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Functional and structural synergy for resolution recovery and partial volume correction in brain PET

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ABSTRACT

Purpose: Positron Emission Tomography (PET) has the unique capability of measuring brain function but its clinical potential is affected by low resolution and lack of morphological detail. Here we propose and evaluate a wavelet synergistic approach that combines functional and structural information from a number of sources (CT, MRI and anatomical probabilistic atlases) for the accurate quantitative recovery of radioactivity concentration in PET images. When the method is combined with anatomical probabilistic atlases, the outcome is a functional volume corrected for partial volume effects.
Methods: The proposed method is based on the multiresolution property of the wavelet transform. First, the target PET image and the corresponding anatomical image (CT/MRI/atlas-based segmented MRI) are decomposed into several resolution elements. Secondly, high-resolution components of the PET image are replaced, in part, with those of the anatomical image after appropriate scaling. The amount of structural input is weighted by the relative high frequency signal content of the two modalities. The method was validated on a digital Zubal phantom and clinical data to evaluate its quantitative potential.
Results: Simulation studies showed the expected relationship between functional recovery and the amount of correct structural detail provided, with perfect recovery achieved when true images were used as anatomical reference. The use of T1-MRI images brought significant improvements in PET image resolution. However improvements were maximized when atlas-based segmented images as anatomical references were used; these results were replicated in clinical data sets.
Conclusion: The synergistic use of functional and structural data, and the incorporation of anatomical probabilistic information in particular, generates morphologically corrected PET images of exquisite quality.

Introduction

Positron emission tomography (PET) has the unmatched ability to image, in absolute quantitative fashion, the distribution of radiolabeled markers with concentrations in the picomolar range. This allows the in-vivo monitoring of functional processes such as perfusion, metabolism, gene and protein expression etc. PET however is hampered by the poor spatial resolution and lack of morphological information, features that are characteristic of CT and MRI. The availability of computational approaches for the between-modalities registration (Woods et al., 1993) but, in particular, the recent availability of combined PET–CT (Beyer et al., 2000) and PET–MRI (Judenhofer et al., 2008; Shao et al., 1997) scanning technology has increased the interest in computational methodologies able to use synergistically multimodal information. In this work we present a statistical model able to combine synergistically PET with morphological data for the resolution recovery of PET data. The model is flexible because the use of structural data is weighted with the relative amount of signal in the functional and morphological images; this allows the preservation of fine functional detail in the absence of matching structural detail. Depending on the quality of structural information that ranges from low (CT) to greater anatomical detail (MRI), the method allows the recovery of the resolution of the PET volume. Moreover, the availability of a registered anatomical image allows the use of standardized morphological information such as, in this case, a probabilistic anatomical atlas. The combined use of the proposed method and the probabilistic anatomical atlas results in an image-based algorithm for the correction of partial volume effects in PET images.

The quantification of small brain structures and the correction of PET signal for underlying morphology may have strong clinical impact (Fazio and Perani, 2000; Leroy et al., 2007). Therefore, accurate

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quantification via a computational technique that may also be widely and easily applicable is of great relevance in nuclear medicine and neuroscience in general.

Resolution recovery for brain PET

Since the finite spatial resolution of PET blurs the distribution of radioligands in images, several authors have proposed resolution recovery (RR) techniques based on the deconvolution of images with the point spread function (PSF) of the scanner (Biemond et al., 1990; Lucy, 1974; Richardson, 1972; Teo et al., 2007). Deconvolution approaches enhance high frequency signal but inevitably increase noise in images and cannot recover anatomical detail that has been lost because of the PSF of the scanner. Alternatively, partial volume correction approaches have been introduced that use PSF and anatomical information derived from segmented MRI images (usually gray and white matter and cerebral spinal fluid relative densities or anatomical segmentation) to correct region of interest (ROI) PET data for the effects of tissue loss (Aston et al., 2002; Labbe et al., 1996; Meltzer et al., 1999, 1990; Rousset et al., 2008, 1998). RR techniques have also been pursued that integrate structural images and position variant PSF into the iterative reconstruction process (Ardekani et al., 1996; Baete et al., 2004; Panin et al., 2006).

Proposed methodology

The methodology presented here stems from previously proposed ideas for RR based on the wavelet transform (WT) (Boussion et al., 2006, 2008; Nunez et al., 2005). In particular Boussion et al. (2008) used co-registered CT images to improve the resolution of PET data using a resolution level dependent factor to scale the CT details into the PET image.

