Analysis of brain Nuclear Magnetic Resonance images for the early diagnosis of Alzheimer's desease

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The main purpose of the MAGIC-5 [1] collaboration is the development of Computer Aided Detection (CAD) systems for the analysis of medical images on distributed databases by using also a GRID platform. The collaboration involves physicists, computer scientists, mathematicians, and physicians from several Italian universities, INFN sections, and hospitals. Up to now, the attention has been focused to the analysis of x-ray mammograms, lung CT scans, and brain NMR images. Here we will briefly report on the work done in order to develop strategies and reliable tools for the early assessment of Alzheimer's disease.

The Alzheimer disease (AD) affects about 500.000 subjects in Italy with serious damages to personality, memory and relation. About 6-10% of the population over 65 is affected, up to 20% for subjects over 80. The typical progress of the disease lasts 8 years since the beginning of the first symptoms, and can extends up to 20 years. This is the most common form of dementia in adult and senior population, and the risk to develop it raises with increasing age. Furthermore AD is difficult to be diagnosed in the early stage, the first step being known as Mild Cognitive Impairment (MCI). Anyway MCI is not necessarily a marker of the disease, because these subjects can evolve either in AD (or other forms of dementia), remain stable, or return to a non pathological condition.

Some recent studies [1] indicates the possibility to recognize, in nuclear magnetic resonance (NMR) images, some precursor signs of the Alzheimer's disease, before the clinical symptoms (such as memory disturbance) are evident. Subjects with tissue loss in the medial temporal lobe (MTL), particularly in the hippocampus, have evidenced cognitive deterioration in the 6-year follow-up, with 90% prediction accuracy. The hippocampal formation essentially consists of gray matter and it is adjacent to other structures with similar characteristics. Therefore NMR images actually display low contrast and hardly distinguishable boundaries along significant portions of its surface. To date, different approaches have been proposed for the extraction and evaluation of the shape and size of the hippocampus, mainly manual and semiautomatic. Fundamental to this purpose is an effective classification of white matter, grey matter and cerebrospinal fluid.

The study of NMR images taken from a wide population of elderly people shows different atrophy grades and, consequently, exhibits an extremely large morphological variability of both the hippocampal formations (right and left). This fact severely hinders the success of most automatic procedures of hippocampal segmentation.

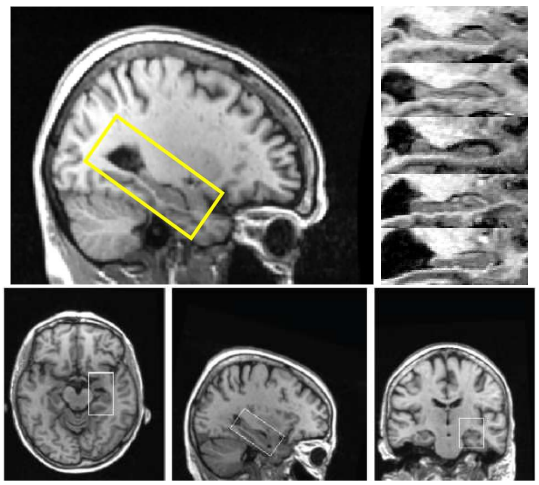

Figure 1. NMR images of the brain showing also the definition of the *hippocampal boxes* used in the analysis (see text).

[1]Medical Applications on a Grid Infrastructure Connection. Web site: http://mag09xl.to.infn.it/site/

