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A 4D neonatal head model for diffuse optical imaging of pre-term to term infants

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ABSTRACT

Diffuse optical tomography is most accurate when an individual's MRI data can be used as a spatial prior for image reconstruction and for visualization of the resulting images of changes in oxy- and deoxy-hemoglobin concentration. As this necessitates an MRI scan to be performed for each study, which undermines many of the advantages of diffuse optical methods, the use of registered atlases to model the individual's anatomy is becoming commonplace. Infant studies require carefully age-matched atlases because of the rapid growth and maturation of the infant brain. In this paper, we present a 4D neonatal head model which, for each week from 29 to 44 weeks post-menstrual age, includes: 1) a multi-layered tissue mask which identifies extra-cerebral layers, cerebrospinal fluid, gray matter, white matter, cerebellum and brainstem, 2) a high-density tetrahedral head mesh, 3) surface meshes for the scalp, gray-matter and white matter layers and 4) cranial landmarks and 10-5 locations on the scalp surface. This package, freely available online at www.ucl.ac.uk/medphys/research/4dneonatalmodel can be applied by users of near-infrared spectroscopy and diffuse optical tomography to optimize probe locations, optimize image reconstruction, register data to cortical locations and ultimately improve the accuracy and interpretation of diffuse optical techniques in newborn populations.

Introduction

Diffuse optical tomography (DOT) is a functional imaging approach, which uses data from multiple sources and detectors of near-infrared light to reconstruct depth-resolved images of the concentration changes of oxy- (HbO) and deoxy- (HbR) hemoglobin (Culver et al., 2003; Dehghani et al., 2009; Gibson et al., 2005; Hielscher et al., 2002; White and Culver, 2010). These values can be calculated from changes in the light intensity measured between a source fiber and a detector fiber located several centimeters apart on the scalp (Boas et al., 2002; Jöbsis, 1977). A high number of channels, arranged densely on the scalp and with multiple source-detector distances in order to probe different depths inside the subject's head, allows the DOT technique to yield significant spatial information. In recent years DOT has been developing quickly, with the aim of improving the accuracy, the resolution and the sensitivity of the reconstructed images (Abdelnour et al., 2010; Boas et al., 2004; Gregg et al., 2010; Heiskala et al., 2012). Eggebrecht et al. (2012) and Zhan et al. (2012) have recently shown that, thanks to the recent advances in array design, signal analysis and head modeling, high-density DOT can achieve a spatial resolution comparable to that of functional magnetic resonance imaging (fMRI).

Diffuse optical techniques provide no information about the anatomical structure of the brain. However, accurate anatomical information is essential if the spatial information present in DOT data is to be fully exploited. Anatomical information not only allows meaningful visualization of the DOT images, but also helps the image reconstruction process itself by restraining the ill-posed inverse problem (Bamett et al, 2003; Boas and Dale, 2005; Guven et al., 2005; Pogue and Paulsen, 1998; Schweiger and Arridge, 1999; Zhang et al., 2005). Diffuse optical image reconstruction necessitates an accurate forward model, which maps a change in optical properties in the target object to a change in the DOT measurements. To produce an accurate forward model, a realistic, multi-layered head model of the different tissues of the human head, each assigned accurate optical properties, is essential. The position of the optical sources and detectors also has to be registered precisely to the head model in order for the forward problem to be solved (Perdue et al., 2012).

The best practice approach to performing DOT image reconstruction is therefore to register the DOT source and detector locations to each subject's individual MRI image, and use that MRI image to construct a subject-specific, multi-layered head model. However, acquiring an

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MRI image for every participant undermines the intrinsic advantages of the DOT technique, i.e. portability and applicability to challenging populations. The use of a generic head model, based on an MRI atlas, is a suitable and effective solution to this problem (Custo et al., 2010; Tsuzuki and Dan, 2013). A number of adult atlases have been applied to DOT (Custo et al., 2010; Ferradal et al., 2013; Habermehl et al., 2012; Tian and Liu, 2013). These include the Colin27 MRI atlas (Collins et al., 1998), which consists of a high-resolution MRI volume of a single individual and the non-linear ICBM152 atlas (Fonov et al., 2011), which constitutes a spatial average of 152 adults. When applied to DOT, each atlas must first be registered to each subject, usually by recording the location of a number of the subject's cranial landmarks and the DOT source and detector positions with a tracking system or with photogrammetric methods (Tsuzuki and Dan, 2013). As the corresponding cranial landmarks can be identified on the chosen atlas, the atlas volume can be transformed to match the subject's cranial dimensions (most simply by an affine transformation, see Singh et al. (2005) and Tsuzuki et al. (2012)). This registered atlas volume will then match the size, and to some extent the shape, of the individual's head, and an accurate forward model can be computed within this space. Using this process, an optical head model can enable an MRI-free approach to diffuse optical image reconstruction.

Both Cooper et al. (2012) and Ferradal et al. (2013) have shown that by employing a generic atlas head model, the localization error associated with DOT reconstruction in adults increases significantly when compared to that obtained using the subject's own MRI. However, atlas-based DOT can obtain a localization accuracy of ~10 mm, which is sufficient to identify the location of an activation within the gross cortical anatomy and even within a given cortical gyrus.

