Pattern Recognition of Alzheimer's disease on PET images

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Abstract

Alzheimer's disease (AD) causes degenerative changes in the nervous tissue, which results in progressive loss of memory and cognitive functions. Alzheimer's disease is the most frequent type of dementia. The prevalence of Alzheimer's disease increases in the elderly patients, and given the fact that population is getting older it is expected that incidence increases. Currently, there is no cure for Alzheimer's disease, but early diagnosis and treatment can slow its progression.

The *Positron Emission Tomography* (PET) examination specifies the functional changes in the human brain and it is an useful tool in analyzing the cerebral blood flow. The regional abnormalities for Alzheimer's disease cause the reduction of blood flow, mainly the temporal lobe, parietal lobe and hippocampus. However, the difficulty of the analysis and interpretation of PET imaging in the diagnosis of Alzheimer's disease led to the use of methods of pattern recognition on PET imaging as a tool for automatic diagnosis of Alzheimer's disease.

In this work, we used the *k*-nearest neighbour and Boosting methods in discrimination between the AD and Normal classes, Mild Cognitive Impairment (MCI) and Normal, and finally between the AD and MCI classes, with the purpose of making them a useful and effective tool in the automatic diagnosis of Alzheimer's disease. The implementation of the MCI class, rarely studied, allows the early diagnosis of Alzheimer's disease through the binary distinction between the MCI and Normal classes. Both methods are afflicted by the problem of "*curse of dimensionality*".

The Boosting algorithm Adaboost achieved better performance than *k*-nearest neighbour method in all discrimination between classes. Thus, the Boosting method adapted better to the problem of "curse of dimensionality" and has serious potential to become a tool for automatic diagnosis of Alzheimer's disease.

Keywords: Alzheimer's disease, PET, automatic diagnosis, *k*-nearest neighbour, Boosting, Adaboost.

1 Introduction

Alzheimer's disease causes degenerative changes in the nervous tissue, which results in progressive loss of memory and cognitive functions. Alzheimer's disease is the most frequent type of dementia [1]. The prevalence of Alzheimer's disease increases in the elderly patients, and given the fact that population is getting older it is expected that incidence increases. Presently, there is no cure for Alzheimer's disease, thus, the main goal of treatment is to minimize the damage and the spread of disease. Only early diagnosis can provide lively and autonomy in last years of life. The temporal lobe, parietal lobe and hippocampus are the most common regional abnormalities for Alzheimer's disease.

When the patient has symptoms of Alzheimer's disease, the first tool used to evaluate patients is cognitive tests. The *Mini Mental State Examination* (MMSE) is the most widely used, and tests the abilities of orientation, memory, language, calculation and constructive capacity. Table below shows the ratings of the MMSE [1].

Table 1: The scale and classification of the MMSE.

Scale	Classification
24-30	Normal
20-23	Mild Cognitive Impairment (MCI)
10-19	Alzheimer
0-9	Terminal Alzheimer

The MCI is a transition state between the Normal and Alzheimer state. Although the patient is in a situation of early Alzheimer, he is able to construct arguments, participate in social activities and live independently. The regional abnormalities for Alzheimer's disease cause the reduction of blood flow and volume. The PET and *Magnetic Resonance Imaging* (MRI) scans are essential to diagnose Alzheimer's disease. The PET and MRI imaging show the functional and structural changes, respectively, in the human brain.

A hard analysis of MRI and mainly PET imaging in the diagnosis of Alzheimer's disease led to the use of methods of pattern recognition on MRI and PET imaging as a tool for automatic diagnosis of Alzheimer's disease. In this work, we used the *k*-nearest neighbour and Boosting methods in discrimination between the AD and Normal classes, MCI and Normal, and finally between the AD and MCI classes, with the purpose of making them a useful and efficient tool in the automatic diagnosis of Alzheimer's disease. The *k*-nearest neighbour method is very simple and intuitive. On other hand, the Boosting method is more complex and has the capacity to improve the accuracy of any classifier, especially the simple classifiers. Both methods are afflicted by the problem of "curse of dimensionality." The "curse of dimensionality" relates to the difficulty of learning over a small number of patterns with high dimension. The volume of the brain in a PET image contains thousands of voxels, which mostly do not have relevant information about Alzheimer's disease and only add uncertainty.