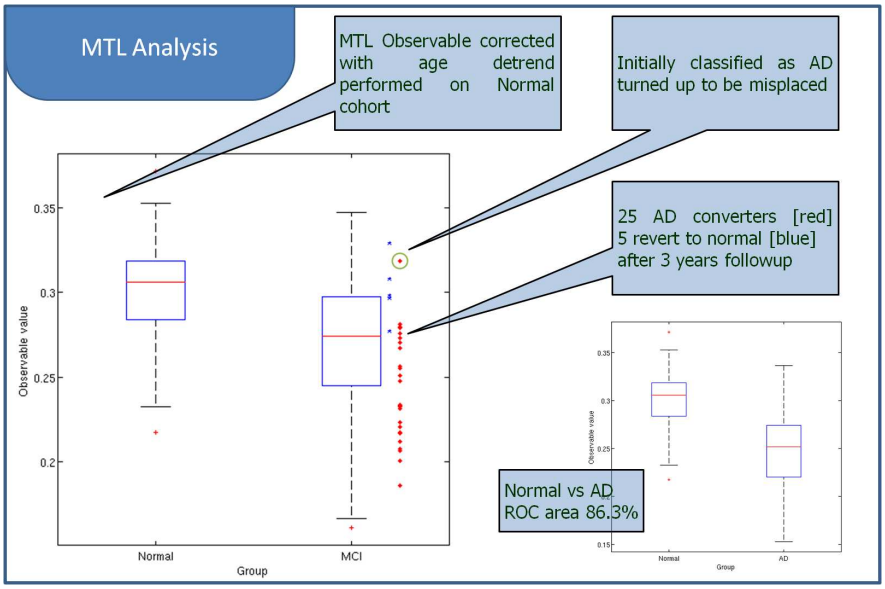

Figure 2. Values of the MTL observable used in the analysis for normal, MCI and AD patients.

In order to circumvent these difficulties, in the framework of the MAGIC-5 collaboration a different approach was proposed, which does not directly tackle the arduous objective of hippocampal segmentation, but simply performs the more straightforward task of extracting from the right and left sides of a given NMR image two small box-shaped fixed-size sub images (Hippocampal Boxes, HB) containing the hippocampi and some adiacent structures (see Fig.1). Following this approach, at first the HBs from a good number of NMR images are extracted by coregistration with an initial manually-segmented HB. This step is based on correlation coefficient maximization. Then clustering techniques are applied and a few HB classes are retained with different hippocampus atrophy degree. The representative HBs of these classes are finally used to classify new NMR images and attribute them a disease level. This procedure looks promising and successfully reproduces the physicians' diagnosis, with sufficiently good predictive power.

The same features are also used to classify MCI patients into likely AD converters and non-converters. Those predictions can be subsequently verified by clinical follow-up data, and the sensitivity/specificity against early detection of AD can be computed. The procedure parameters is being optimized against size and position of the MTL extracted volume as to deliver maximum clinical information. In addition, the developed tools can be used for correlating the hippocampal region and other regions of the brain, thereby improving the probability to find useful markers for early Alzheimer's diagnosis.

The proposed approach, besides being a preliminary step towards other statistical studies on the hippocampus, extracts from the NMR images information useful for diagnostic purposes and, in particular, gives the possibility of performing morphometric studies on the medial temporal lobe in a fully automated way. Our preliminary results on the prediction of AD converters on a 3 to 5 years base are very promising. Furthermore the procedure was able to identify a couple of initially incorrect diagnosis of Alzheimer's disease as shown by further clinical investigation (see Fig.2).

The feasibility of an evaluation of the regional atrophy grade in MTL is also under study. An accuracy comparable with the subjective visual rating scale proposed in [5] is expected. The advantages consist in no subjectivity and in the possibility of processing a large amount of MR images with moderate user intervention.

REFERENCES

1. H.Rusinek et al., Radiology (2003) 229
2. G.Frisoni et al., J. Neurol. Neurosurg. Psychiatry, vol. 74, no. 10, pp. 1371-1381, October 2003
3. (2007) Alzheimers Disease Neuoroimaging Initiative (ADNI). [Online]. Available: http://www.loni.ucla.edu/ADNI/
4. A.Chincarini et al. (The MAGIC-5 Coll), Proceedings of the 14^{th} Annual Meeting of the Organization for Human Brain Mapping, Melbourne, Australia, June 2008.
5. P.Scheltens et al., J. Neurol. Neurosurg. Psychiatry, vol. 55, no. 10, pp. 967-972, October 1992.