1. **Abstract**

This paper proposes a web interface implementation for Alzheimer’s disease (AD) classification based on anatomical features. Our web-based interface combines MRI with demographic and neuropsychological data in order to classify AD. The classification algorithm combines all anatomical features by region with other parameters, creating a multidimensional array, and then runs a twofold cross-validated Support Vector Machine (SVM) for the classification of AD and its prodromal stages.

2. **Introduction**

According to Alzheimer Association (www.alz.org): Alzheimer’s disease is the sixth-leading cause of death in the United States and is the only cause of death in the top 10 in the United States that cannot be prevented, cured, or slowed down. Killing more than breast and prostate cancer combined. While death from other diseases has decreased significantly, from 2000 to 2013, death from Alzheimer’s disease has increased by 71%. In 2015 alone the United States will spend 226 billion dollars to care for people with Alzheimer’s. It is estimated that by 2050 the national cost will reach a trillion, unless something is done. Our interface uses the Alzheimer’s Disease Neuroimaging Initiative database (ADNI), along with other demographic data (age, education, gender) and optionally the neuropsychological test Mini Mental State Examination (MMSE). Our classification employs Support Vector Machine (SVM). The interface allows the user to select among many parameters, such as the SVM kernel, scaling, normalization, Intracrania Volume (ICV) correction and parameter selection. The interface is a first step towards creating a portal for Alzheimer’s disease automated diagnosis. With no cure for the Alzheimer’s disease, an early diagnosis allows people a better chance to be treated and benefiting from treatment, more time to plan for the future, increased chance to participate in clinical trials, an opportunity to participate on their future, before onset of the disease. This is why a diagnosis with minimal input data can be beneficial to prospective AD patients.

3. **Methods**

3.1 Participants

Our current database contains 543 subjects, all obtained from the Alzheimer’s Disease Neuroimaging Initiative - ADNI. Freesurfer volume and area measures are made available as tables in MYSQL, which can be selected by the user running the study. We show 5 possible options regarding features: Subcortical Volumes, Hippocampus Subfield, Cortical Volumes, Average, and Area. Although ADNI provides data fields, we only use in our study gender, education, and age. The datasets are composed of T1-weighted MRI. Quality control (QC), as applied by ADNI, includes visual checks of the image quality by image experts and a priory QC standards for imaging subjects. After studies were included if their MRI passed the QC. All scans were performed in the same scanner.

3.2 Implementation Steps

Our study uses the ADNI database. The subjects are preprocessed in Freesurfer 4.3. We adjust the volumes according to the education, gender, age, and ICV. The MMSE can also be given as an input. The data is broken in two groups (Training / DX), and given to the SVM classification algorithm. DX is the diagnostics group. This separation of the data is typical in SVM classification. Our web interface presents options for the user to select many other options which relate to the algorithm. After the algorithm is trained, with the trained group, for the DX group, we obtain our classification results. Each time the algorithm is run, it creates a new random selection for the two groups. While we use SVM, the classification algorithm can be replaced by any other (such as Neural Networks). Figure 1 shows this process.

4. **Results**

![Figure 3 Parameter Selection](image)

The runtime of the algorithm, for 50 iterations on our current server configuration is about 2-3 minutes. The server is SUSE SLE 11 SP3. We are running the latest version of Drupal (7.38) and libSVM version 3.20. The table above reports the results of running the algorithm with 50 iterations on Normal controls vs. AD groups. The values obtained for subcortical volumes, cortical thickness, and hippocampus subfield provide the best classification results. Given that these are the areas affected by AD, it was expected that these would be more significant. As anticipated, the inclusion of MMSE increases the sensitivity, specificity and accuracy; this is an indication of how important neuropsychological tests are in the diagnosis of Alzheimer’s disease (Figures 3 and 4).

5. **Discussion**

The results reported in Table 1 are only one of the many possible ways our web interface can be used. Many different experiments can be devised by selecting different options such as kernels, scaling, etc. We could also compare aMCI to AD or nMCI to AD. The expected results for those comparisons will not be as good, as brain atrophy in nMCI and aMCI is more subtle than in AD patients.

We noticed that our algorithm produces higher specificity than sensitivity. We believe that is due to the fact that the number of controls is almost double the number of AD patients; hence it is not a bias of the algorithm. We currently process all the volumes in the selected region. However, one step which usually improves classification algorithms is to do feature selection before the classification. This also allows to report which specific sub-volume within the selected volumes have more weight on the classification. We already started implementing F-score based feature selection on our web interface. We are also interested in balancing the data. For instance, if there are 76 AD, and we are comparing them to 199 controls, we could allow for the random selection of only 76 controls, so that the number of subjects in each class is balanced. This might help in getting sensitivity and specificity to even out.

6. **Acknowledgements**

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7. **References**