In this work, it is presented a precise and rigorous study in the automatic diagnosis of Alzheimer's disease. It used a large set of 195 PET images, equally divided into AD, MCI and Normal classes, which provides high precision in the study. It was employed the cross validation in the evaluation of *k*-nearest neighbour and Boosting methods, that ensured rigorous results on the performance of these methods. The implementation of the MCI class, rarely studied, allows the early diagnosis of Alzheimer's disease through the binary distinction between the MCI and Normal classes.

The following section 2 shows performance of classifiers in the distinction between the AD and Normal class. Section 3 explains in detail the *k*-nearest neighbour and Boosting methods. The results of these methods are presented in section 4, and conclusions and future work in section 5.

2 Previous Works Used in Identification of Alzheimer's Disease on PET and MRI Images

In recent years, several studies were initialized with the main purpose of specifying patterns on PET and MRI images of the human brain, able to identify dementias. The PET and MRI images show the activity and three-dimensional structure of the brain. *Single Photon Emission Computed Tomography* (SPECT) images, like the PET images, show the activity of human brain. Many classifiers have been tested in order to verify their accuracy in automatic diagnosis of Alzheimer's disease. Table 2 and 3 show the Accuracy (Acc), Sensitivity (Sen), Specificity (Spe) of many classifiers of the PET/SPECT and MRI images, respectively, the numbers of images used and the methods of evaluation of the classifiers. The evaluation parameters of the classifiers were obtained from the following equations:

$$\text{Sensitivity} = \frac{TP}{TP+FN} \quad (1)$$

$$\text{Accuracy} = \frac{TP+TN}{TP+TN+FP+FN} \quad (2)$$

$$\text{Specificity} = \frac{TN}{TN+FP} \quad (3)$$

where TP, TN, FP, and FN denote true positives, true negatives, false positives, and false negatives, respectively. The TP and TN are the number of Alzheimer´s and the number of Normal images being correctly classified, respectively, while the FP is the number of Normal images being classified as Alzheimer's images, and the FN is the number of Alzheimer's imaging being classified as Normal images.

Table 2: Results of the classifiers on the PET and SPECT images.

Classifier	Accuracy AD/N (%)	Sensitivity AD/N (%)	Specificity AD/N (%)	Nº images AD	Nº images Normal (N)	Evaluation of classifier
NNC [2]	85.05	-	-	58 (22M/36F)	49 (22M/27F)	Cross Validation
OLC [2]	90.84	85.86	**96.79**			
NNC [3]	82.99	-	-	58 (22M/36F)	49 (22M/27F)	Cross Validation
SVM [3]	85.42	-	-			
CPFIC [3]	84.67	-	-			
NMC [4]	84.80	79.30	88.00	29	50	Leave-one-out
PFLD [4]	89.90	82.80	94.00			
Back-propagation[5]	**92.30**	**91.00**	93.00	22	30	16 Training 16 Test
SVM [6]	~ 87.65	84.40	90.90	92	31	90 Training 33 Test
FLD [6]	~ 84.75	82.00	87.50			
LP Boosting [7]	84	84	82	149 (88M/61F)		Cross Validation

Nearest Neighbour Classifier (NNC); Optimal Linear Classifier (OLC); Support Vector Machine (SVM); Characteristic-Point-based Fuzzy Inference Classification (CPFIC); Nearest Mean Classifier (NMC); Pseudo Fisher Linear Distriminant (PFLD); Fisher Linear Distriminant (FLD).

Table 3: Results of the classifiers on the MRI images.

