MACHINE LEARNING-BASED METHOD FOR PERSONALIZED AND COST-EFFECTIVE DETECTION OF ALZHEIMER'S DISEASE

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ABSTRACT

Diagnosis of Alzheimer's disease (AD) is a main problem in now a days, many people's are suffering from the Alzheimer's disease (AD). In this disease having some stages like mild congestive impairment (MIC) (early stage),moderate (middle stage),severe (late stage).In the disease mild congestive impairment (MIC) stage we can't observe in this stage treatment is must be effective, great advantages in diagnosis improving of this diagnosis process. In this work describe and test for a machine learning based diagnosis of Alzheimer's disease it is a classifier model to patient and the machine(computer)and the biomarkers are mostly useful in this diagnosis of alzheimers.Using ADNI data classified AD and control the mild congestive patients report within a year. And patients are having Alzheimer's disease or not it will be says. It is reducing a needed of numbering of biomarkers (i.e MRI,CT,PET etc….).It is used to definitely identified by the Alzheimer's disease using machine learning technique. In this mostly decreasing the saving of time and reducing of cost. Easily find out the stage of Alzheimer disease(AD).It is only taken by the patients details only like age, gender, education,etc….the ADNI having of old patients data. the new subject date and the old patient data will be comparing of the machine to determined which biomarker gives best and effective result. It is use different types of classifiers, like support vector machine(SVM), Logistic regression (LR) Locally weighted learner with logistic regression(LWL-LR)

Index terms-Alzheimer's disease (AD), Biomarkers, Classifiers, Data base, machine learning, MAT LAB Software. Mild congestive impairment.

I. INTRODUCTION

Alzheimer's Disease (AD) is a degenerative brain disease. It is a effect on human thoughts and work. It is also caused by the other diseases and conditions. Like a decline in memory, effected on nerve cells. In Alzheimer's disease, neuronal damage eventually affects parts of the brain that enable a person to carry out basic bodily functions such as walking and swallowing eating etc.. Alzheimer's Disease is a terminal disease with no disease-modifying treatment available as yet. Dementia is an umbrella term which is used to describe a set of symptoms, and there are many different types of dementia including Alzheimer's Disease, vascular dementia, dementia with Lowy bodies, and others, but dementia of the Alzheimer's type (AD) is by far the most common cause of dementia, and this is the type of dementia this thesis is concerned.

It is widely accepted that an early detection of dementia can lead to a more effective intervention and the limiting of morbidity (Petersen et al. Furthermore, Petersen et al. conclude from their work that people who meet the criteria for MCI can be differentiated from healthy control subjects and those with very mild Alzheimer's Disease This group of subjects appear to constitute a clinical entity that can be characterized for treatment interventions.

To date, the diagnosis of most forms of mental disorder has been based on clinical observation. Specifically these include the identification of symptoms that tend to cluster together, the timing of the symptoms' appearance, and their tendency to resolve,

recur or become chronic. There is currently no cure for Alzheimer's Disease and we lack any form of reliable and effective early diagnostic tools. Boise et al. confirm earlier studies regarding low rates of clinical assessment and diagnosis and postulate a possible explanation for this in the subtlety of dementia symptoms combined with the constraints physicians face in their clinical practice.

Alzheimer's disease is clinically diagnosed by performing physical and neurological examinations, and checking other signs of intellectual impairment through standard neuropsychological and cognitive tests. The general approach is based around diagnosis by elimination, i.e. ruling everything else out until Alzheimer's disease remains the last option.

In addition to the above clinical measures, according to Dubois et al. the guidelines for the diagnosis of Alzheimer Disease emphasize the role that can be played by using various Biomarkers. Like magnetic resonance imaging(MRI), positron emission tomography (PET), Computerized tomography (CT), Single photon emission computed tomography (SPECT) etc…There are analysis of genetic risk profiles though these are expensive and difficult to scale to large numbers of assessments There is no single test that can show whether a person has or does not have Alzheimer's Disease. While physicians can almost always determine if a person has dementia, it may be difficult to determine the exact cause.

