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A Proposed System for the Early Detection of Alzheimer's Disease

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ABSTRACT
In the medical field, the early detection of Alzheimer's disease (AD) is a crucial factor for management of the disease and providing appropriate treatment, which can be more effective if the disease is detected in as timely a manner as possible. With the recent tremendous revolution in radiology in general and the medical imaging modalities in particular, medical diagnosis has witnessed great progress. However, human interpretation of the brain Magnetic Resonance Imaging (MRI) images, regardless of being normal or abnormal, may lead to misclassification of AD, particularly when detected at its early stages. This issue has given rise to the need for an automated detection system for classifying AD. The present research paper proposes an automated system for the early detection of AD based on the effective Grey Level Co-Occurrence Matrix (GLCM) analysis technique. The proposed system for the early detection of AD has been validated for use after being tested by a group of computer experts and a group of end users; and the results obtained have proved to be satisfactory. In addition, the classification accuracy of the proposed system for the early detection of AD has been verified by a number of neurologists in Mansoura University and has achieved a high classification accuracy rate of 90.53%.
Keywords - Alzheimer's disease, early detection, risk factors, image processing, GLCM.

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I. INTRODUCTION

It is a well-known fact that the brain is the central organ of the human nervous system; and any impairment caused to it because of any disease can lead to entire failure of the human structural organization [1].

The medical diagnosis systems have proved that a normal human brain contains approximately one hundred billion neurons (cell nerves), with each neuron having long branching extensions that enable individual neurons to connect with other neurons forming the so-called synapses (structures that transmit nervous impulses between neurons). This allows information to flow in tiny bursts of chemicals released by the neurons and transmitted to other neurons. In addition, the human brain contains one hundred trillion synapses, which allow signals to travel rapidly through the brain's neuronal circuits, creating the cellular basis of memories, thoughts, sensations, emotions, movements and skills. The accumulation of the beta-amyloid protein fragment (also called "beta-amyloid plaques") outside neurons and the accumulation of an abnormal form of the tau protein (also called "tau tangles") inside neurons represent two main hallmarks associated with Alzheimer's disease [2].

Alzheimer's disease is the most common type of dementia (cognitive decline). It is marked by decline in the memory, thinking abilities and multifactorial disorders, with ageing being considered the major known cause for its occurrence and development [3].

Historically, the discovery of AD dates back to the year 1906, when it was defined for the first time by German Psychiatrist Alois Alzheimer while treating a 51-year-old woman named August Dieter. The woman suffered from some abnormal symptoms such as agitation and confusion, which affected her memory, speech and behavior. Over five years of treatment preceding the patient's eventual death, Dr. Alzheimer concluded that her condition corresponded to the definition of what was then known as dementia. The newly discovered disorder was first discussed in medical research in 1907 and was called Alzheimer's disease in 1910[4].

Theoretically, subsequent medical studies have proved that the early diagnosis of AD can prevent worsening of the patient's condition, despite the fact that the disease is known to be incurable. Actually, the mechanism of distinguishing AD from Normal Cognition (NC) depends on analyzing the MRI data obtained from the human brain images. Practically speaking, the brain MRI analysis shows some features of AD as compared to NC, such as reduction in the volume of grey matter in the temporal lobe, hippocampal formation, insula and left thalamus [5].

Over the past decades, the analysis and interpretation of medical image mainly depended on the medical expert's shrewdness. However, this

procedure was not completely accurate, due to complexity of some patients' images and the analysis subjectivity, which resulted in big differences among various interpreters. Hence, it was necessary to devise new mechanisms for analyzing images and diagnosing diseases to help doctors in providing the appropriate treatment. Among the most important of those mechanisms are image processing techniques [6].

Generally, image processing is a form of signal processing for which the input is an image, such as a photograph or video frame; and the output is either an image or a set of features characterizing the given image in high accuracy [7]. In the medical field, image processing is a special branch of computer vision concerned with detecting various diseases in a non-invasive way using a variety of medical imaging methods, including X-ray, Ultrasonography, Computed Tomography (CT) and MRI [8].

In image processing applications, the quality of input images plays a major role in making any image analysis task a success, because the higher the quality of input image, the easier and simpler the analysis task. On the other hand, automatic image processing is not such an easy task because it involves many processes that make it difficult to perform a fully automatic, such as object detection, feature extraction, image matching etc [9].

Feature extraction is the method of capturing significant key features of the image for the indexing and retrieval purposes [10]. Today, feature extraction has become desperately needed in the medical field, because the medical domain contains a large amount of data generated from the medical imaging and medical test reports explaining the patient's health status [11].