Classifier	Accuracy AD/N (%)	Sensitivity AD/N (%)	Specificity AD/N (%)	Nº images AD	Nº images Normal (N)	Evaluation of classifier
LDA [8]	84.00	82.00	85.00	75	75	Leave-one-out
QDA [8]	83.30	84.00	83.00			
SVM [8]	**92.00**	**91.00**	93.00			
AdaboostSVM [9]	86.00	80.00	92.00	49F	49F	Cross Validation
LDA [10]	91.00	79.00	**100**	24	40	30 Training 34 Tests
Back-propagation [11]	83.65	82.60	84.70	25 (5M/20F)	27 (17M/10F)	Training Tests

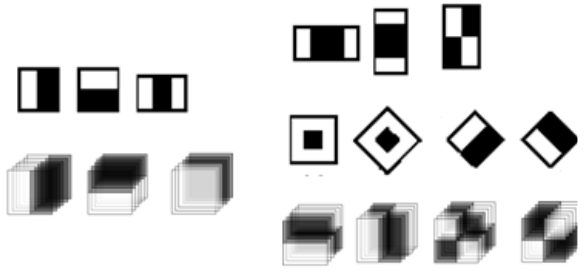
Linear Discriminant Analysis (LDA); Quadratic Discriminant Analysis (QDA).

Although the PET and MRI scans expose different information of the human brain, but the accuracy in discrimination between AD and Normal class are quite similar. In most studies, the specificity is higher than sensitivity, thus, it is easier recognize the Normal images. In a rigorous analysis of the results is necessary to take into account the number of images used and the method of evaluation of the classifier. The SVM classifier was used in many studies, and consistently achieved high ratios of accuracy. Thus, the SVM classifier referred to in table 3, achieved an accuracy of 92% on a rigorous method of evaluation of the classifier structure and with a high number of images. This result is a reference and a goal.

3 Automatic Diagnosis of Alzheimer's Disease

In this section, we present the k-nearest neighbour and Boosting methods as a tools for automatic diagnosis of Alzheimer's disease on PET images. The k-nearest neighbour method has been previously used in the automatic diagnosis of Alzheimer's disease, and achieved good results [2,3]. The k-nearest neighbour method is very simple and intuitive. Basically, it determines the k closest training patterns to the pattern x and assigns the majority class. The simple implementation and the performance of this method provided the platform and reference to use a more complex method. The Boosting method is a complex method to improve the accuracy of any classifier, particularly the simple ones. The references to use Boosting method on PET imaging are scarce [7], but on MRI imaging was reached good performance [9,12]. The Boosting method has the great advantage of being resistant to overfitting and has the capacity to adapt to the problem of "curse of dimensionality".

In this work, we used the Haar features and voxels intensities as features. The Haar features contain information about a brain area or volume instead of single voxel intensity. Figure 1 shows examples of Haar features [13].



a) b)

Figure 1: Haar features; a) simple; b) extensions [13].

The final value of a Haar feature is the difference between the sum of the voxels within white and black rectangular regions. The shape and size model of the Haar feature ($T_k(x,y,z)$) covers all positions of the PET image ($I(x,y,z)$) for features extraction (equation 4).

$$f_k(x_0,y_0,z_0) = \\ = \iiint I(x,y,z)\,.\,T_k(x-x_0,y-y_0,z-z_0)dxdydz \qquad (4)$$

3.1 The k-nearest neighbour method

The k-nearest neighbour method is a supervised learning system. This method is a particular case of the *maximum a posteriori* classification (MAP), which consists minimizing the probability of error of this classifier. Thus, the pattern x is associated to the majority class ($\hat{c}$) from the classes set $\Omega = \{c_1, \dots, c_p\}$ defined by:

$$\hat{c} = arg \max_{c\epsilon\Omega} P(c|x), \qquad (5)$$

where $P(c|x)$ is the probability of occurrence class c, given that pattern x was observed, called the *posterior probability*. Through the Bayes' theorem it is possible to determine the *posterior probability*:

$$P(c|x) = \frac{p(x|c)P(c)}{p(x)} \qquad (6)$$

The first step in implementing the k-nearest neighbour method is to choose the k patterns' number involved in the classification. The result of the classification depends essentially on the value chosen for k. A small sphere is centered at a pattern x, and the radius of the sphere grows up until it contains precisely k training patterns. Suppose that patterns set contains N_k patterns in class C_k and N patterns in total, so that $\sum_k N_k = N$. Then radius of the sphere grows up until encompasses k patterns. Suppose this sphere, of volume V, contains k_k patterns from class C_k . Then we can use the estimated unconditional density (7) to give approximations for the class-conditional densities (8) [14]:

$$p(x) = \frac{k}{NV} \qquad (7)$$

$$p(x|C_k) = \frac{K_k}{N_k V} \qquad (8)$$

$$P(C_k) = \frac{N_k}{N} \qquad (9)$$

Now, Bayes' theorem gives,

$$\boldsymbol{P(C_k|x) = \frac{p(x|C_k)P(C_k)}{p(x)} = \frac{K_k}{K}} \qquad (10)$$

To minimize the probability of misclassifying the pattern x, it should be assigned to the class C_k which the ratio k_k/k is greatest. The value for k must be an odd number to eliminate the possibility of having classes with the same frequency. The k-nearest neighbour method has the disadvantage of the results deriving some estimates of the probability density sensitive to irrelevant features, and it is computationally slow for high values of k and high training patterns.

3.2 Boosting method

The Boosting method is also a method of supervised learning. The Boosting method works by running the *weak classifiers* on the training set multiple times, each time focusing the weak classifiers attention on different training set patterns. In the end of iterations cycle it make the combination of all weak classifiers previously trained, to obtain a *strong classifier*. Thus, combinations of classifiers have a capacity to achieve better performance than any individual classifier. Overall, the Boosting method is an excellent method to improve the accuracy of any classifier, especially the weaker classifiers. There are two variants of Boosting method [15]: Adaboost (binary classification), and Adaboost.M1 and Adaboost.M2 (multiclass classification).

3.2.1 Adaboost

The Adaboost (Adaptative Boosting) is a variant of Boosting, introduced in 1995 by Freund and Schapire, and like the name suggests, adjusts adaptively to the errors returned by the weak classifier, along the iterations. The variant Adaboost is used both to select the features and to train the classifier, with the goal to optimize the binary classification. The Adaboost takes as input a training set (x_i, y_i), where each pattern x_i belongs to some instance space, and each label y_i is in some label set $\{0,1\}$. The Adaboost construct a strong classifier as linear combination of weak classifiers. The Adaboost performs repeatedly the weak classifier, extracting and combining the best separation *hypothesis* of the classes and the respective features in the recognition of patterns of Alzheimer's disease, to create a unique and effective strong classifier. The weak classifier calculates the best separation hypothesis, along the thousands of features, which provide the smallest error in the binary distinction. A weak classifier $(h_j(x))$ thus consist of a feature (f_j), a threshold (θ_j) and a parity (p_j) indicating the direction of the inequality sign [13]:

$$h_j(x) = \begin{cases} 1 \; if \; p_j f_j(x) < p_j \theta_j \\ 0 \quad otherwise \end{cases} \tag{11}$$

One of the main ideas of the Adaboost is to maintain a distribution or set of weights over the training set. Initially, all weights are set equally, but on each iteration, the weights of incorrectly classified patterns are increased so that the weaker classifier is forced to focus on this pattern in the training set. Figure 2 shows all the steps in the execution of Adaboost [13].

The most basic theoretical property of Adaboost concerns of its capacity to reduce the training error. Any separation hypothesis between binary and equivalents classes has an error rate lower or equal 1/2. Thus, if each weak hypothesis is slightly better than 1/2, then the training error drops exponentially fast. The Adaboost has disadvantages, such as dependence on a good choice of a weak classifier. If the weak classifier has a poor performance along the iterations, the strong classifier tends to be worst. Also, the performance of Adaboost is degraded in the presence of ambiguous features, due to high error rates of the weak classifier. Finally, the Adaboost has a high overload in the selection the best features on a large feature set.

