FETAL BRAIN MAPPING

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ABSTRACT

Advances in fast 2D MRI have led to its growing clinical use in un-sedated fetal brain studies, as a tool for challenging neurodevelopmental cases. The availability of this 2D data has motivated new engineering developments that combine fast multi-slice MRI scans with computer vision techniques to provide a route to full 3D fetal brain image formation in a significant fraction of imaging studies. Critically, this promises a route to studying early human brain development with realistic populations, rather than in a fraction of individuals where motion does not occur. This article will briefly review the problem of slice motion estimation, techniques for 3D image reconstruction and look at new methods that have been developed to model and segment early developing tissue zones within the human fetal brain. Finally, a brief review covering some of the early applications of these methods to study fetal brain growth is included.

Index Terms— Brain Mapping, Fetal MRI, Brain Development, Computational Developmental Anatomy

1. INTRODUCTION

Unlike fetal ultrasound, signal levels in MRI limit the lower bound on acquisition time and lead to compromises between resolution, contrast properties and speed. However, given enough signal, MRI provides unique tissue contrast that is inaccessible to ultrasound. These allow, for example the delineation of subtle developing tissue zones within the fetal brain such as the sub-plate and germinal matrix. As a result, clinicians have driven the use of fast 2D MRI to help provide additional clues in challenging neurodevelopmental abnormalities. However, 2D MRI for visual clinical interpretation does not provide the true 3D anatomical representation required for more quantitative population studies such as those commonly carried out in the adult and the developing child. Even with accelerated MRI techniques such as those using parallel imaging, sparse reconstruction or spiral imaging, it is not currently possible to acquire full 3D images with useable contrast to reliably study the moving fetal head.

2. FETAL HEAD MOTION ESTIMATION

The problem of motion correction in MRI has a long history. However, the methods have most commonly made use of the assumptions of a rigid anatomy moving within an empty air background, such as the case of adult head or joint motion, allowing the trivial separation of moving object signal from background. This has permitted approaches to be developed in the naturally acquired k-space domain of MRI data, or to make use of 3D tracking of anatomy using additional fast locator scans. The problem of local object motion correction within a complex anatomical field such as the maternal anatomy is significantly more challenging and has led to spatial domain solutions that can make use of anatomical context to simplify the localization of motion estimates to the fetal head. The first approaches to fetal MRI motion correction [1] were motivated by the clinical use of multiple fast multi-slice acquisitions to provide coverage of the fetal anatomy in multiple image planes required by the clinical radiologist. These data generally are able to freeze motion within the majority of the slices acquired, but then suffer from the resulting unknown 3D relationship between the acquired slices, as the fetus moves between slice acquisitions. The resulting problem can be related to those of image mosaicing in computer vision, image stacking in histology, and slice to volume image matching. The key differences being that there is minimal (line) overlap between the acquired component images (unlike photogrammetric mosiaicing), there is full 3D motion between image slices and therefore no simple data ordering (unlike histology slice data), and that there is no reference volume with which to match the acquired slices (unlike slice to volume matching problems). Approaches to a solution can be divided into those based on a reconstruction step [2] which form an intermediate estimate of the 3D image to which 2D slices are matched, and those that consider matching of slice intersections directly [5] without the need for a volume reconstruction, as illustrated in Figure 1.

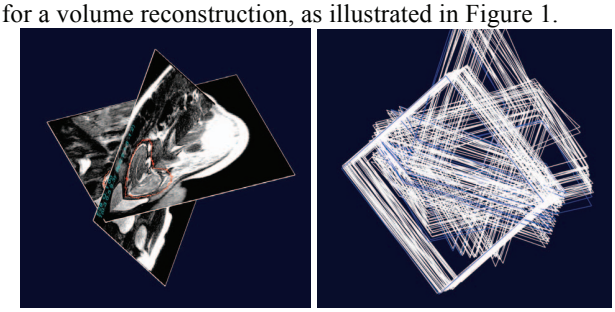

Figure 1: Example clinical MRI slices (left) from two orthogonally planned multi-slice MRI acquisitions of the fetal brain showing surrounding maternal anatomy. Right image shows the head-motion corrected location of all 5 multi-slice datasets.