Diffuse optical techniques are widely used on term and preterm infants and have a long history of application to this population (Austin et al., 2006; Cooper et al., 2011; Elwell et al., 2005; White et al., 2012). This is partly due to the non-invasive nature of the technique and the fact that it is silent and applicable at the bedside (Fournier et al., 2012; Liao et al., 2012; Lloyd-Fox et al., 2010). DOT instrumentation can be applied in the Neonatal Intensive Care Unit (NICU), and recording can be continuous and long-term (Ancora et al., 2013; Lin et al., 2013). Infants are also very suitable for DOT techniques because of their smaller head sizes, thinner skulls and minimal hair, all of which make obtaining measurements of the brain more straightforward than is usually the case in adults.

Despite the widespread use of DOT in the neonatal field, there are a limited number of studies that have attempted to produce accurate infant head models (Dehaes et al., 2011; Fournier et al., 2012; Heiskala et al., 2009; White et al., 2012). Acquiring an MRI image of a newborn baby is challenging and is rarely performed unless clinically necessary. There are also difficulties in dealing with newborn MRIs because of a lack of established automatic tools to segment the neonatal MRI images into different tissue types (cerebrospinal fluid (CSF), gray (GM) and white matter (WM) for example). Indeed, automatic segmentation of the neonatal brain tissues remains a challenging problem because the contrast between the tissues is different and usually lower than that in adults and the within-tissue intensity variability is high (Altaye et al., 2008; Prastawa et al., 2005). The tools available for adult MRI segmentation cannot always be utilized without introducing significant errors (Wilke et al., 2003). As a result, there are a limited number of high-resolution MRI data-sets available for newborns and even fewer for preterm babies.

Because the brain of the newborn infant is developing extremely quickly, accurate DOT reconstruction requires head models that are carefully age-matched. The brain structure of a 30 weeks PMA (post menstrual age) newborn is markedly different from that of a full term (40 weeks) baby (Battin and Rutherford, 2002). A single generic atlas, which can be applied to adults spanning a wide range of ages, will not be suitable for neonatal DOT. An atlas with age-specific infant MRIs, from pre-term to term, is therefore needed to produce suitable optical head models. DOT image reconstruction can then be performed using the correct, age-matched anatomy.

A small number of term-age MRI atlases have been constructed and described in the literature. The atlas proposed by Shi et al. (2011) was built by registering and spatially averaging MRIs obtained from 95 infants aged between 38.7 and 46.4 weeks PMA to produce a single, term-age atlas volume. Similarly, the atlas proposed by Oishi et al. (2011) used data from 25 infants aged between 38 and 41 weeks PMA and the atlas proposed by Heiskala et al. (2009) used 7 infants aged between 39 and 41 weeks PMA. The atlas proposed by Sanchez et al. (2011) averaged MRIs acquired on 23 babies aged between 8 days to 29 days after birth.

Although these single-age atlases have many applications, the ideal neonatal atlas should be built from MRI data obtained over a wide pre-term to term age range, and would ideally include enough data at each age to allow an atlas to be dynamically produced for any arbitrary age within that range. The atlas proposed by Kuklisova-Murgasova et al. (2011) does just that. Using MRI images recorded on 142 infants ranging from 29 weeks PMA to 47 weeks PMA and using a weighted averaging approach this atlas allows the production of tissue probability maps for any age in this range, and the resulting volumes are publicly available for 29 to 44 weeks in one week intervals (www.brain-development.org).

Although this 4D atlas provides a great resource for producing age-matched head models for DOT, there is one significant difficulty preventing the use of the volumes that are currently available online. Because DOT requires a forward model to be computed based on the scalp locations of each source and detector, a model of the extra-cerebral tissues is essential. For a number of reasons, including data protection and a more accurate registration and segmentation, the scalp and skull layers visible in the MRI data are usually stripped out of the image prior to that data being included in the atlas. In order to produce DOT head models, it is first necessary to retrieve the extra-cerebral tissue layers.

The aim of this paper is to present a 4D optical head model for preterm and term newborns ranging from 29 weeks PMA to 44 weeks PMA that can be used by researchers to perform DOT image reconstruction on an accurate, age-matched anatomy. Each step of the construction of the 4D optical head model is presented and discussed. The final package, available online at www.ucl.ac.uk/medphys/research/4dneonatalmodel contains, for each age: 1) a multi-layered tissue mask which identifies extra-cerebral layers, cerebrospinal fluid, gray matter, white matter, cerebellum and brainstem, 2) a high-density volumetric, multi-layered tetrahedral head mesh, 3) The scalp, white matter and gray matter surface meshes and 4) all the coordinates for the 10-5 positions and cranial landmarks on the scalp.

Materials and methods

Subjects

The MRI atlas on which we based our models was built using 324 (160 female) T2-weighted fast-spin echo images acquired on 3T Philips Intera system with MR sequence parameter TR = 1712 ms, TE = 160 ms, flip angle 90° and voxel size 0.86 × 0.86 × 1 mm. The original atlas (Kuklisova-Murgasova et al., 2011) was built using 142 T2-weighted images; new images have been acquired since its release and have been added to the average volumes on which our head models are based. The age range of the newborns at the time of scanning was 26.7 to 47.1 weeks PMA.

MRI atlas pre-processing

Because of the necessity of including scalp and skull information in the final atlas, the same process of affine registration to an average reference space and voxel-wised weighted intensity averaging, with