Adaboost

- Given examples images $(x_i, y_i) \ldots (x_n, y_n)$, where $y_i = 0,1$ for negative and positive examples, respectively.
- Initialize weights $w_{t,i} = 1/m$, where m is the total number of images.
- For $t = 1, \ldots, T$
  1. Normalize the weights,
     - $w_{t,i} = \frac{w_{t,i}}{\sum_{i=1}^{n} w_{t,i}}$;
  2. For each feature, j, train a classifier h_j which is restricted to using a single feature. The error is evaluated with respect to w_j,
     - $E_j = \sum_i w_i \, |h_j(x_i) - y_i|$;
  3. Choose the classifier, h_t, with yhe lowest error E_t;
  4. Update the weights,
     - $w_{t+1,i} = w_{t,i} \beta_t^{1-e_i}$, where $\beta_t = \frac{e_t}{1-e_t}$
     - $e_i = 0$ if example x_i is classified correctly and $e_i = 1$ otherwise;
- Strong classifier,

$$h(x) = \begin{cases} 1 \; \sum_{t=1}^{T} \alpha_t h_t(x) \geq \frac{1}{2} \sum_{t=1}^{T} \alpha_t \\ 0 \qquad\qquad otherwise \end{cases} \qquad \alpha_t = \log \frac{1}{\beta_t}$$

Figure 2: Adaboost steps [13].

4 Experimental Results

4.1 Database

The *Alzheimer's Disease Neuroimaging Initiative* (ADNI) provides an integrated environment for safely archiving, visualizing and sharing medical imaging data. “This project is the most comprehensive effort to date to identify neuroimaging and other biomarkers of the cognitive changes associated with MCI and Alzheimer’s Disease AD” [16]. Each PET volume dimensions is 128 by 128 by 60 voxels. The 195 pre-processing images we used in this work were taken from ADNI. In total 195 images were used, including 65 patients with AD, 65 patients with MCI, and 65 Normal ones. Table 4 shows the characteristics of images PET.

Table 4: Characteristics of PET images

Class	AD	Normal	MCI
Images	65	65	65
Male/ Females	40M/25F	43M/22F	44M/21F
Average age	76.994	76.660	77.318
Stantard deviation	6.846	4.688	7.635
MMSE	21.154 8min/27max	29.323 24min/30max	26 20min/30max
Average weight	76.598	75.985	75.566
Stantard deviation	13.997	12.924	13.138

The cognitive test MMSE may offer a misdiagnosis of the patient. In this PET images set, there are patients in the AD class which have results in the cognitive test at the scale of Normal.

4.2 Pre-processing

The 195 PET images from the database ADNI are subject to complex processes of pre-processing, to make images from different scanners in uniform images, and with the same format, such that it is possible to make direct comparison, of the voxels intensities, between images with pre-processing. The different positions of the patients during the exam, as well as, the different anatomies and morphologies among patients, cause the same voxel location in two images corresponds to different anatomical locations in the brain. To correct this problem it is necessary to perform *spatial normalization*. Upon certification of the correct overlap of voxels of PET imaging in brain anatomy, it is necessary to scale the voxels intensities by *intensity normalization*. Different amounts of FDG injected at the time of image acquisition, the sensitivity of the scanner and the different development of the disease among patients, causing disproportion in the voxels intensities. Finally, each image set is filtered with a scanner-specific filter function to produce images of a uniform isotropic resolution of 8 mm Full Width Half Maximum (FWHM).