The GLCM method proposed in 1973 by Haralick et.al is considered one of the earliest and most popular techniques for extracting the statistical image features [12]. GLCM is defined as a two-dimensional histogram of grey levels for a pair of pixels, which are separated by a fixed spatial relationship [13]. In practical terms, GLCM can extract a large number of significant image texture features, such as energy, entropy, contrast, homogeneity etc [14].

This paper aims to develop a GLCM-based system for the early detection of AD for patients in general, and patients in the university sector in particular. The paper is organized in several sections. Section I is the introduction. Section II presents an overview of the risk factors of Alzheimer's disease and Section III defines the study problem. Section IV provides details of the proposed system and Section V discusses the obtained results. Finally, the conclusion and future orientation.

II. OVERVIEW OF THE RISK FACTORS OF ALZHEIMER'S DISEASE

Despite the fact that the role of healthcare in dealing with AD is indispensable, we need to find out the main risk factors causing this disease to be able to develop therapeutic agents that can slow down or even prevent its development completely. Over long periods, scientific studies mainly focused on ageing as the only cause of AD, but the most recent studies revealed that there were other risk factors for this disease [15]. Those risk factors can be classified into the following two main types[16,17,18,19,20,21,22,23]:

1- ***Genetic Risk Factors***

According to scientific studies, the symptoms of Alzheimer's disease occur in the majority of patients in their old age, including the early form that occurs in individuals less than 65 years and the late form that occurs in individuals aged 65 years or more. Some scientists have confirmed that genetic factors play a major role in the development of AD in about 70% of patients, and they attributed the early form of AD to mutations in the Amyloid Precursor Protein (APP) gen (located in chromosome 21q21), Presenilin-1 (PSEN-1) gen (located in chromosome 14q24.3) and Presenilin-2 (PSEN-2) gen (located in chromosome 1q31-q42). However, they attributed the late form of AD to polymorphism in the Apolipoprotein E (APOE) gene (located in chromosome 19), particularly the presence of the ε4 polymorphic allele.

2- ***Acquired Risk Factors***

Numerous scientific studies have confirmed that genetic factors are not the only cause of AD, and that there are other acquired factors for the development of AD. The following subsection provides an overview of the most important acquired risk factors.

2.1- Cerebrovascular Diseases

The results of analyzing the brains of Alzheimer's patients have proved that any cerebrovascular changes such as hemorrhagic infarcts, small and large ischemic cortical infarcts, vasculopathies and changes in the cerebral white matter increase the risk of developing AD.

2.2- Hypertension

Hypertension is considered another risk factor for developing AD, because it can cause changes in the vascular walls, which lead to

hypoperfusion, ischemia, cerebral hypoxia and dysfunction in the blood-brain barrier.

2.3- Type 2 Diabetes

Many epidemiological studies have revealed that developing type 2 diabetes has many negative effects, including toxicity of hyperglycemia (high blood sugar), cerebrovascular damage, vascular inflammation, which increases the probabilities of developing AD.

2.4- Obesity

The role of obesity as a risk factor for developing AD remains uncertain according to the heterogeneous results of some studies. On the other hand, other studies have significantly linked obesity (Body Mass Index - BMI ≥30 kg / m2) in midlife with developing AD in later life stages.

2.5- Dyslipidemia

The high levels of cholesterol as a risk factor for developing AD have already demonstrated, as revealed by the results of some studies, that cholesterol levels in patients with AD compared to healthy individuals are higher by 10%. The explanation of those results is that high cholesterol level causes an increase in both amyloid β-protein (Aβ) deposition and the formation of neurofibrillary tangles (NFT) in some regions of the brain. Also, it leads to cognitive decline, neuritis, dysfunction of cholinergic neurons and cerebral microbleeds.

2.6- Marital Status

Studies have shown that there is a relationship between singleness and the development of AD, as the results of those studies have revealed that single individuals have an increased risk of developing AD, as compared to married or cohabiting individuals, indicating that this effect is more obvious in carriers of the ε4 allele of the APOE gene.

2.7- Stress

Stress is characterized by overactivity of the Hypothalamic-Pituitary-Adrenal (HPA) axis that leads to increased production of the cortisol levels in the human body. However, linking the risk of developing AD with the high levels of cortisol is a matter of disagreement among various scientific studies. Some of those studies have revealed that the high cortisol levels increase Aβ peptide deposition in some regions of the brain such as hypothalamus and prefrontal cortex, which in turn leads to developing AD in the long run. Other studies, however, have shown that there is no connection between high cortisol levels and AD development.

