Brain perfusional SPECT imaging implementation for the early diagnosis and prognosis in Alzheimer disease

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Introduction.
The study of brain perfusion has a key role in the diagnosis of dementing disorders. In fact, it is known that some specific forms of dementia, such as Alzheimer's disease (AD), show distinctive patterns of cerebral hypoperfusion, which is found in posterior temporoparietal associative cortex. These findings can be obtained by widely available techniques, such as Single Photon Computed Emission Tomography (SPECT) in patients with aspecific or absent structural deficits. A key problem with Single Photon Emission Tomography (SPECT) is image reconstruction from raw data collected from the gamma camera. The most widely used method is the Filtered Backprojection (FBP), but this method does not fully take into account how the actual shape of the crystal and the performances of the collimator may affect data acquisition. Moreover, the choice of different types of frequency filter is virtually the only possibility of operator intervention during the reconstruction phase. With the aim of improving SPECT imaging quality, a new experimental algorithm, i.e., the Conjugate Gradient reconstruction technique with Modified Matrix (CGMM) [3], has been applied. It utilises linear equations to link radioactivity distribution within the object under study to the counts of photons measured by the crystal (this is achieved using coefficients proper to each individual detecting system). Detailed phantom studies [6] and a study on a single patient [5] have fully demonstrated clear advantages of the new reconstruction techniques in terms of spatial resolution and overall image, allowing better identification both of normal anatomical structures and of pathological findings. The aim of the program was to compare SPECT images as obtained by the new CGMM algorithm with those deriving from conventional FBP method in a group of patients affected with mild AD (scoring higher than 14 at the Mini-Mental State Examination, MMSE) and in a group of aged healhty controls. Perfusional results deriving from the two reconstruction techniques have been correlated with neuropsychological and neurophysiological data.

Subjects.
Twenty-two patients affected with probable AD (8 males and 14 females, aged 53-81 years, mean age: 72.9 + 7.8) according to the NINCDS-ADRDA criteria [4] were studied. Eleven healthy volunteers (3 males and 8 females, aged between 52 and 75 years, mean: 64.5 + 7.5) formed the control group.

Methods.
From the whole of neuropsychological assessment, including multiple tests for cognitive functions, the synoptic score on MMSE and on Buschke-Fuld memory tests [1] were taken into consideration for the purpose of this study. The Buschke-test was considered as the total number of words recalled at the six items. SPECT acquisitions were performed by a brain-dedicated equipment (CERASPECT, Digital Scintigraphics, Waltham, MA), 90-180 min. after the i.v. injection of 740 to 925 MBq of freshly prepared 99mTc-HMPAO with the patients seated in a reclining chair in a quiet, dimly lit room, with eyes closed.

Reconstruction methods.

A) Filtered Backprojection: sixty-four axial slices parallel to the cantho-meatal line, 1.67 mm thick, were reconstructed on a 128×128 matrix (1 pixel = 1.67 mm) using a 2-d Butterworth filtered backprojection (cut-off 0.80 cm, order 10). The reconstructed images were corrected for attenuation with Chang's first-order method, applying an attenuation coefficient equal to 0.15/cm [2].

B) Conjugate Gradients with Modified Matrix: two-dimensional (2D) CGMM image reconstruction was performed after preliminary filtering projections in the axial direction to improve the signal-to-noise ratio (1D Butterwoth filter, cut-off equal to 20% of Nyquist, order 10). Sixty-four transaxial in a similar

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manner as with the conventional FBP technique (1 pixel = 1.67 mm), after Chang's first order attenuation correction (0.15/cm), and brain reorientation along the bicommessural line.

SPECT images underwent rotation of $+30°$ on the sagittal plane as suggested by Onishi et al. [7] to better identify both the hippocampus and the hippocampal gyrus. The three contiguous transaxial slices passing through the hippocampal structures identified in this way were summed up to obtain a 5-mm thick section. Finally, two irregular but symmetrical ROIs were hand-drawn around the two hippocampal regions. Normalisation of SPECT data was obtained by computing ROI/thalamic ratios (mean counts per pixel in each ROI over mean counts per pixel in the two thalami). If a greater than 10% asymmetry was found between the two thalami, the thalamus with higher perfusion was chosen as reference region. Drawings of the hippocampal region were randomly performed in the FBP or in the CGMM image, and then automatically transferred to the other image by a software option, so as to obtain a ROI of identical volume in the two images.

Statistic.

The Pearson Rank test was employed to study the relationship between SPECT and neuropsychological data, both in controls and in patients. The difference between the hippocampal ROI value in each patient and the corresponding mean value of controls was assessed by Z statistics.

Results.

The visual comparison between images as obtained by the two reconstruction methods shows that the CGMM method allowed a better identification of the anatomical structures in most cases. Moreover, the heterogeneity of perfusion patterns within the cerebral cortex was fairly better appreciable with this CGMM than with FBP.

Z statistics showed a similar number of AD patients with hippocampal hypoperfusion with the two reconstruction methods, but hypoperfusion was more symmetric with CGMM than with FBP. In controls, no significant correlation was found between hippocampal perfusion (both FBP and CGMM values) and the Buschke-Fuld indexes. In AD patients, the correlation between hippocampal perfusion and MMSE score was highly significant ($p < 0.001$) in both hemispheres with both the reconstruction methods. On the contrary, the correlation between hippocampal perfusion and the total of words recalled was significant ($r = 0.44$; $p < 0.02$ in the left hemisphere, $r = 0.39$; $p < 0.05$ in the right hemisphere) only with CGMM method.

Correlative analysis between hippocampal perfusion and both quantitative Electroencephalographic and hormonal data are being investigated in other groups of AD patients.

Comment.

The visual analysis has clearly shown that the methods, such as the CGMM, which take into account the structural characteristics of the crystal actually allows better images in comparison to the traditional FBP method. Such a better visualisation of cerebral structures is well appreciable in a comparison of FBP and CGMM images with a scheme of the Talairach's atlas [8]. However, a faster processing of raw data is needed before proposing the CGMM method for routine clinical use. Hardware improvement may significantly shorten the time needed without increasing the cost. The better quality of images is supported by the results of correlation with widely accepted neuropsychological indexes, such as the MMSE and the Buschke-Fuld scores. In fact, the correlations achieved with CGMM better than with FBP point to a more proficient use of this method to clinical purposes, at least in AD, but presumably in other pathological conditions as well.

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