3. 3D IMAGE RECONSTRUCTION

Once accurate transformations that bring the fetal head slices into collective correspondence have been estimated, the scattered slice data must be accurately reconstructed on a regularly sampled 3D voxel lattice. One of the key factors here is that clinical multi-slice data is commonly acquired for visual inspection with highly anisotropic resolution: fine pixels in plane, but thick slices to provide adequate signal to noise for clinical inspection. However, sets of multi-slice clinical studies are commonly acquired with approximately orthogonal directions, so the studies collectively provide complementary resolution that can be exploited in the process of reconstruction onto a regular lattice. However, a second confounding issue is that of motion induced variable data density. In order to support a given reconstruction resolution we need to ensure adequate data sampling. The first techniques were aimed at general clinical studies where there was significant motion, few sets of slice stacks and therefore variable density, and therefore employed kernel based Gaussian [1] or B-Spline [3] scattered data interpolation to robustly estimate values onto a regular lattice, as illustrated in Figure 2. These interpolation methods were later adapted to make better use of the complementary data resolution in different axes [4]. More recently methods aimed specifically at making use of high numbers of multi-slice datasets have explored the use of super-resolution reconstruction techniques [5,6].

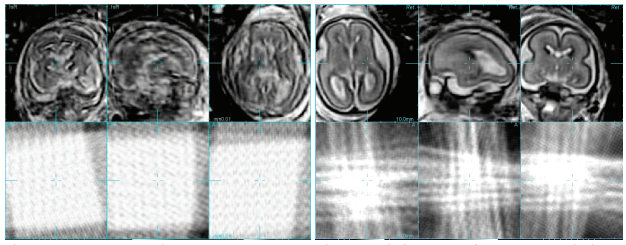

Figure 2: Example 3D reconstructions of from a fast T2 weighted multi-slice MRI study of the moving human fetal brain before (left) and after (right) slice motion correction, in a case of more severe fetal motion. The lower rows show corresponding slice voxel density supporting the reconstruction. Reconstruction onto a regular voxel lattice was achieved in this case using a simple distance weighted scattered data interpolation, but provides robustness to the large variations in data density that arise because of fetal head motions during the study.

A second important issues relating to fusion of the data is that of MRI intensity bias arising from the spatially varying imaging coil sensitivity over the maternal abdomen. Because the fetus moves within the coil profile, the same anatomy can be imaged twice but appear with different intensity bias patterns. These differences induce artifacts in the final fused data. As a result, the problem of resolving inconsistencies in intensity bias must be addressed in cases of significant fetal head motion. Extending slice motion estimation approaches, techniques have been developed to provide relative bias estimation between sets of intersecting slice stacks [7] that can significantly reduce bias related artifacts and improve contrast between developing tissue zones. Combining these processing algorithms, practical software tools [9] have begun to emerge that allow a user to quickly combine multiple clinical multi-slice studies exported as DICOM format, into a single high-resolution volumetric dataset.

4. ATLAS CONSTRUCTION AND TISSUE SEGMENTATION

The use of age-specific templates, in children and neonates has been shown to improve automated tissue segmentation significantly. Because the speed of changes in the developing brain occur on the order of weeks or days and because the age of a fetus is relatively uncertain, an atlas aimed at a specific gestational age is both difficult to construct and of limited use in the analysis of new studies. Thus, the focus of research has been to develop continuous or parametric atlases of the fetus, explicitly modeling changes in shape, size, MRI contrast, and tissue probability at every point in the fetal brain [10]. This modeling enables the synthesis, for any given gestational age, of a specialized MRI template with representative tissue contrast and tissue probabilities.

Given the difficulty and ethical considerations of carrying out repeat imaging on the same expectant mother, this atlas cannot be constructed directly from repeated longitudinal imaging as in adult analysis, but is naturally constructed from many different fetuses, each scanned at different ages. However, this allows the atlas to form a mean growth trajectory that is representative of a population and also encodes the natural variation of development together with uncertainties in the estimation of fetal age. Such an approach, when used to provide subject specific priors to a conventional EM tissue labeling, has been shown to significantly improve the ability to extract transient tissue structures such as the germinal matrix, as illustrated in Figure 3.