2.8- Depression

Studies have shown that suffering from depression by adults in their early life stages increases deposition of Aβ peptide with ageing, and is therefore considered a risk factor for developing AD at old age.

2.9- Sleep Disorder

Studies have generally demonstrated that individuals with sleep disorder and more specifically those with sleep disorder caused by breathing difficulties impairment have an increased risk of developing AD.

2.10- Smoking

Studies have shown that smoking may increase the risk of developing AD through a variety of mechanisms. Smoking increases the production of free radicals, causes oxidative stress and promotes pro-inflammatory action in the immune system, leading to the activation of phagocytes, additional oxidative damage and cerebrovascular diseases, which eventually leads to the development of AD.

III. PROBLEM DEFINITION

Just a few years ago, the world has moved into the digital age, marked by the emergence of new technologies that have generated a wide range of changes in various areas of the human life.

The tremendous revolution in medical imaging techniques has played a significant role in the entire healthcare continuum, by providing wellness, screening, early diagnosis, treatment and follow-up.

For long decades, the medical data extracted from medical imaging has been interpreted by the medical expert. However, over time and for various reasons, a wide variety of unfathomable diseases appeared, which doctors were unable to diagnose with complete accuracy. This situation gave rise to the demanding need for devising new technologies to detect and diagnose such diseases accurately.

Nowadays, image processing has become one of the most accurate and effective technologies that help doctors in diagnosing different types of diseases, including AD.

The current study employs the image processing techniques to build a GLCM-based system for the detection of AD in early stages of human life.

IV. PROPOSED SYSTEM

This section of the paper discusses the details of the proposed system for the early detection of AD, namely system overview, system requirements and system implementation.

a. System Overview

In the proposed system for the early detection of AD, two samples of the human brain images are needed. The first is the normal sample of the human brain image. The second is the query sample of the human brain image submitted to the verification process. The basic steps included in the proposed system for the early detection of AD can be summarized and outlined in Fig.1 below.

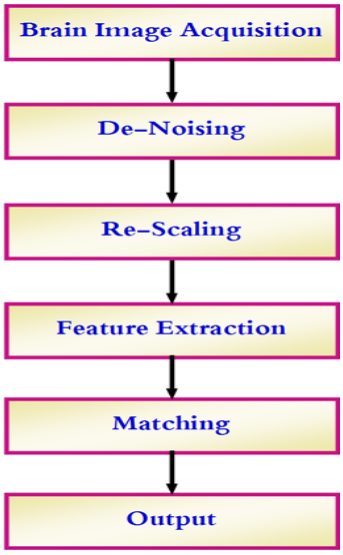

Fig.1: Design flow of the proposed methodology

Every step in this diagram will be briefly presented as follows:

1- Brain Image Acquisition

Uploading human brain images to the computer device is the initial stage in the order of workflow execution. The normal and query human brain MRI images are acquired by a flatbed scanner or a digital camera.

2- De-Noising

The human brain MRI scans are often sensitive to imaging noise and artifacts. Therefore, a group of image enhancement filters has been used to improve the quality of the captured brain MRI images.

3- Re-Scaling

Commonly, the human brain MRI images captured through a flatbed scanner or a digital camera are too large. In order to minimize the processing operations, the dimensions of the captured brain images are resampled to be adjusted to a more appropriate size.

4- Feature Extraction

The significant features of the captured human brain MRI images are extracted using the GLCM technique so that they can be used later in the matching step. The major features of the normal brain MRI image are extracted and stored in the features vector (V1); while the major features of the query brain MRI image are extracted and stored in the features vector (V2). Practically speaking, the two feature vectors are calculated according to the following steps:

4.1- Constructing V1

The full steps for constructing the texture features vector (V1) of the normal human brain MRI image are as follows:

(Step-1): Read the normal brain MRI scan image in a grayscale space.

(Step-2): Remove the noise form the entire normal brain MRI image.

(Step-3): Adjust the dimensions of the normal brain MRI image to a certain size.

(Step-4): Create the GLCM from the enhanced version of the normal brain MRI image in 0°, 45°, 90° and 135° degree directions.

(Step-5): Extract only the major two-order statistical features form the created GLCMs: Energy, Contrast, Homogeneity and Correlation.

(Step-6): Calculate the average value of the Energy samples.

(Step-7): Calculate the average value of the Contrast samples.

(Step-8): Calculate the average value of the Homogeneity samples.

(Step-9): Calculate the average value of the Correlation samples.

(Step-10): Combine all the resulted average values into a one-dimensional texture features representation called V1.

