the 3D MRI images of different stages of AD is illustrated below with efficient techniques

Step 1: Reorientation of the 3D MRI images of different stages of AD to the standard MNI template.
Step 2: Applying a median filter to reduce noises in the spatial values of the voxels in the ROI for the detection of the atrophy.
Step 3: Use of eight histogram clipping, the proposed methodology subdivides the images into eight clips based on histogram values of the voxels.
Step 4: Eight clips are integrated based on the voxels distribution for the enhancement of the region using defined clipping parameters.
Step 5: The number of clips/subdivisions and the threshold value defines the efficient enhancement of the images
Step 6: The threshold for clipping and enhancement is based on the probabilistic distribution of the voxels in the histogram.
Step 7: The output image as a result defines to be more efficient for the detection and segmentation of the ROI, hippocampus.

Thus the pre-processing algorithm for the 3D MRI images of the different stages of AD for the identification of progressive stages of AD and analysis of Alzheimer's Disease is defined.

4 CONCLUSION

Alzheimer's disease is a neurological condition that impairs brain function and causes cognitive deterioration. Alzheimer's disease can be detected in several phases, including CN, EMCI, LMCI, and severe AD, based on blood tests, neurotransmitter levels, signal imaging techniques, and other factors. MRI, fMRI, PET, and SPECT are the imaging modalities used for 3D MRI picture diagnosis [24, 25]. Magnetic resonance imaging specifies the structural regions to precisely pinpoint the anomalies in the body's various sections. The hippocampus is one of many indicators of Alzheimer's disease. The hippocampus's atrophy can be utilized to both identify the phases of Alzheimer's disease and forecast the brain's cognitive alterations. Therefore, it is required to segment and analyze the hippocampal region in order to determine the phases of AD [20]. MRI scans in 3D from the ADNI database are taken into consideration for the diagnosis and prediction procedure. Based on the voxels, pre-processing of the 3D MRI images is carried out. Filtering, which lowers noise, is the first stage of pre-processing; the three filters are said to be more effective for voxel-level spatial fluctuations. The improvement method based on the histogram is the next pre-processing step. Histogram enhancement of the regions of the images is used to analyze the voxel distribution in the images. The regions of interest should be enhanced using the histogram-based eight-clipping enhancement technique. Different statistical variations among the image parameters in 3D are determined using multidimensional scaling and the Kruskal-Wallis test [26]. Statistical analysis of the parameters defines that median filter and histogram-based eight clipping enhancement are 98% significant and efficient pre-processing algorithms for the detection of stages of AD. Thus, utilizing the resulting images, it is possible to identify the stages of AD and the degree of hippocampal atrophy. The pre-processed pictures will eventually allow for the segmentation and classification of the hippocampal region in relation to the various phases of AD.

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