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Medical imaging analysis: Automatic hippocampus segmentation

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Summary. — Alzheimer's disease (AD) is a major cause of disability in the developed countries and places. The objective of our research is to increase the likelihood of early recognition and assessment of Alzheimer Disease so that concern can be eliminated if it is not warranted; treatable conditions can be identified and addressed appropriately; and non-reversible conditions can be diagnosed early enough to permit the patient and family to plan for contingencies such as long-term care. We developed computational tools for the automatic analysis of Medial Temporal Lobe atrophy starting from large sets of structural MR images and we are providing an IT infrastructure built on a high available, high scalable computing cluster, integrated with our neuroimages analysis tools.

PACS 87.57.nm – Segmentation.

1. – Purpose

Dementia is a major cause of disability in the developed countries and places. An important public health concern of developed countries is aging of the population and the associated increases in the prevalence of various dementias, particularly Alzheimer's disease (AD). In fact as life expectancy increases together with the birth rate decrease in industrialized countries, we face a noticeable escalation in population aging and, consequently, a burst in Alzheimer disease incidence. The tragic outcome of this disease and the health system increasing costs render the economical burden often unbearable for the families as well as for the social health networks. Numerous studies have explored the effect of Alzheimer's disease on brain structure. For these reasons, it is of paramount importance to develop strategies and reliable tools for the early assessment of the disease, in the effort to limit its consequences. The objective of our research is to increase the likelihood of early recognition and assessment of Alzheimer Disease so that 1) concern can be eliminated if it is not warranted; 2) treatable conditions can be identified and addressed appropriately; and 3) non-reversible conditions can be diagnosed early enough to permit the patient and family to plan for contingencies such as long-term care.

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2. – Methods

We developed computational tools for the automatic analysis of Medial Temporal Lobe atrophy starting from large sets of structural MR images. The algorithm is based on a combination of different kinds of templates and image registration techniques. It can accept input images from a variety of formats and scanner acquisition conditions. The procedure takes a raw MR image, normalizes it to the ICBM152, and extracts two regions containing portion of the medial temporal lobe (MTL) around each hippocampus. Templates are constructed from a cohort of 200 MR images containing a random sample of Normal, AD and MCI populations. We developed an algorithm that extracts from each MR two sub images (right and left side), containing the hippocampal formations plus a portion of the adjacent tissues and cavities. Then, a small number of templates is selected among the previously obtained volumes, able to describe the morphological variability present in the whole population.

With these templates we are able to find the right and left hippocampal formations in any new MR image, using statistical indicators to assess the precision on this volume extraction. MR images ranging from normalcy to extreme atrophy can be successfully processed. The extracted sub images are finally analyzed both with linear and non-linear methods such as Voxel Based Morphometry and neural networks classifiers. The computed features are chosen to maximize the area under the ROC curve between Normal and AD cohorts. The same features are then used to classify MCI patients into likely AD converters and non-converters. The procedure predictions are subsequently verified by clinical follow-ups data, and the sensitivity/specificity against early detection of AD is computed. The procedure parameters have been 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.

3. – Computing resources

In order to improve the collaboration efficiency among several developers working in different sites, we are providing an IT infrastructure built on a high available, high scalable computing cluster, integrated with our neuroimages analysis tools.

The analysis suite relies on Matlab and the ITK (Insight Toolkit) libraries [1], which implement leading-edge algorithms for registering and segmenting multidimensional medical images. Every computing job is a combination of an arbitrary number of software modules connected through a client/server, visual, multi-platform application (LONI Pipeline) [2]. Each module is submitted to the central infrastructure by the developer, where an IT manager will validate it and make it available in a shared repository through the Pipeline server. SUN Grid Engine (SGE) batch system is used to submit and run jobs on the execution nodes. SGE look after the optimization of the available resources providing a remarkable scalability (thousand of nodes). The LONI Pipeline server is fully integrated with SGE using SUN's Java DRMAA bindings. The bindings allow jobs to be natively submitted from the LONI Pipeline to the grid without the need for external scripts. The images database was developed based on a C++ frontend to a MySQL server and provides all the basic methods to access, modify and insert images. At the moment we are working on the implementation of authentication and authorization procedures. We are also evaluating other database candidates such as XNAT (eXtensible Neuroimage Archive Toolkit) [3], which may meet all our requirements.

The computing farm is composed of two execution nodes: 16 Intel E5410 cores and 32 GB of RAM (2GB per core). The batch system master nodes is installed as a XEN virtual machine and is able to live migrate from one physical machine to another, in order to keep the system available during maintenance operation (*i.e.* hardware/software upgrade or reconfiguration). The storage system contains the images database and files, and the software modules repository. It relies on a 4Gb/s Fiber Channel SAN (Storage Area Network) with fully redundant path. All disks are exported to the execution nodes by one IBM GPFS (General Parallel File System) filesystem server, connected to LAN by a two-GE (Gigabit Ethernet) bonding. The total disk space available is 2TB but it is easily expandible. INFN-Genova data center, which host the whole infrastructure, is provided with UPS (Uninterruptable Power Supply) to protect against supply interruptions, and with an automatic unattended computing nodes installation. No single point of failure are present in the whole system to achieve a high availability.

Once terminated the images database configuration and the performance and reliability testing, the infrastructure will be ready to run the analysis jobs. The next step will be the development of a web portal to allow neurologists to submit MRI images to the system, obtaining a value which will help them in the diagnosis.

4. – Results

The proposed approach, besides being a preliminary step towards the unsupervised segmentation of the hippocampus, extracts from the MR image 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. We extracted and analyzed more than 500 1.5 Tesla T1 images in a matter of a few hours. The images and the clinical data come from two major Italian hospitals and from the ADNI consortium, and they span a variety of acquisition scanners. Our preliminary results on the prediction of AD converters on a 3 to 5 years base are very encouraging. Furthermore the procedure was able to identify a couple of incorrect diagnosis of Alzheimer's disease as shown by further clinical investigation.

5. – Conclusions

The automated analysis of MTL atrophy in the segmented volume is readily applied to the early assessment of Alzheimer Disease (AD), leading to discriminating converters from Mild Cognitive Impairment (MCI) to AD with an average three-years follow-up. This procedure can quickly and reliably provide additional information in early diagnosis of AD, and we believe it can become a routine test to aid clinicians evaluate the patient, together with the more traditional tools. In addition, the ability to incorporate different kinds of templates makes the algorithm suitable for the automatic extraction of MTL structures affected by different pathologies.

REFERENCES

[1] `http://www.itk.org`.
[2] `http://pipeline.loni.ucla.edu`.
[3] `http://www.xnat.org/`.