4.2- Constructing V2

The full steps for constructing the texture features vector (V2) of the query human brain MRI image are as follows:

(Step-1): Read the query brain MRI scan image in a grayscale space.

(Step-2): Remove the noise form the entire query brain MRI image.

(Step-3): Adjust the size of the query brain MRI image to the size of the normal brain MRI image.

(Step-4): Create the GLCM from the enhanced version of the query brain MRI image in 0°, 45°, 90° and 135° degree directions.

(Step-5): Extract only the major two-order statistical features form the created GLCMs: Energy, Contrast, Homogeneity and Correlation.

(Step-6): Calculate the average value of the Energy samples.

(Step-7): Calculate the average value of the Contrast samples.

(Step-8): Calculate the average value of the Homogeneity samples.

(Step-9): Calculate the average value of the Correlation samples.

(Step-10): Combine all the resulted average values into a one-dimensional texture features representation called V2.

5- Matching

For determining the presence of Alzheimer's disease in the query human brain MRI scan image, it should be compared to the normal human brain MRI scan image. The comparison process aims to calculate the Similarity Factor (SF) between the significant features of the normal human brain MRI image stored in the vector (V1) and the significant features of the query human brain MRI image stored in the vector (V2). Practically speaking, the SF is calculated according to the following formula:

$$DIFF=ED(V1,V2) \quad (1)$$
$$SF=(1-DIFF)*100$$

Where,
ED: Euclidean distance value between V1 and V2

6- Output

The final output of the proposed system for the early detection of AD is either "Positive AD" or "Negative AD", based on the SF value previously computed. Practically speaking, the final outcomes is calculated according to the following formula:

```
IF SF=100 Then
PRINT Negative AD
OTHERWISE
PRINT Positive AD
```
(2)

b. System Requirements

To use the proposed system for the early detection of AD without any bugs, it is recommended to run it on a computer device having the minimum recommended hardware and software specifications. These include: Intel® Core™ i5 Processor, 2.53 GHz Processor Speed, 4 GB RAM, 500 GB Internal Hard Drive, 15.6 Inch High Resolution 1366 X 768 Screen, Windows 7 Operating System and Matlab R2013a Programming Language.

c. System Implementation

The initial prototype of the proposed system for the early detection of AD has been implemented using Matlab platform on a 64-bit Windows 7 operating system. The main screen of the proposed early AD detection system is shown in Fig.2 below.

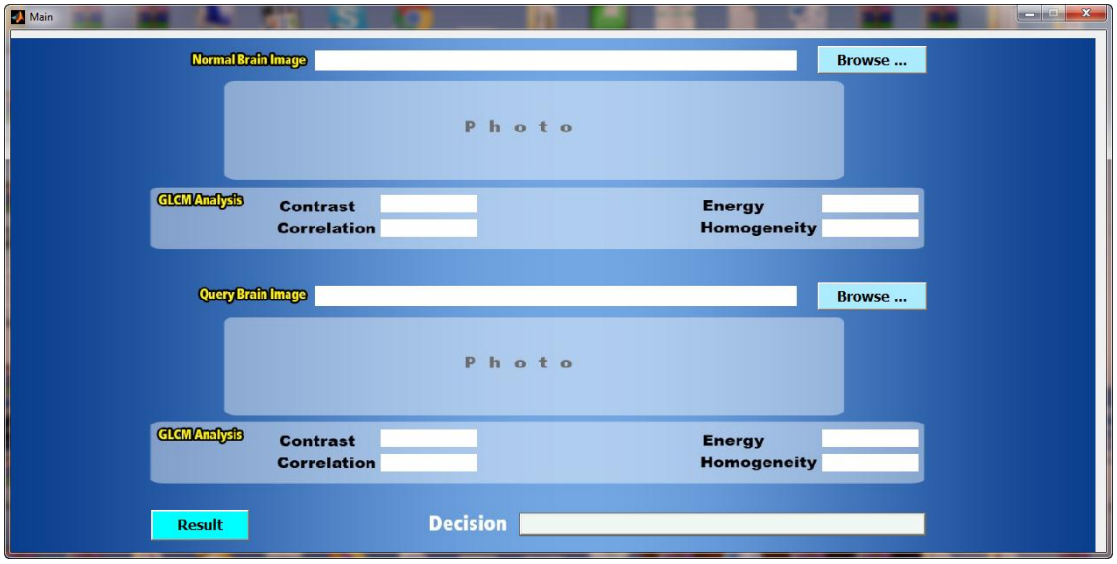

Fig.2: Main screen of the proposed system for the early detection of AD

In the case of uploading the two human brain MRI images and the absence of the disease, the major features of both human brain MRI images are displayed and a report with the result of "Negative AD" is presented after the button "Result" is pressed, as shown in Fig.3 below.

