A Four-dimensional Atlas of Neonatal Brain MRI

Ahmed Serag[1]
a.serag09@imperial.ac.uk
Paul Aljabar[1]
paul.aljabar@imperial.ac.uk
Serena Counsell[2]
serena.counsell@imperial.ac.uk
James Boardman[3]
j.boardman@imperial.ac.uk
Jo V. Hajnal[4]
jo.hajnal@csc.mrc.ac.uk
Daniel Rueckert[1]
d.rueckert@imperial.ac.uk

[1] Biomedical Image Analysis Group, Imperial College London, London, UK
[2] Centre for the Developing Brain, Imperial College London, London, UK
[3] Simpson Centre for Reproductive Health, Royal Infirmary of Edinburgh, Edinburgh, UK
[4] MRC Clinical Sciences Centre, Imperial College London, London, UK

Abstract

In this paper we present an approach for constructing a 4D brain atlas of MR images of preterm infants aged between 26-44 weeks of gestation at time of scan. The method used for the creation of an average 4D atlas is based on the use of pair-wise non-rigid registration to eliminate bias in the atlas towards any of the original images. In addition, we use kernel regression to produce age-dependent anatomical templates. The resulting unbiased 4D atlas is much sharper than currently available atlases created using affine registration.

1 Introduction

Due to their importance in the analysis of population data, average atlases have received increasing attention in the area of medical image analysis. Average atlases are useful in detecting abnormalities by measuring the variations in anatomy between an atlas and an individual subject. An established method of atlas construction is to select a reference image and register all subject images to the selected reference. However, such an atlas is biased towards the chosen subject. To reduce or avoid bias in the atlas towards any of the registered subjects, many alternative atlas creation approaches have been proposed. [1] suggest a method in which the bias towards a specific reference can be reduced by carring out pair-wise registration on all pairs of images in the population, and each image is deformed by the average of the the deformation fields estimated between the image and all other images. The atlas is thus built by averaging all the deformed images.

There are also examples of spatio-temporal atlases in the literature. Davis et al. [2] produced a time-varying non-rigid templates using kernel-based regression. Recently, [3] extended the kernel-based regression approach to build a 4D probabilistic atlas of preterm subjects, at gestational ages of 29-44 weeks. These images were aligned using affine registration and this leads to fuzziness in the resulting atlas. This is because affine registrations only account for global variations in translation, rotation, scaling and shearing. Moreover, it can be difficult to register an individual subject with clear anatomical structures to a fuzzy mean image which may not provide sufficient anatomical information to guide the registration process.

In this paper we present an approach for constructing a 4D atlas of the developing brain using non-rigid registration of MR brain images of preterm infants. In order to achieve this, we develop a four-dimensional extension of the approach of Seghers et al. [1]. In addition, we use kernel regression to produce age-dependent anatomical templates. The result is an unbiased spatio-temporal atlas which is much sharper than currently available atlases derived via linear registrations.

2 Methods

2.1 Subjects

The atlas approach presented was applied to a database of MR images of prematurely born neonates consisting of 205 images. The images were scanned between 26.71 to 44.29 weeks. Infants who had major focal lesions on imaging were excluded from the study. The images were acquired on 3T Philips Intera system with the following parameters: T2-weighted fast spin-echo (FSE): TR = 8700 ms, TE = 160 ms, flip angle = 90 degrees, acquisition plane = axial, voxel size = 1.15 x 1.18 x 2 mm, FOV = 220 mm, acquired matrix = 192 x 186. All images were preprocessed using [4] (brain extraction) and [5] (bias field correction).

2.2 Kernel Regression

In this work, kernel regression [6] is used to construct a 4D time-varying brain atlas. The technique is used across the population of interest to compute the average brain template at any given age, using weighted support from the neighbors of the age selected. The kernel serves to interpolate between the subjects (since there may be no subjects at exactly the age of interest). Moreover, it serves to average out the inter-subject variation. In our work, we use a Gaussian kernel as the weight function:

$$w(t_k,t) = \frac{1}{\sigma\sqrt{2\pi}} e^{\frac{-(t_k-t)^2}{2\sigma^2}}$$

The width of the kernel, σ, is a parameter that is tuned to have a comparable number of subjects at every time-interval.