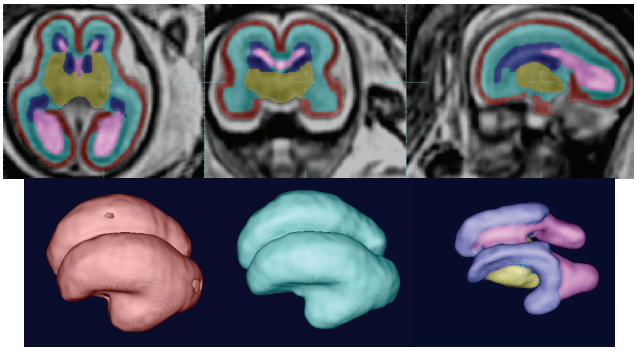

Figure 3: Example automated Spatio-temporal atlas based segmentation of the developing tissues zones from 3D motion corrected MRI (top tow). Lower row shows 3D rendering of cortical plate (left), Sub-plate (middle) and

combined germinal matrix, ventricle and deep grey matter (right).

5. SHAPE ANALYSIS: MAPPING BRAIN GROWTH

One of the key motivations for the study of fetal MRI is its promise of revealing a clearer picture of early normal human brain growth, which is impossible to acquire from postmortem or animal studies. Many tools have been developed to probe adult brain shape and these have begun to be adapted to study the rapid changes underway in fetal brain anatomy. At a local level, the growth of a sulcated neonatal brain from a smooth fetal brain requires a complex series of local tissue volume changes to form an individually unique cortical folding pattern. Tensor-based morphometry (TBM) uses accurate spatial normalization of brain anatomy into a common coordinate frame to study patterns of size differences in local anatomy. Such an approach requires modification to be used in the early developing brain because of the dramatic changes in tissue contrast occurring over short timescales. Direct deformable registration of fetal MRI of ages varying by only a few weeks can induce artifactual deformations as image warping attempts to account for the presence of inconsistent tissue types when mapping from one fetal age to another. By first employing automated age specific tissue segmentation to extract age-consistent tissue boundaries for alignment, recent work has shown that it is possible to apply groupwize alignment to bring fetuses of different gestational ages into accurate alignment for TBM studies [11]. As a result it has been shown to be possible to successfully to map patterns of the spatial variation of tissue growth rate as sulci begin to form.

An alternative quantitation of brain growth emerges from the study of brain surface curvature. The application of this type of analysis to fetal brain MRI is only possible without accurate 3D reconstruction and tissue segmentation to extract a representative tessellation of tissue surfaces. The application of automated age specific segmentation has enabled this approach to the study of the boundary between the cortical plate and sub-plate [12], allowing the construction of the first 4D map of the time and location of active folding in early sulcal formation. In addition, the use of symmetric groupwise registration has allowed the accurate study of the emergence of the very earliest signs of asymmetry in the brain that may reflect to functional specializations in the cortex.

6. DISCUSSION OF FUTURE DIRECTIONS

The majority of studies so far have focused on conventional structural imaging, and the use of T2W MRI data of fetal brain tissues. The use different contrasts such as T1W, susceptibility weighted and diffusion weighted data promises to reveal much more information about the subtle changes in tissues zones that occur during the period of cell migration from the germinal matrix to form the cortical plate. Diffusion weighted imaging in particular is of significant interest because of its ability to reveal the presence and formation of white matter connectivity that underlies sulcal formation. Early attempts at adapting motion correction techniques to the more challenging DTI problem [14,15] are promising, but are not yet at the stage of more general application to larger studies.

The new field of human fetal brain mapping [15] is just beginning to emerge as new tools provide a route to studying larger scale populations of fetuses. Critically, this will allow the construction of much more accurate models of normal brain growth that precisely map the location and time of developmental events in 4 dimensions and reveal how these events, such as sulcal formation, can vary in time and space in a healthy pregnancy. In the future, such maps will allow us to examine how factors such as diet, stress, substance abuse or genes can perturb this trajectory away from normal variation, and hopefully better understand how those changes relate to functional and cognitive outcomes after birth.

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