Alzheimer's disease epidemiology and risk factors

In the developed world, Alzheimer's disease accounts for 50–60% of all dementia cases. Vascular, lewd body and frontal lobe are some of the other causes of dementia. The prevalence of dementia increases with age, rising from 1% in the 60-64 to between 24 and 33% in those 85 years or older. In 2001, an estimated 24.3 million people had dementia, this is expected to double every two decades as life expectancy also increases; rising to 81.1 million in 2040. The countries and regions of the world which are the most affected are Western Europe, the USA and China. By 2040 these countries and region will be home to 55.7% of the total affected population.

Diagnosis & clinical symptoms of Alzheimer's disease

Classification and Diagnostic criteria

The classification and the criteria used to diagnose dementia and Alzheimer's disease is set out in the Diagnostic and Statistical Manual of Mental Disorders (4th ed, text revision, DSM- IV-TR) (APA) and the International Statistical Classification of Diseases and Health –related Problems, 10th revision (ICD-10). The DSM-IV-TR (APA) and ICD-10 classifies dementia as memory impairment with one or more impairment(s) in other cognitivedomains.

The ICD-10 defines Alzheimer's disease as "a primary degenerative cerebral disease of unknown etiology with characteristic neuropathological and neurochemical features. The disorder is usually insidious in onset and develops slowly but steadily over a period of several years.

The main cognitive symptoms of Alzheimer's disease are amnesia, aphasia, apraxia, agnosia, and executive dysfunction. Over the course of the illness these symptoms become more pronounced, owing to an increase in disease severity. There are also non-cognitive symptoms that are prominently manifested during the course of the disease. These are the behavioral and psychological symptoms. Symptoms such as agitation, apathy, depression, hallucinations and delusions occur at some stage in most patients. They cause significant distress to both patients and their carers and lead to early institutionalization of patients.

A.DNI Database:

II.USEDTTERIALSMA

In this database are download and it is a main part of this paper and it is having from known patients data for Alzheimer's disease(AD) patients and the no disease patients data and mild congestive implement(MIC) patients all information is there in the database. it is mainly considered by the values are observed by the so many patients details of taken by the age, gender, education etc...In this database used by the to known the patient having Alzheimer's disease (AD) or not. The α

B.General cost of the Biomarkers:

Generally the cost of the biomarkers are high like Magnetic resonance imaging (MRI), positron emission tomography (PET), Computerized tomography (CT), Single photon emission computed tomography (SPECT) these are very costly biomarkers(Using brain scanning purpose).But, the ADNI Database used we will taken by the patient details only like age, gender, year of education etc..Compare by those techniques machine learning based test will be reduced by the cost and time.

Magnetic Resonance Imaging (MRI)

Magnetic resonance imaging is a medical imaging technique used in radiology to form pictures of the anatomy and the physiological processes of the body in both health and disease. MRI scanners use strong magnetic fields, electric field gradients, and radio waves to generate images of the organs in the body. MRI does not involve X-rays and the use of ionizing radiation, which distinguishes it from CT or CAT scans. Magnetic resonance imaging is a medical application of nuclear magnetic resonance (NMR). NMR can also be used for imaging in other NMR applications such as NMR spectroscopy.

MRI was originally called 'NMRI' (nuclear magnetic resonance imaging) and is a form of NMR, though the use of 'nuclear' in the acronym was dropped to avoid negative associations with the word. Certain atomic nuclei are able to absorb and emit radio frequency energy when placed in an external magnetic field. In clinical and research MRI, hydrogen atoms are most often used to generate a detectable radio-frequency signal that is received by antennas in close proximity to the anatomy being examined. Hydrogen atoms are naturally abundant in people and other biological organisms, particularly in water and fat. For this reason, most MRI scans essentially map the location of water and fat in the body. Pulses of radio waves excite the nuclear spin energy transition, and magnetic field gradients localize the signal in space. By varying the parameters of the pulse sequence, different contrasts may be generated between tissues based on the relaxation properties of the hydrogen atoms therein.

