Poster #3973

Developmental Brain ADC Atlas Creation from Clinical Images

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Introduction

-Development of age-specific brain atlases for diffusion-weighted images would significantly enhance clinicians' ability to consistently detect subtle abnormalities.

- Here we test the ability to leverage a large number of MRIs within the clinical PACS to create age-specific normative brain atlases.

- The Apparent Diffusion Coefficient (ADC) provides a measure of water content in the brain, and thus a surrogate marker for myelin development [1].

-Myelination undergoes dramatic changes from birth to 6 yrs of age and thus ADC can track brain development over time within and potentially across subjects [2].

- Prior developmental brain atlases have focused primarily on T1 or T2 showing volumetric changes with age [3,4], with only one including an FA atlas and ADC values [5]. Also, most cover narrow age ranges (29-44 gestational weeks [5], 0-2 year old [3], 37-53 post-conceptional weeks, or >4 years old [4]). Our proposed atlases densely sample 0-6 years.

Methods

Image Retrieval

-The Informatics for Integrating Biology and the Bedside (i2b2, www.i2b2.org) software suite enables the repurposing of healthcare data for clinical research.

-A recently developed software plug-in, the Medical Imaging Informatics Bench to Bedside (mi2b2, www.mi2b2.org) workbench, allows clinical images to be retrieved from institutional Picture Archiving and Communication System (PACS) databases by IRB-approved investigators.

-At Partners HealthCare institutions, the Research Patient Data Registry (RPDR) serves as our institutional instance and the i2b2 precursor;

-The mi2b2 workbench and the RPDR precursor together enable the repurposing of electronic medical records (EMRs) and medical images for research;

-The detailed data request submitted to RPDR returned the EMRs of 4745 pediatric patients with a head MRI. From them 1600 patients were <6yr at the time of scan, with potentially normative brain MRI acquired after 2006.

- The collected ADC maps went through the following inspection to keep the "normative" subjects only.

Defining "Normative" Cohort

-A licensed pediatrician manually reviewed the radiology reports and medical records to remove patients having diagnosis of any neuropsychiatric disease with known structural changes (e.g. stroke, trauma, HIV, CNS cancer etc).

- Also manually reviewed the ADC maps of subjects to keep the ones with high image qualities and visually absence of any structural-affecting pathologies.

- As a result, we have included a cohort of clinical ADC maps from 152 normative subjects who had scans during 2006-2013 and were free of any major neuropsychiatric diseases at the time of the scan.

- The included ADC maps have typical image sizes of 128x128x64 voxels and voxel sizes of 2.0x2.0x2.0 mm^3, and were all acquired from a 3T Siemens Trio MRI scanner with diffusion parameter b=1000 s/mm^2.

Age Stratification

The 152 subjects were divided into 15 age groups, more densely into weeks or months in the first 2 years to capture the fast myelination and neurodevelopment, and then yearly afterwards (8 subjects in wk0, 8 in wk1, 7 in wk2, 9 in wk3, 11 in mon1, 12 in mon2, 10 in mon3, 7 in mon4, 9 in mon5, 11 in yr0.5-1, 12 in yr1-2, 13 in yr2-3, 12 in yr3-4, 13 in yr4-5 and 10 in yr5-6).

Automated Image Analysis

Brain Extraction

-To remove extra-meningial tissues and non-brain structures (skull, eyes, nose, neck, etc), a fully-automated multi-atlas skull-stripping algorithm, originally developed for structural images of adults, has been adapted for the ADC maps of children 0-6 years old.
- Specifically, our prior knowledge came from a set of 15 ADC maps with manual annotations of brain masks.

- An extensively validated, publicly-available deformable registration tool, DRAMMS [7] (http://www.cbica.upenn.edu/sbia/software/dramms), were used to non-linearly propagate the brain masks from the 15 manually-annotated ADC maps to the subject ADC map (computations run on an SGE cluster);

- Automated selection out of 15 annotated ADC maps by computing, ranking and thresholding the correlation coefficients of the warped and the target ADC maps, followed by STAPLE-based label fusion, leading to the final brain mask in the target ADC map (see Figure 1 for some representative results).

- Visual inspections of the obtained brain masks demonstrated close agreements with expert inference; more detail of the algorithm and quantitative validation results pending a journal publication.