2.3 Registration

In the age range of study, the brain development incorporates global (size and shape) and local (structure's evolution) variations. Any estimated atlas needs to reflect these global and local changes in order to be representative for the population of interest. Therefore, for a given pair of images, registration was carried out in two steps. A global transformation was first estimated using a 12 parameter affine registration. Subsequently, using the result of the affine registration as a starting point, a non-rigid registration step was carried out. We describe one image as the 'target' and the second image as the 'source'. After registration, the obtained transformation maps locations in the target to locations in the source.

Let $\mathbf{T}_{global}$ represent a global affine transformation and $\mathbf{T}_{local}$ a local non-rigid displacement field. The global transformation can be represented by a translation vector $\mathbf{d}$ and a 9 parameter affine matrix M encoding rotations, scales and shears: $\mathbf{T}_{global}(\mathbf{x}) = M\mathbf{x} + \mathbf{d}$. The complete transformation $\mathbf{T}$ that accounts for both global and local differences between a pair of images is modelled as the sum of these local and global components:

$$\mathbf{T}(\mathbf{x}) = \mathbf{T}_{global}(\mathbf{x}) + \mathbf{T}_{local}(\mathbf{x}) = M\mathbf{x} + \mathbf{d} + \mathbf{T}_{local}(\mathbf{x}) \tag{1}$$

for each location $\mathbf{x}$ in the target image. The non-rigid deformations were represented using the free-form deformation (FFD) model proposed by Rueckert et al. [7].

2.4 Atlas Construction

The method used for the creation of age-dependent average space atlas is based on the use of pair-wise registrations and transformation averaging in a four-dimensional extension of the approach of Seghers et al. [1]. Within a time-interval, we carried out pair-wise registrations by, in turn, selecting all images within the time-interval as target image and subsequently, by averaging the resulting transformations, the images are transformed into a mean image. The pair-wise registrations eliminate bias in the atlas towards any of the original images. This method is illustrated in Figure 1.

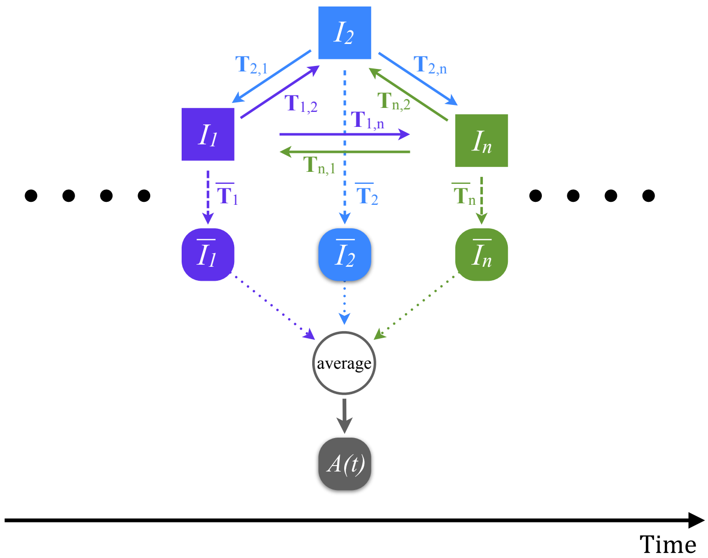

Figure 1: The procedure to construct an age-dependent atlas. Within a time-interval, the scans of all subjects are registered to all others and then used to construct a mean shape image for each scan. The mean shape images are subsequently averaged after appropriate intensity rescaling to compensate for global intensity differences in the original data. The procedure is repeated at every time-interval in order to create a spatio-temporal atlas.