Positron-emission tomography (PET)

Positron-emission tomography (PET) is a nuclear medicine functional imaging technique that is used to observe metabolic processes in the body as an aid to the diagnosis of disease. The system detects pairs of gamma rays emitted indirectly by a positron- emitting radionuclide(tracer), which is introduced into the body on a biologically active molecule. Three-dimensional images of tracer concentration within the body are then constructed by computer analysis. In modern PET-CT scanners, three-dimensional imaging is often accomplished with the aid of a CT X-ray scan performed on the patient during the same session, in the same machine. If the biologically active molecule chosen for PET is fludeoxyglucose(FDG), an analogue of glucose, the concentrations of tracer imaged will indicate tissue metabolic activity as it corresponds to the regional glucose uptake. Use of this tracer to explore the possibility of cancer metastasis (i.e., spreading to other sites) is the most common type of PET scan in standard medical care (90% of current scans). Less often, other radioactive tracers are used to image the tissue concentration of other types of molecules of interest. One of the disadvantages of PET scanners is their operating cost.

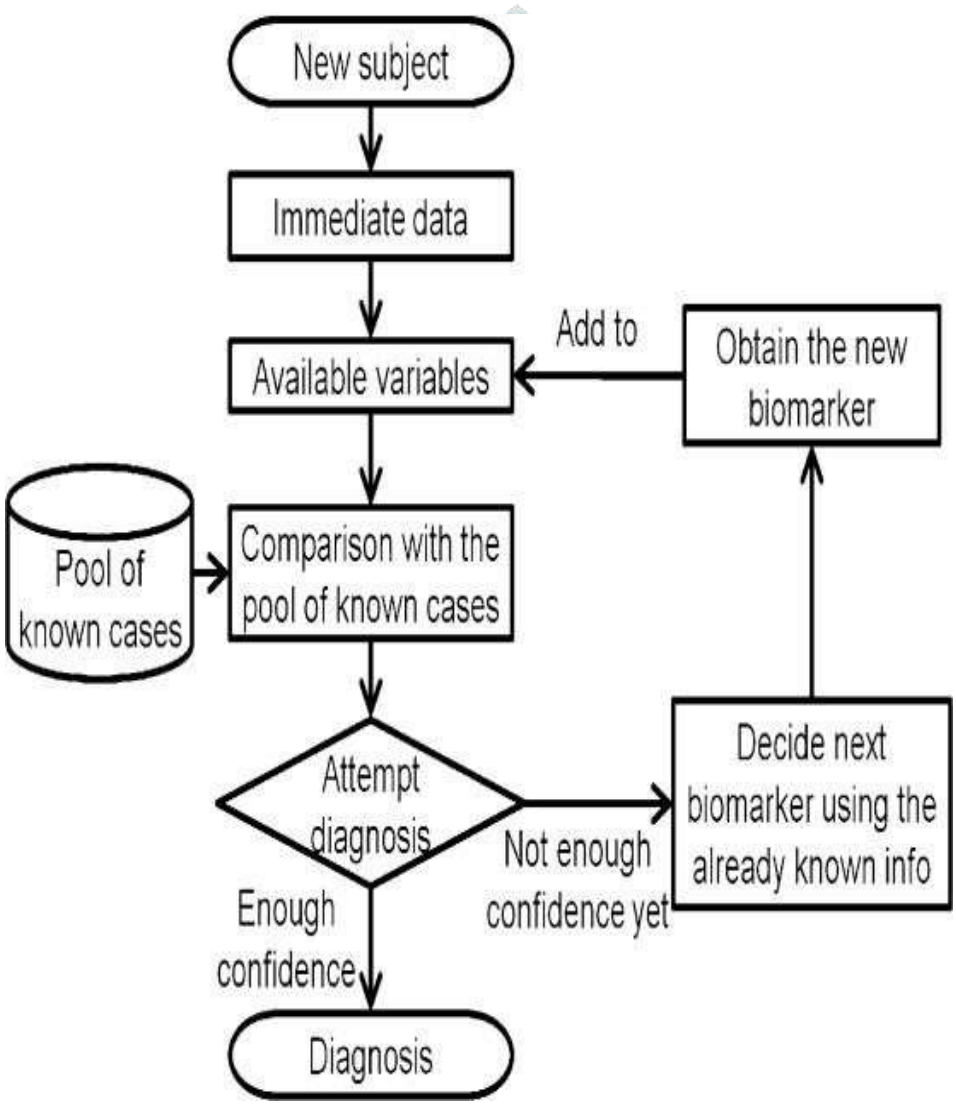
PET imaging is best performed using a dedicated PET scanner. It is also possible to acquire PET images using a