4.3 Masks

Brain images have some irrelevant information in the recognition of Alzheimer's disease. The irrelevant information only increment ambiguity and decrement the accuracy of classification. The masks include the regional abnormalities for Alzheimer’s disease. Masks only use the slices 15 to 45, because the rest are extra cranium and imperceptible in the recognition of Alzheimer's disease. We used two types of masks, called mask M1 and mask M2, with different functions. Mask M1 encompasses the entire brain, but eliminates the posterior frontal lobe and surrounding the ends the brain. Mask M2 eliminates the frontal lobe, surrounding the ends and the "corpus callosum".

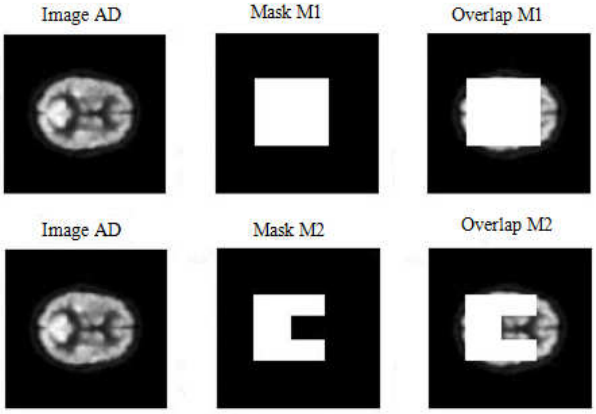


Figure 3: Location masks M1 and M2.

4.4 Results of k-nearest neighbour method

The k-nearest neighbour method was the first method used in this work in the identification of Alzheimer's disease. For each PET image, the sum of the difference between all voxels of this image and the all voxels of remaining PET images was calculated. Thus, the difference from one image to another image is measured by a single value. Two metrics were applied in the summation, the $L_1$and L_2 norm (equation 12 and 13).

$$L_1 = \|I - I'\|_1 = \sum_{k,l,m} |I(k,l,m) - I'(k,l,m)| \quad (12)$$

$$L_2 = \|I - I'\|_2 = \sqrt{\sum_{k,l,m} (I(k,l,m) - I'(k,l,m))^2} \quad (13)$$

The distances matrix dimensions are 130 by 130, with the first 65 positions belonging to the class $c_1$and remaining positions belonging to the class c_2. The 129 values on each column classify the PET image inserted in this line. If the PET image to be classified belongs to class c_1, it is expected that the first 65 values are smaller than other values. Thus, after the choice of the k nearest neighbour, the k smallest positions on the 129 positions are determined. If class $c_1$is bigger than class c_2 on the k smallest positions, the PET image is correctly classified. In case the PET image is classified

to belong to class c_2, the highest k values are determined. Table 5 shows the results of the k nearest neighbor method for the best k values.

A five-fold cross validation was performed on the k-nearest neighbor method. The training set was divided into five subsets. The binary distinction on the masks achieved better performance than the use of all voxels of brain volume. On other hand, the L_2 norm obtained better results than the L_1, because the L_2 norm accentuates the differences between the images. The distinction between AD and Normal classes was achieved an accuracy of 83.85% on mask M1 and using L_2 norm. The specificity was very high, thus it was easier to recognize the Normal images than the AD images. The distinction between AD and MCI classes was achieved an accuracy of 65.39%, on M2 mask and using L_2 norm. Both values of sensitivity and specificity were very low, thus, the inclusion of MCI class creates high problems in the correct classification Alzheimer's disease in different stages of evolution. The distinction between MCI and Normal classes the accuracy is a little higher than the distinction between AD and MCI, achieving an accuracy of 68.74%. This accuracy results mainly the low sensitivity, thus, many MCI images were classified as Normal images. The MCI class is a transitory state between the Normal state and the Alzheimer state, which makes it difficult to discriminate between MCI state and the adjacent states.

Table 5: Results of a *k* nearest neighbour method (% percentage).