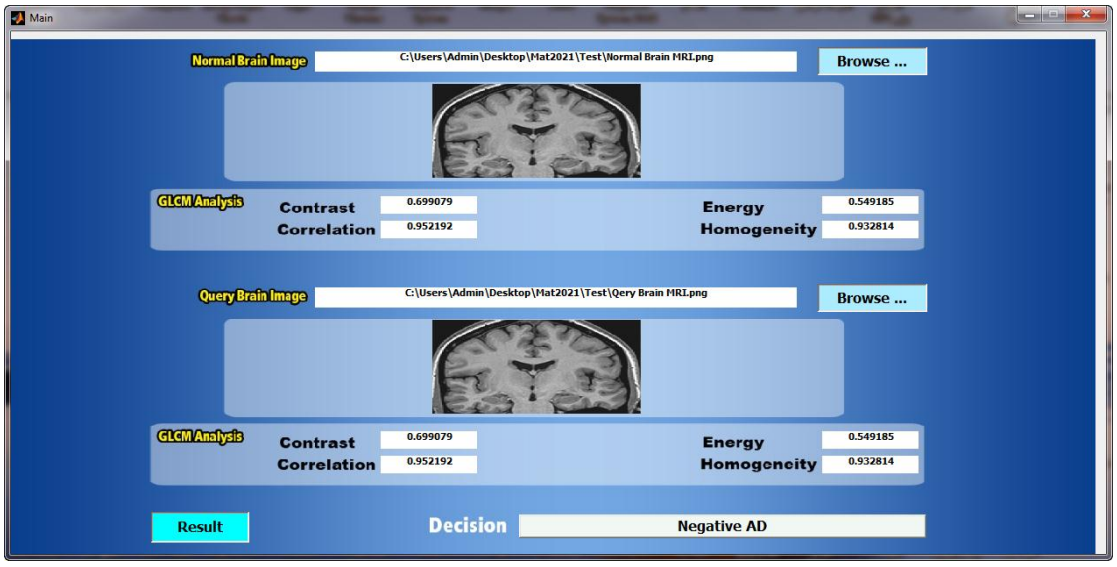

Fig.3: Negative AD report

On the other hand, in the case of uploading the two human brain MRI images and the presence of the disease, the major features of both human brain MRI images are displayed and a report with the result of "Positive AD" is presented after the button "Result" is pressed, as shown in Fig.4 below.

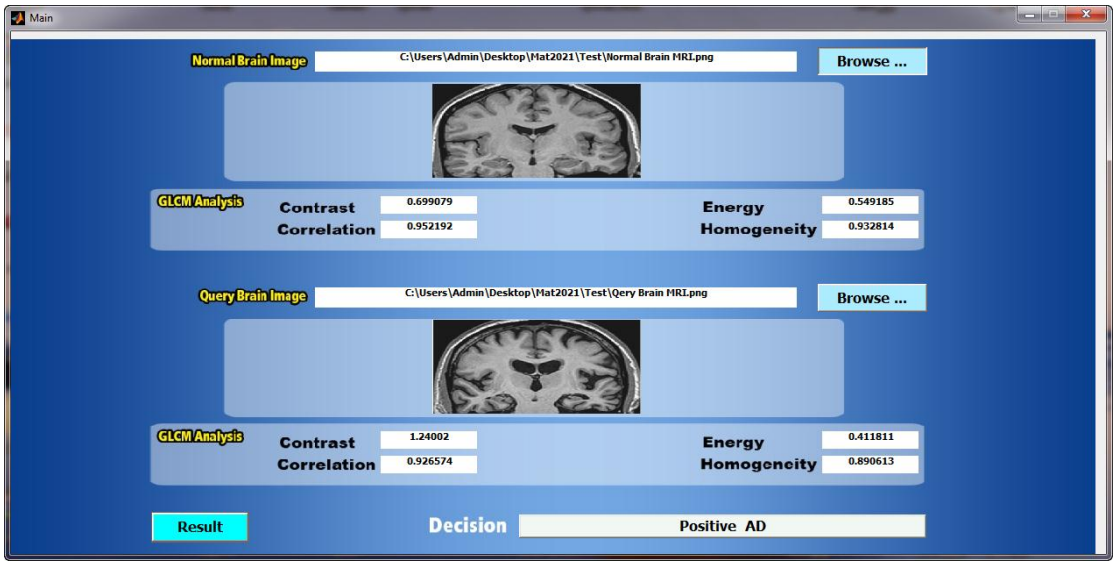

Fig.4: Positive AD report

V. EXPERIMENTAL RESULTS

After the prototype of the proposed system for the early detection of AD has been fully prepared and implemented, its effectiveness is verified through a set of experimental tests divided into two levels. The paper will discuss these tests in detail as follows:

a. *Validity Test*

For measuring the validity of the proposed system for the early detection of AD, a set of experiments is conducted by two teams of human evaluators. The first team comprises a group of experts with a background in computer science; while the second team comprises a group of typical

end users. The evaluation scope of these experiments is based on four major evaluation criteria: appearance, familiarity, functionality and timeliness.

For determining the extent of meeting the evaluation criteria by the proposed early AD detection system, a satisfaction questionnaire form is prepared. The questionnaire form contains a number of questions for measuring the evaluators' satisfaction with various aspects of the proposed system for the early detection of AD. The satisfaction of each evaluation criterion is divided into five levels according to the satisfaction score value presented in Table.1 below.

Table.1: Classification of the satisfaction factor scores and levels

Satisfaction Score	Satisfaction Level
1 - 3	Unacceptable
4-5	Poor
6-7	Good
7-8	V.Good
9-10	Excellent

The feedback of the two evaluation classes is collected and simply analyzed through descriptive quantitative statistical metrics. The results of the experts' satisfaction with the proposed system for the early detection of AD are recorded in Table.2 and summarized in Fig.5 below. On the other hand, the satisfaction results of their counterparts from the end users are recorded in Table.3 and summarized in Fig.6 below.

Table.2: Results of the experts' satisfaction with the proposed system for the early detection of AD

Eval. No	Levels of Experts' Satisfaction			
	Appearance	Familiarity	Functionality	Timeliness
Eval-1	Excellent	V.Good	Excellent	Excellent
Eval-2	V.Good	Excellent	V.Good	V.Good
Eval-3	Excellent	V.Good	Excellent	Excellent
Eval-4	V.Good	Excellent	V.Good	V.Good
…..	…..	…..	…..	…..
Eval-N	V.Good	V.Good	Excellent	Excellent
Overall Average	**(88%)**	**(86%)**	**(90%)**	**(91%)**

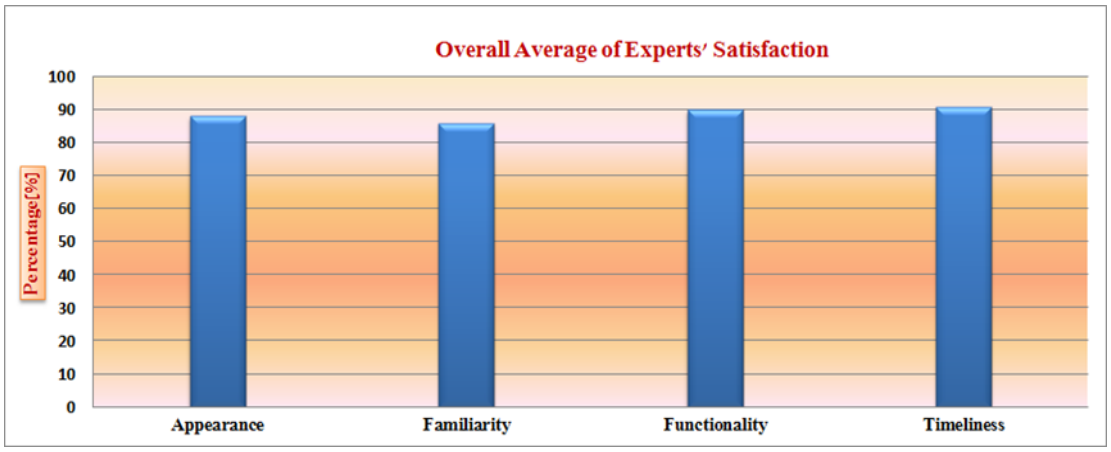

Fig.5: Overall average of the experts' satisfaction with the proposed system for the early detection of AD

Table.3: Results of the end users' satisfaction with the proposed system for the early detection of AD

Eval. No	Levels of End Users' Satisfaction			
	Appearance	Familiarity	Functionality	Timeliness
Eval-1	Excellent	Excellent	Excellent	Excellent
Eval-2	Excellent	Excellent	Excellent	Excellent
Eval-3	Excellent	Excellent	Excellent	V.Good
Eval-4	Excellent	V.Good	Excellent	Excellent
…..	…	…	…	…
Eval-N	Excellent	Excellent	V.Good	Excellent
Overall Average	**(95%)**	**(93%)**	**(92%)**	**(92%)**