conventional dual-head gamma camera fitted with a coincidence detector. Although the quality of gamma-camera PET is considerably lower and acquisition is slower, this method allows institutions with low demand for PET to provide on-site imaging, instead of referring patients to another centre or relying on a visit by a mobile scanner.

III.PROCESS

In this process mainly used by the block diagram carefully observed that process i.e. First of all we will taken bye the New subject details and we will taken by the Immediate data it means we will taken by the new patient age, gender and year of education like as detains are taken and the useful information will be taken next process is the available data and the known pool cases(i.e.ADNI Database) compare and attempt the diagnosis the result will be diagnosis otherwise Decide next biomarker using the already known information next obtain The next biomarker added by the available data in this process observed by the block diagram1.

A. Personalized classification



Instance-based classifiers (e.g., k nearest neighbors), also known as memory-based classifiers, combine the information from the training set with that of the new subject to create an ad hoc classification model . Other methods (e.g., neural networks) process all data in advance to create one decision model that is applied to all cases. The former may be sensitive to noisy data, whereas the latter are unable to do any personalization. An alternative is locally weighted learning which weights each training instance by its distance to the new subject to reflect how relevant each case in the training set is with regard to the subject to be classified. Then,

the weighted instances are used to train a classifier. Locally weighted learning is similar to memory-based classifiers because all computation is deferred to the moment the subject to be classified arrives so that an ad hoc decision rule is created. Thus, it allows us to tailor the classifier to each patient by allocating the most importance in training to the cases most similar to the patient.In this work used to the classification model so classification is depends upon the α values. there are a locally weighted learning very linearly values in this values are ranging from 0 to 1 the output of logistic regression method ranges from 0 to 1,It can be seen as the probability Pr that the subject being classified is a positive case. If *Pr **is*** high (Pr>1- α) surly patient diagnosis is positive, Pr<1- α not confidence in the diagnosis another biomarker is needed, Pr< α most probably the subject is a negative case. the diagnostic process ends. Otherwise α <Pr< 1 – α, there is not enough confidence in the diagnosis, and more biomarkers are needed. Using only the training set, all variables are normalized to the [0,1] range and synthetic minority oversampling technique is used to equalize the frequency of the classes.

B.Selection of Additional Biomarkers

Feature selection is used to decide which variables are most informative for a task. The feature selection considered in most articles is difficult to be directly applied in clinical settings because it assumes that all biomarkers are readily available and it is not personalized. a personalized approach based on the distance between the new subject and known cases in the Pool may solve such problems. The personalized approach selects the biomarkers one by one. It starts by taking the already available data and weights that account for the similarity between the subject and known cases in the Pool. Performance of this “old” setting. Then, in turn, each other potential biomarker available for the subjects in the Pool is added to the set of features to create a “new” set of variables. Ten runs of a tenfold cross validation are run again within the Pool so that the difference between the “old” and the “new” performance is computed for every biomarker. The one that maximizes this difference is selected. The “old” and “new” classifications are computed using the weights of the previous diagnosis attempt because cases similar to the new subject will tend to remain similar when more biomarkers are added.