Classes		**AD/Normal**			**AD / MCI**			**MCI/ Normal**		
Mask/ Metric	Value de K	Sen.	Esp.	Acc.	Sens.	Esp.	Acc.	Sens.	Esp.	Acc.
Brain L1	5	58.46	90.77	74.62	55.38	67.69	61.54	44.62	75.38	60.00
	9	50.77	92.31	71.55	56.92	67.69	62.41	44.62	72.31	58.47
	15	55.38	90.77	73.08	**64.62**	60.00	62.31	35.38	76.96	56.15
Brain L2	5	61.54	89.23	75.39	55.38	61.54	58.46	43.08	75.38	59.23
	9	53.85	92.31	73.08	58.46	61.54	60.00	35.38	87.69	61.54
	15	50.77	89.23	70.00	56.92	53.85	55.34	36.92	84.62	60.77
Mask M1 L1	5	66.15	92.31	79.23	44.62	63.07	53.85	**52.31**	81.54	66.93
	9	66.15	95.38	80.77	56.92	60.00	58.46	46.15	83.08	64.62
	15	67.69	95.38	81.54	53.85	58.46	56.16	40.00	89.23	64.62
Mask M1 L2	5	**70.77**	95.38	83.08	50.77	60.00	55.39	44.61	84.62	64.62
	9	**70.77**	96.92	**83.85**	53.85	66.15	60.00	**52.31**	80.00	66.16
	15	64.62	95.32	80.00	55.28	63.08	59.23	44.62	92.31	**68.74**
Mask M2 L1	5	64.62	93.85	79.24	52.31	66.15	59.23	40.00	83.08	61.54
	9	63.08	98.46	80.77	60.00	70.77	**65.39**	33.64	84.23	59.04
	15	66.15	98.46	82.31	55.38	72.31	63.85	38.46	92.31	65.39
Mask M2 L2	5	66.15	90.77	78.46	53.85	66.15	60.00	44.62	80.00	62.31
	9	64.62	96.92	80.77	50.77	67.69	59.23	30.77	90.77	60.77
	15	66.15	**100**	83.08	56.92	**73.85**	**65.39**	36.92	**95.38**	66.15

4.5 Results of a Boosting method

The Boosting method Adaboost was chosen to classify the PET images, which has the advantage of being resistant to overfitting. First of all, Adaboost was used in the extraction feature. We used the voxels intensities as features, and on masks M1 and M2 the features vector has 79.856 and 73.160 thousand of intensities values, respectively. Also we used the Haar features and their average as features, and on masks M1 and M2 the features vector has 124.296 and 109.472 thousand of intensities values, respectively. Figure 4 represents the Haar features used.

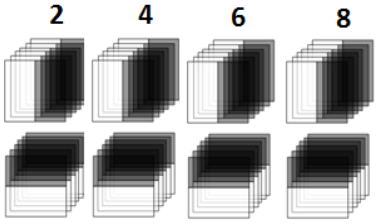


Figure 4: The Haar features used.

The Adaboost runs for 300 times to select the best features along the cyclical performance of the weak classifier, to obtain a precise strong classifier. Thus, for each PET test image, the strong classifier run along the 300 features selected, and in the end assigns a class to PET test image. If the value of the label test image, y_i, is equal to the return of strong classifier, the PET image is correctly classified and, if the values do not match, the PET image is incorrectly classified. A five-fold cross validation was performed on Adaboost. The training set was divided into five subsets with 26 images. Noted, the high overload in the implementation the cross validation. Table 6 shows the Adaboost results using Haar features and voxels intensities as features on the masks M1 e M2. The fact that AD and Normal images belonging to two quite different states, resulted in the selection of the best discriminative features able to correctly identify the two states. Thus, the distinction between AD and normal classes achieved a high accuracy of 89.23%. As happened with

the *k*-nearest neighbour, the specificity was higher than sensitivity, thus it was easier to recognize the Normal images than the AD images. The distinction between AD and MCI adjacent classes, the accuracy decreased to the value of 66.15%. In sync with the accuracy, sensitivity and specificity also decreased their percentages. The distinction between MCI and Normal classes achieved an accuracy of 70.77%. The lack of homogeneity of PET images within the same classes makes classification very hard. Mostly the MCI images produce ambiguity in the classification, which cause the decrease of accuracy.