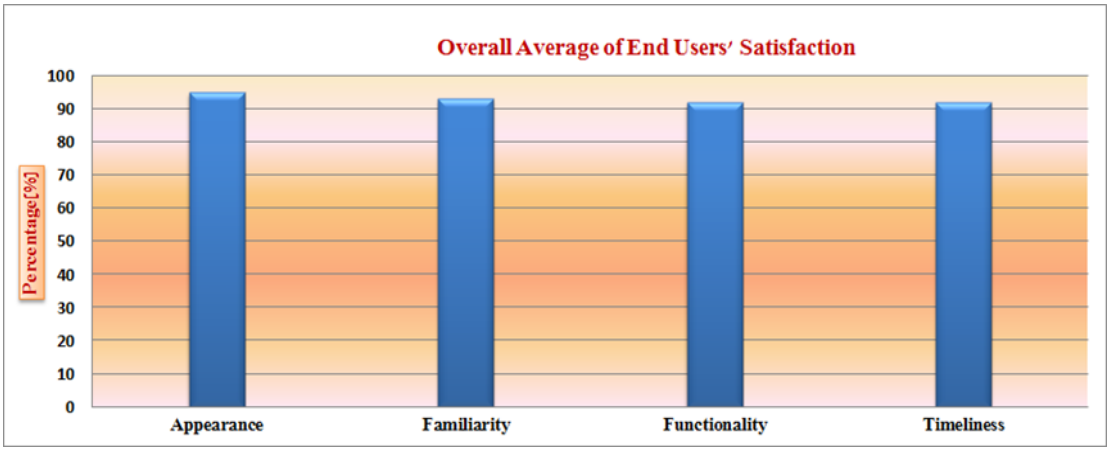

Fig.6: Overall average of the end users' satisfaction with the proposed system for the early detection of AD

Generally, the abovementioned results show that the two evaluation teams are unequally satisfied with the proposed system for the early detection of AD. The same results have revealed that the overall average of experts' satisfaction on the appearance criterion is 88% and that the overall average of end users' satisfaction on the appearance criterion is 95%. The results have also revealed that the overall average of experts' satisfaction on the familiarity criterion is 86%' and that the overall average of end users' satisfaction on the familiarity criterion is 93%. In addition, the results have shown that the overall average of experts' satisfaction on the functionality criterion is 90% and that the overall average of end users' satisfaction on the functionality criterion is 92%. Finally, the results have shown that the overall average of experts' satisfaction on the timeliness criterion is 91% and that the overall average of end users' satisfaction on the timeliness criterion is 92%.

The justification for the difference between the two evaluation teams in acceptance of the proposed system for the early detection of AD is that the experts have more experience and knowledge than the end-users. This enables them to evaluate different aspects of the proposed system accurately unlike the end-users who often focus more on the outward appearance of the proposed system than on the functional aspect, which makes their assessment somewhat doubtful.

b. ***Classification Accuracy Test***

For verifying the classification accuracy of the proposed system for the early detection of AD, the system was tested by a number of neurologists at Mansoura University. The tests were performed on a large sample of human brain MRI images, with the test sample of the brain MRI images being divided into four groups according to age and gender. The results of testing the classification accuracy of the proposed early AD detection system were recorded in Table.4 and shown in Fig.7 below.

Table.4: Results of the classification accuracy test of the proposed early AD detection system

Dataset Group	Classification Accuracy [%]
Male	88.5
Female	91.7
Age From 45 To 65	89.6
Age Over 65	92.3
Overall Average	**90.53**