The performance in this selection procedure is measured with two criteria

1) Accuracy (ratio of correctly classified cases)

2) Area under the ROC curve

Three confidence thresholds α are studied (0.10, 0.15, and 0.20). These values are chosen because the diagnostic accuracy of AD in common clinical practice is about 80% , and it is expected that an ideal biomarker for AD should have sensitivity and specificity of no less than 80% . For a fair comparison with bulk-data classifiers, a classical logistic regression based on all variables is applied to both tasks. We also compare our results with those of a system where logistic regression is combined with locally weighted learning, but no feature selection is used at all. This is an intermediate development where the decision rule is personalized but there is no feature selection what so ever.

IV. EVALUATION

We evaluate our approach using leave-one-out cross validation. One participant is considered the new subject and is left out for testing, while the remaining participants are considered the Pool of known cases (training set). This process is repeated as many times as subjects, leaving a different one out each time . The method is assessed against four criteria: Final accuracy, final AUC, number of biomarkers to achieve a confident classification, and cost of such biomarkers.

Two classification tasks are considered :

(1) CN versus AD

2) nMCI versus cMCI, while the system operates in two modes: minimization of number or cost of biomarkers.

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V. Support Vector Machine

Support Vector Machine (SVM) is an algorithm that was developed for pattern classification but has recently been adapted for other uses, such as finding regression and distribution estimation. It has been used in many fields such as bioinformatics, and is currently a very active research area in many universities and research institutes which include the National University of Singapore (NUS) and Massachusetts Institute of Technology (MIT).Although the SVM can be applied to various optimization problems such as regression, the classic problem is that of data classification. The basic idea is shown in figure

- The data points are identified as being positive or negative, and the problem is to find a hyper-plane that separates the data points by a maximazlargin.
- The above figure only shows the 2-dimensional case where the data points are linearly separable. The mathematics of the problem to be solved is the following:

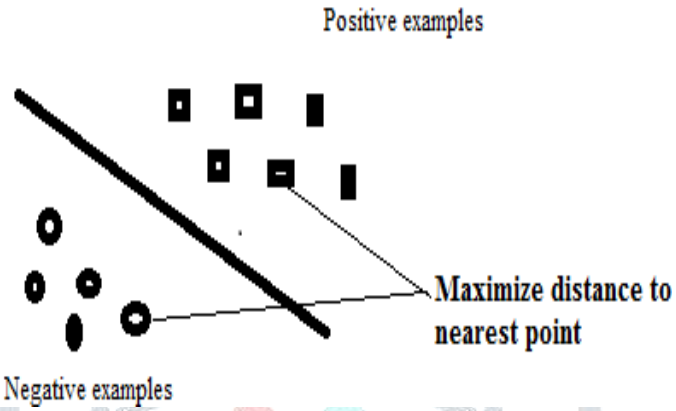
$$\min_{w,b} \frac{1}{2} w ,$$

$$s.t \quad y_i = +1 \Rightarrow w \cdot x_i + b \geq +1$$

$$y_i = -1 \Rightarrow w \cdot x_i - b \leq -1$$

The identification of the each data point x_i is y_i, which can take a value of +1 or -1 (representing positive or negative respectively). The solution hyper-plane is the following:

$$u = \vec{w} \cdot \vec{x} + b$$



Data Classification

Definition:

A support vector machine constructs a hyper plane or set of hyper planes in a high or infinite-dimensional space, which can be used for classification, regression, or other tasks. Intuitively, a good separation is achieved by the hyper plane that has the largest distance to the nearest training-data point of any class (so-called functional margin), since in general the larger the margin the lower the generalization error of the classifier. Whereas the original problem may be stated in a finite dimensional space, it often happens that the sets to discriminate are not linearly separable in that space. For this reason, it was proposed that the original finite-dimensional space be mapped into a much higher-dimensional space, presumably making the separation easier in that space. To keep the computational load reasonable, the mappings used by SVM schemes are designed to ensure that dot products may be computed easily in terms of the variables in the original space, by defining them in terms of a kernel function K(x,y) selected to suit the problem. The hyper planes in the higher- dimensional space are defined as the set of points whose dot product with a vector in that space is constant.