The methodology develops previous work (Turkheimer et al., 2008) that used CT/MRI information in a synergistic fashion to denoise functional data. In this instance though, the existing local functional/structural relations are exploited for an accurate and realistic recovery of the resolution of PET images. We labeled the method as "Structural–Functional Synergistic" Resolution Recovery (SFS-RR). SFS-RR uses the WT to decompose the functional (e.g., PET) and the structural reference image (e.g. CT/MRI) into several resolution elements and then replaces the high-resolution component of the functional image with the anatomical image with an appropriate local scaling. Functional and anatomical distributions however may differ (Shidahara et al., 2007; Soret et al., 2007; Teo et al., 2007; Tohka and Reilhac, 2008); to suppress the effects of distribution mismatch, on one hand the proposed methodology handles the substitution of functional with structural details flexibly by evaluating the local ratio between functional and structural signal in the wavelet domain. This however may not be sufficient as no single structural image may provide the anatomical support for the functional study at hand. We therefore developed the synergy concept further and investigated the possibility of using an anatomical frequency-based brain atlas (Hammers et al., 2003) as structural information to inform the SFS-RR. The use of a probabilistic brain atlas, as shown in the following section, makes the SFS-RR into an image-based approach for the partial volume correction of PET images.

In the present study, the performance of SFS-RR was assessed using accurate simulations and clinical brain data for [^{18}F]FDG and [^{11}C]raclopride as representative of the wider range of PET data of relevance for the methodology.

Materials and methods

Wavelet transform

The wavelet transform (WT) produces a time/frequency signal decomposition (Mallat, 1999). The WT decomposes the signal $f(x)$ through a high band-pass function Ψ and a low-pass scaling function Φ as:

$$f(x) = \sum_k \sum_{j=1}^{J} d_j(k) \cdot \psi_{j.k}(x) + \sum_k C_J(k) \cdot \phi_{J.k}(x) \quad (1)$$

The second term on the right side of Eq. (1) represents low frequency components of the signal. The functions $\psi_{j,k}$ are orthonormal basis elements generated by dilated (j) and translated (k) versions of Ψ. The $d_j(k)$ in Eq. (1) are the wavelet coefficients which are given by the scalar product of the original signal with the $\psi_{j,k}$ basis elements. The coefficients $d_j(k)$ indicate elements of the decomposed signal at position k within frequency band j, where j is usually referred to as the decomposition/resolution level, or simply level. For two-dimensional images, the 1D WT is firstly applied to the horizontal direction (0°), followed by a decimation where every odd numbered element is removed. Thereafter, the 1D WT and the decimation are applied to the vertical direction (90°). As a result, images can be decomposed within three directions (0, 45 and 90°) with each wavelet coefficient indexed as $d_j(q, k)$ where q is the quadrant.

In this work, differently from the previous synergistic approach (Turkheimer et al., 2008), we used the dual-tree complex wavelet transform (CWT) that decomposes the image into multiple directional features (Kingsbury, 2001; Selesnick and Li, 2003) and therefore preserves better the sharp morphological detail. The CWT decomposes 2D images into six quadrants with directionalities (15, 45, 75, −15, −45 and −75°) labeled D_{45}, H_{15}, V_{75}, D_{-45}, H_{-15}, V_{-75} and one residual quadrant. Each wavelet coefficient of the 2D image is indexed as $d_j(q, k)$ where $q = 1...6$. In the 3D dual-tree CWT utilized in this study $q = 1…28$.

Resolution recovery using wavelet

The basic idea of SFS-RR using wavelets (Boussion et al., 2006, 2008; Nunez et al., 2005) consists of (a) the decomposition of the target PET image and the corresponding anatomical image into several resolutions using the WT and (b) the replacement of the high-resolution component of the PET image from the anatomical image.

Let the high-resolution wavelet coefficients of the PET image be d^{PET} and let d^{ana} be the correspondent anatomical wavelet coefficients. We define the scaling procedure as:

$$d_j^{\mathrm{corr}}(q,k) = \alpha_j \cdot d_j^{\mathrm{ana}}(q,k) \quad (2)$$

where d^{corr} is the resolution recovered wavelet coefficient that will replace the correspondent d^{PET}. The variables q and k correspond to the quadrant and the position in wavelet domain respectively and α is the scaling factor. In general however, the relation between d^{PET} and d^{ana} will vary throughout the image. This is captured by expanding Eq. (2) into the following model.

$$d_j^{\mathrm{corr}}(q,k) = \beta_j \cdot \left\{ \gamma_j \cdot \left(\alpha_j \cdot d_j^{\mathrm{ana}}(q,k) \right) + \left(1 - \gamma_j \right) \cdot d_j^{\mathrm{PET}}(q,k) \right\} \quad (3)$$

In Eq. (3), β is the SFS-RR coefficient accounting for the difference in resolutions between the two images. The parameter γ is a branching factor that weights the anatomical information versus the functional in the recovery process.

β as the SFS-RR coefficient

The magnitude of wavelet coefficients in high frequency depends on the spatial resolution of the image. SFS-RR requires the conversion of the magnitude of wavelet coefficients d^{PET} to high-resolution. The recovery coefficient β, which varies throughout resolutions, is obtained as the ratio of the wavelet coefficients of the original anatomical image and the same anatomical image smoothed with a 3-dimensional Gaussian filter to PET scanner resolution. In the instance of the data used here we utilized the filter's full width at half