Let $I_1, \ldots, I_n$ represent the images for all subjects within a time-interval. Each image I_i is in turn selected as a reference template (target image), yielding transformations $\mathbf{T}_{i,j}$ for $j = 1, \ldots, n$. These transformations can be averaged to produce $\bar{\mathbf{T}}_i$:

$$\bar{\mathbf{T}}_i = \frac{1}{n} \sum_{j=1}^{n} \mathbf{T}_{i,j} \tag{2}$$

for each image i at a given time-interval. Details of averaging global and local transformations can be found in Aljabar et al. [8]. Hence, we define the mean shape image $\bar{I}_i$ as the image obtained from I_i by the spatial transformation

$$\bar{I}_i = I_i \circ \bar{\mathbf{T}}_i^{-1} \tag{3}$$

When building a 4D atlas of the developing brain, we aim to create a continuous spatio-temporal model dependent on a parameter t which represents time, which in our case is gestational age scan. Let $t_1, \ldots, t_n$ denote the scan time gestational ages of the database subjects. To create such a spatio-temporal atlas we use kernel regression, similar to [2, 3]. Therefore, equation (2) is extended to incorporate the weights derived from kernel regression:

$$\bar{\mathbf{T}}_i = \frac{\sum_{j=1}^{n} w(t_j,t)\mathbf{T}_{i,j}}{\sum_{j=1}^{n} w(t_j,t)} \tag{4}$$

The average atlas with mean shape and mean intensities at the age t can be estimated as

$$\mathscr{A}(t) = \frac{\sum_{i=1}^{n} w(t_i,t)\bar{I}_i}{\sum_{i=1}^{n} w(t_i,t)} \tag{5}$$

where mean shape images are voxel-wise weighted intensity averages which represent the age-dependent average space atlas $\mathscr{A}$ at age t. However, before performing intensity averaging, appropriate intensity rescaling has to be applied to compensate for global intensity differences between the images within the time-interval of interest [1].

3 Results

In Figure 2, the final atlas is compared with an atlas constructed using affine registration [3], and can be seen to be clearly sharper. The importance of a sharp mean image in image registration is demonstrated in Figure 3. Each of the input images was non-rigidly registered to the atlas at the corresponding time-point. Cross-correlation was then used to quantify the degree of similarity between the atlas and each individual image. Figure 3 shows the average cross-correlation at every time-point. The new atlas shares a much higher similarity with the input images compared with the affine atlas from [3]. This is because lack of details in the atlas can impair detailed correspondences being identified.

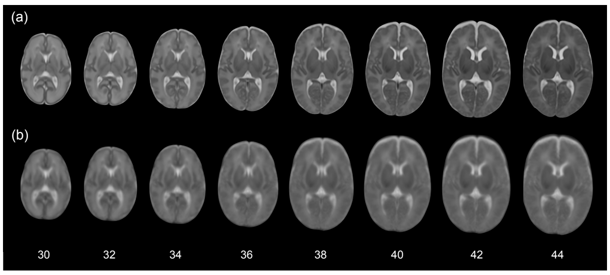

Figure 2: Comparison of our atlas (a) with the affine atlas (b) at 30, 32, 34, 36, 38, 40, 42, and 44 weeks GA.

4 Conclusion

In this paper we present an approach for constructing a 4D brain atlas of MR images of preterm infants. This results in a spatio-temporal atlas which is much sharper than currently available linearly produced atlases. Such a sharp atlas offers the potential to improve the

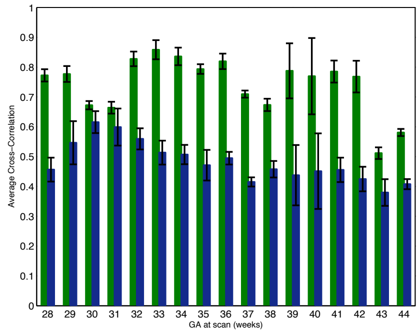

Figure 3: Average similarity measure results between individual images and the new atlas (green), the affine atlas (blue).

registration process between the atlas and individual subjects with clear anatomical structures, and can lead to more precise analyses and detection of abnormalities by measuring the anatomical variation between the atlas and the individual subject. To our knowledge this is the first time that such a spatio-temporal atlas with this level of clarity and detail has been constructed using a large number of subjects and for such a wide range of ages. The atlas is publicly available at www.brain-development.org.

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