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Early Diagnosis of Alzheimer's Disease Using a Grid Implementation of Statistical Parametric Mapping Analysis

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A voxel based statistical analysis of perfusional medical images may provide powerful support to the early diagnosis for Alzheimer's Disease (AD). A Statistical Parametric Mapping algorithm (SPM), based on the comparison of the candidate with normal cases, has been validated by the neurological research community to quantify ipometabolic patterns in brain PET/SPECT studies. Since suitable "normal patient" PET/SPECT images are rare and usually sparse and scattered across hospitals and research institutions, the Data Grid distributed analysis paradigm ("move code rather than input data") is well suited for implementing a remote statistical analysis use case, described as follow.

Summary

The SPM software library was originally developed and is made freely available by the Functional Imaging Lab (FIL) at the Wellcome Department of Imaging Neuroscience (London University College) for activation studies in functional MR.
Since then, the use of SPM was extended and, through a specifically defined analysis protocol, SPM routines are presently the standard within the neurological research community as regards a voxel based analysis of PET/SPECT studies for the early diagnosis of AD.
In order to achieve correct results, the SPM software library provides a number of functionalities related to image processing and statistical analysis: normalization, co-registration, smoothing, parameter estimation, statistical mapping.
The statistical parametric mapping algorithm (the most important functionality for our goal) performs a statistical analysis in order to compare, on a voxel-by-voxel base, the perfusion values in the test images against the corresponding values in normal images.

As a result of a previous research project [1], remote access to SPM is being made available through the Italian Portal of Neuroinformatics providing doctors from peripheral hospitals with an invaluable tool to increase the "comparison database" and therefore improving the AD diagnosis. The portal contains a section entirely dedicated to the statistical analysis of PET/SPECT images, accessible by authorized users only. Doctors or researchers accessing the portal may thus be supported in running analysis tasks on suspect AD patient studies. Directly from the portal, a user can upload the suspect AD image and select the normal cases for statistical calculation.
The SPM application is available to authorized users without downloading any software tool. In order to use it, no particular hardware resource or specific computer knowledge is needed.

In order to evaluate the potential advantage of porting such an implementation to a Grid environment, it is worth noting that during the statistical parametric mapping a large set of images of normal patients is required to be used for comparison. This is because the accuracy of ipoperfusion maps is strictly related to the number of normal studies compared to the test image.
On the other hand, due to ethical issues and to the high costs of neuroimaging technologies, PET and SPECT studies on normal subjects are very rare. The NEST-DD project, funded by the European Commission [2], collected a database of about 100 images in order to make available the first large dataset for these studies.
Moreover the images of normal subjects are covered by privacy and security issues and for this reason they cannot be freely moved on the net or published by the centre that made the analysis. As a consequence, only doctors working at very large institutions, locally owning large databases of normal images, can usually carry out SPM-based analyses.
Starting from these considerations, the aim of our project has been to enable doctors from small peripheral hospitals to use large sets of normal PET/SPECT images provided by medical research institutes distributed on the net, by remotely extracting the information needed for the statistical analysis from the normal images and collecting it without moving the original image files.

Furthermore, the execution time of the analysis must be compatible with an interactive clinical application in a busy medical environment. The time required for the analysis can be reduced, since:
- some aspects of calculation could be parallelized and distributed on the computational resources associated to the remote databases of normal images;
- the time required for data transfers over the network would be reduced, since the code amounts to just few KB, compared to images sizing up to 100 MB.
The use of GRID technologies well matches all of the above issues and allows easy access to distributed data as well as to distributed computational resources.

Grid implementation has been carried on GILDA Infrastructure that provides a series of sites and services spread all over Italy and the rest of the world on which LCG and gLite middleware are installed and several Virtual Organisations are enabled.
A LCG node has been installed at University of Genoa for the implementation of biomedical applications and in particular for this application.

The objectives of the LCG-based implementation are:
- to distribute PET/SPECT images on different storage resources available on the GRID and register them on a catalogue.
- to insert and manage metadata in order to make the user able to select normal images for the statistical analysis using their own attributes.
- to access images from User Interface using Logical File Names (LFN) without moving them from storage resources.

To reach the first result, LCG File Catalog (LFC) was selected: it allows users and applications to locate files (or replicas) on the LCG Grid maintaining mappings between logical and physical file names.
As next step, the ARDA Metadata Grid Application (AMGA) has been integrated, fulfilling also the second requirement. Actually, LCG does not provide a satisfactory metadata management system and AMGA fills this hole. The collected metadata are associated to files stored on the LCG Grid through a reference on the LFC catalogue system and are used to select images directly through the portal.
AMGA provides the ability to allow only certain people to access specified attributes. This is very important because all medical data should be considered as sensitive to preserve patient privacy.
To meet the third requirement, LCG Data Management and File access tools have been selected.
In particular lcg_util and Grid File Access Library (GFAL) tools was used to transparently interact with LFC catalog and to perform calls for storage management and file access using the correct protocol for file transfer.

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[2] K. Herholz, E. Salmon, D. Perani, J-C. Baron, V. Holthoff, L. Frolich, P. Schonknecht, K. Ito, R. Mielke, E. Kalbe, G. Zundorf, X. Delbeuck, O. Pelati, D. Anchisi, F. Fazio, N. Kerrouche, B. Desgranges, F. Eustache, B. Beuthien-Baumann, C. Menzel, J. Schroder, T. Kato, Y. Arahata, M. Henze, and W-D. Heiss "Discrimination between Alzheimer Dementia and Controls by Automated Analysis of Multicenter FDG PET"NeuroImage 17, 302–316 (2002)

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