VI.RESULTS

LR-AUC and Accuracy 90.246335 81.269868

LWL-LR- AUC and Accuracy 90.307007 86.323592

TABLE. I-LR &LWL-LR AUC AND ACCURACY

Alpha values	LR With AUC	LR With ACC	LR With AUC Accuracy	LR With ACC Accuracy	LWL-LR With AUC	LWL-LR With ACC	LWL-LR With AUC Accuracy	LWL-LR With ACC Accuracy
0.05	90.764742	90.675939	81.576131	84.217613	89.061921	89.587663	80.971318	81.868726
0.1	90.719108	90.471946	82.784982	86.557407	86.137816	89.361599	82.769230	84.387444
0.15	87.375052	90.325884	88.002805	86.787352	84.369494	86.052468	86.554779	86.948266
0.2	86.883005	84.135091	89.571669	87.922073	83.369371	85.536796	87.060461	87.655168
0.25	83.780323	83.285693	89.575068	88.491293	83.254663	83.275569	87.431325	89.502220
MRI & PET								

The logistic regression(LR) and Locally weighted learner(LWL-LR)with logistic regressions been applied classifier to total data. Other rows correspond to total personalized classifiers with different values of α and criteria to select the sequence of biomarker

SVM Final AUC and Accuracy 90.565584 90.770745

TABLE-II-SVM AUC AND ACCURACY

Alpha values	SVM With AUC	SVM With ACC	SVM With AUC Accuracy	SVM With ACC Accuracy
0.05	90.495124	90.325046	90.471238	89.810437
0.1	90.483222	90.013831	90.808360	90.338970
0.15	91.258439	90.789048	91.261574	90.792183
0.2	90.659178	90.189787	90.946387	90.476992
0.25	90.496995	90.024138	91.740671	91.078978
CT-SCAN				

The Support vector machine (SVM) Classifier is used it is a reducing the number of biomarkers.

VII.CONCLUSION

In this work tested a machine learning approach for personalized and cost-effective detection of AD based on:

1) locally weighted learning and
2) a sequential selection of biomarkers to reduce their number or cost for confident diagnosis.

Two classification tasks were addressed: CN–AD and cMCI– nMCI. The approach is closer to the clinical setting, where not all biomarkers are available at once. It also considers which previous cases are more relevant for the patient. The personalized classifiers tried to minimize the number or cost of the biomarkers included in the process. In both modes, the classifications were considerably more cost-effective than those based on all variables as there were important reductions in the diagnosis cost. On the other hand, the system optimizing the cost tended to select inexpensive biomarkers first and only if these were not conclusive were more expensive tests chosen. The overall classification performance was better when the system tried to minimize the number of biomarkers.

The system assumes that not all biomarkers are available at once and it could be modified to account for other criteria than just cost when selecting the biomarkers This could be done by deriving appropriate "modified costs" accounting for the relative effects of such factors The "modified costs" could also incorporate the clinician's prior expertise to guide the system towards specific biomarker combinations. We acknowledge that the classification performance of the system is not high enough to replace clinical diagnosis and that it is sometimes lower than that obtained considering all variables at once. However, this is not an inherent limitation of the method because its aim is to support, and not replace, the clinician, who must always make the final decision on clinical diagnosis.

The SVM classifier is used and it is a reducing the area under curvy (AUC) And Accuracy values and it is an also reduce the needed of biomarkers.

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