Atlas Construction

- An atlas was constructed for each stratified age group;
- A unbiased atlas construction strategy was used [8], extending the pair-wise deformable registration DRAMMS [7] into a population-wise registration, without the need for the explicit and bias-inducing selection of any individual's image as the template (software available at http://www.cbica.upenn.edu/sbia/software/dramms);
- The constructed atlas reflects the average geometry and the average ADC intensity in a specific age group (see Figure 2 for example).

Results

Typical Brain Extraction Results in ADC Maps for 0-6 yo Children

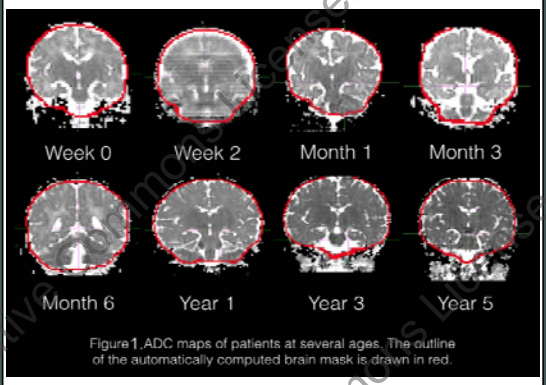

Figure 1. ADC maps of patients at several ages. The outline of the automatically computed brain mask is drawn in red.

Atlas Construction to Represent Mean Shape and Mean Intensity in a Typical Age Group

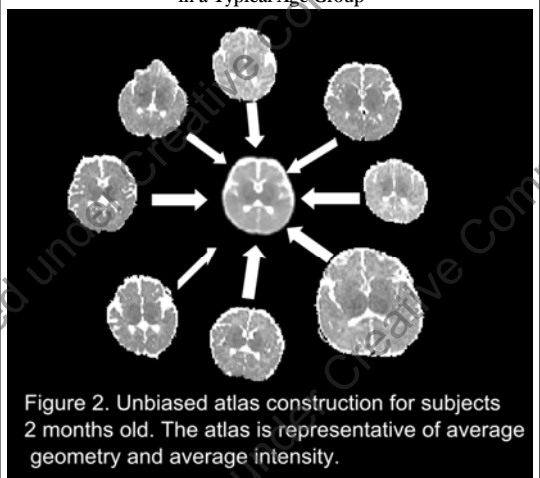

Figure 2. Unbiased atlas construction for subjects 2 months old. The atlas is representative of average geometry and average intensity.

Age-Specific ADC Atlases to Visualize Development

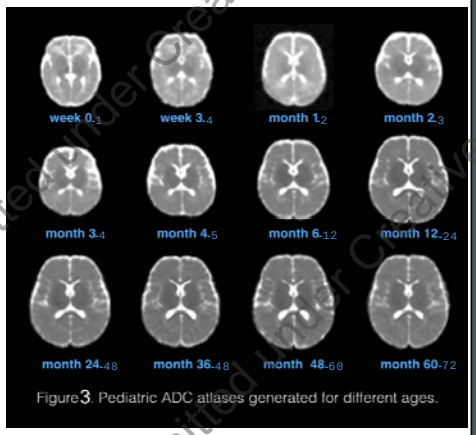

Figure 3. Pediatric ADC atlases generated for different ages.

Discussions and Future Work

- The mi2b2 workbench can query and access valuable large numbers of PACS data.

- In this pilot study, we established a pipeline to construct atlases densely sampling 0-6 yr age range. The atlases display ADC values and visualize early neuro-development .
-The brain develops fast from birth to 2 years, and then develops at a relatively slower pace till 6 years;
- Visual inspections found that the average ADC values decrease with age (as the atlases become overall darker), revealing the myelination process in early life, which agrees with known clinical knowledge;

- Our future work will be
1) to collect larger number of structural and diffusion data using the mi2b2 workbench;
2) to better understand the differences in the constructed atlases from data acquired at different scanners and in different institutions;
3) to quantitatively study ADC trends for whole brain, various tissue types and structures, and
4) to quantify the volumetric and myelination-related ADC value changes in this age span.

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Acknowledgements

We gratefully acknowledge support from NIH 1 UL1 RR 025758-01, 1 U24 RR 025736-01 R01 EB014947-01 and Partners HealthCare System.