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Generation of realistic HMPAO SPECT images using a subresolution sandwich phantom

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ABSTRACT

Traditional interpretation of rCBF SPECT data is of a qualitative nature and is dependent on the observer's understanding of the normal distribution of the tracer. The use of a normal database in quantitative regional analysis facilitates the detection of functional abnormality in individual and group studies by accounting for inter-subject variability. The ability to simulate realistic images would allow various important areas related to the use of normal databases to be studied. These include the optimisation of the detection of abnormal blood flow and the portability of normal databases between gamma camera systems. To investigate this further we have constructed a hardware phantom and scanned various configurations of radioactive brain patterns and simulated skull configurations.

Methods: A subresolution sandwich phantom was constructed with a simulated skull which was assembled using a high-resolution segmented MR scan printed with a $^{99m}TcO_4-$ mixture and scanned using a double-headed gamma camera with parallel-hole collimators. Various different grey-to-white matter (GM:WM) ratios and aluminium simulated skull configurations were used. A single difference measure between the phantom data and a control database mean image was used for optimisation. The realism of phantom data was assessed using statistical parametric mapping (SPM) and ROI analysis.

Results: Optimisation was achieved with a range of WM:GM ratios from 1.9 to 2.4:1 with various simulated skull configurations.

Conclusion: The ability to simulate realistic HMPAO SPECT scans has been demonstrated using a subresolution sandwich phantom. Further work, involving scanning the optimised phantom on different gamma camera systems and comparison with camera-specific normal databases should further refine the phantom configuration.

Introduction

Historically, most rCBF SPECT images have been assessed by visual interpretation of 2D images through the brain. Such interpretation is subjective and dependent on the operator's understanding of normality. Consequently the technique of anatomic standardisation and comparison of patients with controls and/or other patient groups is increasingly used in clinical practice and research (Huang et al., 2003; Imabayashi et al., 2004; Matsuda et al., 2007; Van Laere et al., 2002b).

Several software packages are available that allow automated whole-brain analysis of brain SPECT studies based on anatomic standardisation. The Statistical Parametric Mapping (SPM) software package (Frith et al., 1997) is well-known, freely available and strongly supported by many brain imaging researchers (Stamatakis et al., 2002; Van Laere et al., 2002b). Much of the work in this study used SPM5. The application of other voxel- and VOI/ROI-based analysis techniques to rCBF SPECT is also popular (Huang et al., 2002; Imabayashi et al., 2004; Volkow et al., 2002).

Only a few studies have been carried out on several topics of interest related to the use of normal database comparisons. Topics of interest include the optimisation of various processing steps (*e.g.* reconstruction, anatomic standardisation, normalisation and comparison) and the portability of normal databases between gamma camera systems (Barnden et al., 2004; Matsuda et al., 2004; Van Laere et al., 2001). The conventional method of addressing these issues is to create what Van Laere et al. (2002a) refers to as 'signal known exactly (SKE) conditions' *i.e.* where the cerebral activity distribution is known. As it is the comparison and portability of *normal* brain images under study, an ideal hardware phantom should, when scanned, produce as close to a normal distribution as possible.

Existing commercially-produced hardware phantoms for radionuclide brain studies, notably the Hoffman phantom (Hoffman et al., 1990), are difficult to accurately and reproducibly adapt for lesion and activation studies. More importantly, the 4:1 ratio between the grey and the white matter volumes in the Hoffman phantom are inappropriate for HMPAO SPECT studies of normal function, where the

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ratio is approximately 2:1 (Wirestam et al., 2000). The cerebellum is a popular area for count normalisation; the phantom only includes the top part of the cerebellum which means scaling to peak or average cerebellar uptake is not possible.

In this study we have constructed a hardware phantom based on a stacked 'sandwich' design, modified slightly from the phantom used by Van Laere et al. (2002a), which was in turn based on a design by Larsson et al. (2000). The principle is based on discrete sampling of radioactivity in 3D objects by means of subresolution-spaced equidistant 2D planes, on which *a priori*-defined radioactive distributions are printed using radioactive dye. Previous studies using this type of phantom have concentrated on validation of scatter and attenuation correction techniques (Larsson et al., 2000) and performance assessment of neuroactivation studies (Van Laere et al., 2002a). Both used sections of the digitised mathematical Hoffman phantom as a cerebral template and neither study simulated the skull.

The aim of this study was to use a realistic cerebral template with a simulated skull to generate realistic HMPAO SPECT images. Ideally, the phantom projection data should be processed in exactly the same way as clinical data; for the centres involved in this work, most clinical studies involve the investigation of dementia. Realistic HMPAO SPECT simulation would have applications in (particularly multicentre) quality assurance (Heikkinen et al., 1998), assessment of the portability of normal databases and the optimisation of processing techniques through the use of lesions simulated in a normal distribution (Grova et al., 2003; Stamatakis et al., 1999; Ward et al., 2005).

Materials and methods

Sandwich rCBF phantom

The basic design for the phantom was taken from Van Laere et al. (2002a). The phantom consists of 53 4 mm PMMA (polymethylmetacrylate, density 1.10 g cm^{-3}) discs of 200 mm outer diameter, kept together by four PMMA screw rods for compression of the radioactive sheets as well as the reproducible placement of the preformatted printer sheets (see Fig. 1).

rCBF activity distribution software templates

The SPM canonical single subject T1 template was used to create a software phantom for the creation of the stacked printout slices. SPM99 was used to segment the template into grey and white matter volumes. It should be noted that all subsequent image analyses used SPM5. The original template consists of a $91 \times 109 \times 91$ matrix MRI scan with 2 mm cubic voxels. After segmentation, Matlab (Mathworks, Inc., Natick, MA, USA) was used to rescale the images to $2 \times 2 \times 4$ mm rectangular voxels suitable for use in the phantom. Non-brain areas were then cropped from the grey and white matter segments using MRIcro (Rorden and Brett, 2000). Matlab was then used to recombine the grey and white matter images in digital intensity ratios between 1.3 and 4:1 (see Fig. 2). For each of the different ratios, MRIcro was then used to produce individual portable network graphics files for each of the 36 transverse slices in the image volume. Finally, each of the slice images were imported into successive worksheets in a Microsoft Excel workbook and resized so that the printed slice would fit on the preformatted paper for the printer. A separate workbook was produced for each digital intensity ratio.

Aluminium skull simulation

The effective skull thickness has been measured for three empty skulls (Turkington et al., 1993). For the skull regions surrounding most of the brain, the effective skull thickness varied considerably, but was generally less than 6 mm. For all three skulls the thickness was greater than 10 mm in the lower bone, which is the area surrounding the cerebellum. Data from Hubbell and Seltzer (1995) indicates that the attenuation properties of 6 mm of bone and 4 mm are similar at 140 keV. Consequently, two separate aluminium sheaths of 2 mm thickness were made to enclose the entire length of the phantom. Other semi-circular aluminium sections of varying thicknesses and heights were also made to simulate thicker areas of skull, particularly at the bottom of the brain.

Radioactive sheet printout

The black ink container of a digital inkjet printer (Hewlett Packard Deskjet 930C) was used. The ink container of the black ink cartridge was modified to allow refilling. A solution of 10 ml black ink and 2 ml $^{99m}TcO_4-$ in aqueous solution containing approximately 1.2 GBq (32 mCi) was mixed and inserted into the printer cartridge. The ink cartridge was then sealed, inverted and left for 20 min for the air pressure inside and outside the cartridge to equalise. Several test sheets (depicting a geometric pattern) were then printed and visually

Fig. 1. Partially disassembled (left) and fully assembled (right) views of the sandwich rCBF phantom.