Table 6: Adaboost's Results (% percentage).

Features/ Mask	**AD/Normal**			**AD/MCI**			**MCI/Normal**		
	Sen.	Esp.	Acc.	Sens.	Esp.	Acc.	Sens.	Esp.	Acc.
Voxels/ M1	83.08	87.69	85.39	64.54	58.46	61.54	63.08	75.38	69.23
Voxels/ M2	80.00	**92.31**	86.15	**69.23**	**63.08**	**66.15**	58.46	73.85	66.15
Haar/M1	**87.69**	87.69	87.69	61.54	52.31	56.96	64.62	**76.92**	**70.77**
Haar/M2	86.15	**92.31**	**89.23**	53.84	58.46	56.15	**69.23**	63.08	66.08

Figure 5 shows the 6 regions more affect by Alzheimer's disease determined by Adaboost. It should be noted, as was expected, the 6 main regions determined by the Adaboost are in the parietal and temporal lobe. The region most commonly selected is in slice 16 and overlap in the hippocampus region.

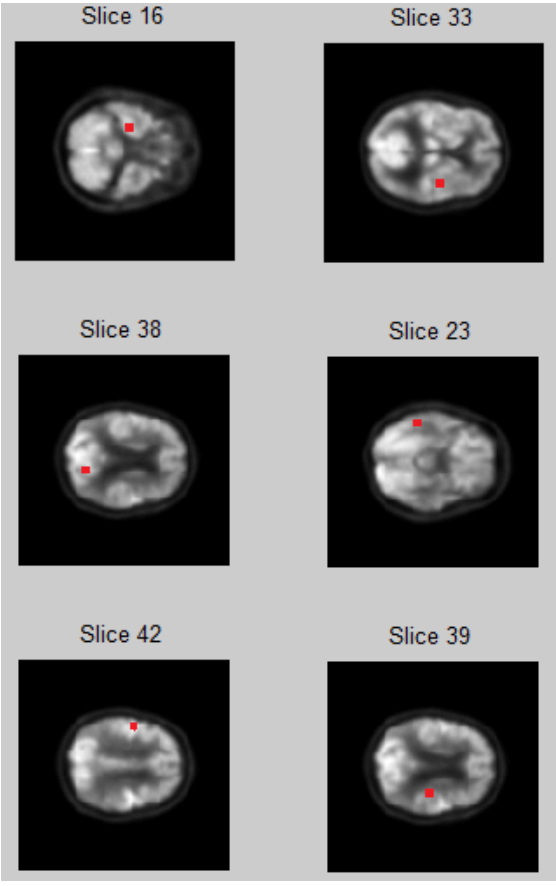


Figure 5: The 6 main regions determined by Adaboost

5 Conclusions

The difficulty of the analysis and interpretation of PET imaging in the diagnosis of Alzheimer's disease led to the use of the *k*-nearest neighbour and the Boosting methods as a tool for automatic diagnosis of Alzheimer's disease. The advantage of Boosting algorithm prevailed and it was possible to achieve better performance in all binary distinctions. The discrimination between AD and Normal classes had the best performance. The fact that AD and Normal classes are not transitory states allowed selecting more discriminative features and to achieve an accurate of 89.23%.

This work implemented the MCI class, rarely studied in automatic systems but essential in the early diagnosis of Alzheimer's disease. The fact that a MCI state is a transition state led to a reduction accuracy, achieving 70.77% and 66.15% in the distinguish between MCI and Normal classes, and AD and MCI classes, respectively. For future work one might want to use more selective and restrict masks over the regional abnormalities for Alzheimer's disease. Also to implement other weak classifiers, like decisions tree or SVM. In conclusion, the Boosting method Adaboost achieved better performance in identification of Alzheimer's disease, and has serious potential to become a tool for automatic diagnosis of Alzheimer's disease.

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