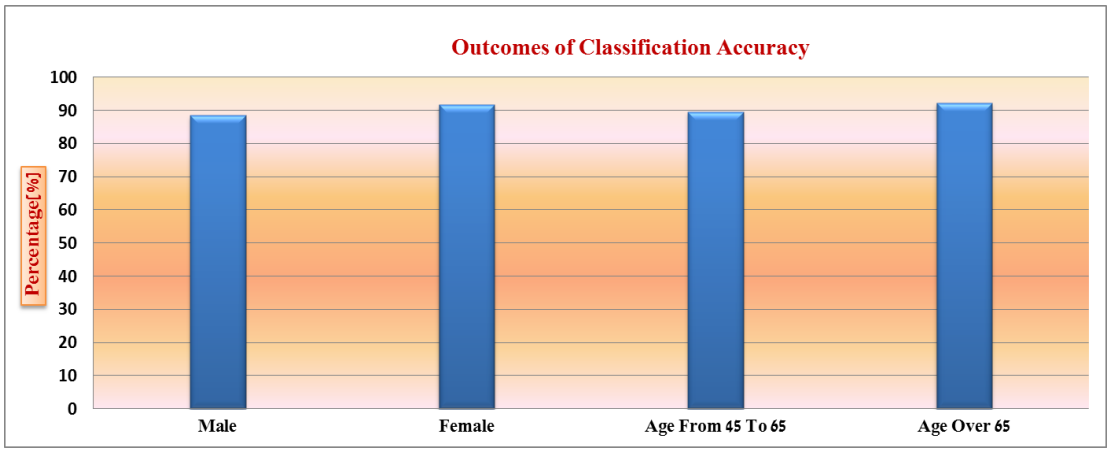

Fig.7: Classification accuracy of the proposed system for the early detection of AD

Generally, the abovementioned results confirm that the classification accuracy of Alzheimer's disease is higher for women than for men, and higher for those over the age of sixty-five. These results are in line with the results of the study published in [4], which employed Support Vector Machine (SVM) classifier for the early detection of Alzheimer's disease. They have concluded that the highest classification accuracy is achieved in the case of the group of older people (aged between 66 and 90), and the group of females.

Comparing those results to the results reached by some previous studies, we realize that the proposed system has achieved a satisfactory classification accuracy. For example, its classification accuracy is greater than the classification accuracy achieved by the study of Fraser et al, which employed logistic regression method and reported a classification rate in distinguishing AD up to 81.92% as shown in Fig.8 below [24].

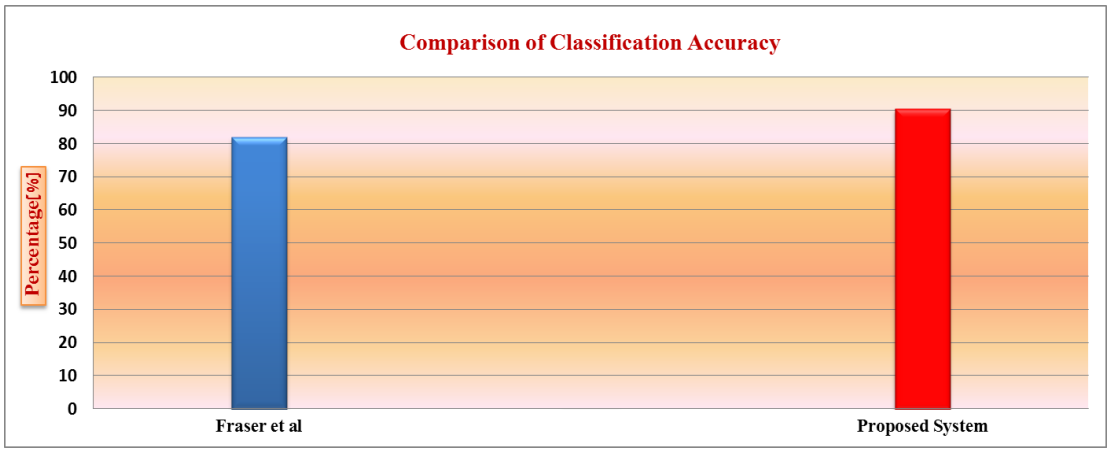

Fig.8: Comparison of the classification accuracy of the proposed early AD detection system with related studies

Based on these positive results, we can confirm that the proposed system for the early detection of AD has achieved its goals efficiently, and accordingly it can be used on a large scale for detecting AD at its early stages.

VI. CONCLUSION AND FUTURE WORK

Over the past few years, the automatic detection and classification of Alzheimer's disease became an important issue in our life, because of the inability of the conventional medical diagnosis to detect this vague disease, particularly in young people. In this paper, some image processing techniques were employed for the early detection of Alzheimer's disease. The features of both the normal human brain MRI image and the query human brain MRI image were extracted using the GLCM. After that, the extracted features were compared to report

either a Positive AD if the disease is present or a Negative AD if the disease is absent. The proposed early AD detection system firstly received acceptance of the two evaluation teams, one of which comprised a group of computer experts while the other comprised a group of end users. Then, it achieved a classification accuracy of 90.53%, which is considered a high percentage when compared to the percentage achieved by the similar related studies.

For future work, the researcher plans to collect the patient's acoustic features and combine them with the features of human brain MRI image to improve the AD classification accuracy.

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