Evaluation of White Matter in Preterm Infants With Fetal Growth Restriction


Departments of Radiology and Psychiatry, Children's Hospital Boston. September 24, 2009.
Road Map

• Introduction
• Material and Methods
  • DTI Atlas for Group Comparison
  • Towards a Robust Group Comparison
• Results
• Conclusion
Road Map

- Introduction
- Material and Methods
  - DTI Atlas for Group Comparison
  - Towards a Robust Group Comparison
- Results
- Conclusion
Introduction

• Fetal Growth Restriction (FGR)
  • Weight below 10th percentile of normal weight for gestational age
  • Often caused by placental function disruption
  • Often linked to prematurity
  • Occurs during accelerated brain development

• Prematurity and FGR may lead to disabilities
  • Motor skills, cognitive function
  • Lower neurodevelopmental score

• Early care in the Newborn Intensive Care Unit (NICU) crucial to FGR infants development
The NIDCAP Program

• NIDCAP = Newborn Individualized Development Care and Assessment Program

• Objectives
  • Better neurodevelopment of FGR preterm-born children
  • Support brain structure maturation

• How
  • Minimize environmental stress for the baby
  • Observation and evaluation of the infant’s behavior
  • Adaptation of care to get closer to the intra-uterine environment
Previous Study on NIDCAP

• Randomized study on 30 AGA preterm-born children
  • Two groups: 14 in standard care / 16 in NIDCAP program
  • Influence of NIDCAP on brain development

• Comparison at two time points
  • Do differences exist? Are they maintained at a later stage?
  • 2 weeks: comparison of DTI derived scalar parameters
  • 9 months: behavioral assessment (mental / motor scale)

• Better maturation at 2 weeks (PLIC on left side)
  • Consistent with brain functional differences
  • Lasting effects at 9 months behavioral assessment

Challenges

- Problems
  - Scalar measures: loss of information
  - Predefined regions of interest, manually drawn
  - Movement artifacts, distortion in the images

- Objective: study of NIDCAP influence on white matter
  - Local and automatic evaluation over the whole brain
  - Use the whole tensor and be robust to image artifacts

- Our approach
  - Construction of an age adapted common coordinate system
  - Robust comparison of populations
Road Map

- Introduction
- Material and Methods
  - DTI Atlas for Group Comparison
  - Towards a Robust Group Comparison
- Results
- Conclusion
DTI Atlas for Group Comparison

- Goal: Compare populations to detect groupwise differences

Controls Group

NIDCAP Group
DTI Atlas for Group Comparison

- Goal: Compare populations to detect groupwise differences

Controls Group

Atlas = Common coordinate system

NIDCAP Group
Average Image Construction

• Challenges
  • Very early acquisitions (42 weeks PMA)
  • Specific anatomy → External adult reference standard not adapted

• Our approach
  • Build a geometrically unbiased DTI atlas from the populations

• Atlas construction method [Guimond et al., 2000]
  • Iteration over two steps
    • Registration of all DT images on the current reference
    • Build a new reference (from images and transformations)

Road Map

• Introduction
• Material and Methods
  • DTI Atlas for Group Comparison
  • Towards a Robust Group Comparison
• Results
• Conclusion
DTI Group Comparison

- Objective: Detect groupwise differences between populations
- Cramers test [Whitcher et al., 2007]
  - Use of the full tensor: Log-Euclidean distance on tensors
  - Permutation testing: No assumption on a specific PDF for the statistic
- Output: voxel-wise probability of the existence of differences

DTI Group Comparison

- **Objective:** Detect groupwise differences between populations
- **Cramers test [Whitcher et al., 2007]**
  - Use of the full tensor: Log-Euclidean distance on tensors
  - Permutation testing: No assumption on a specific PDF for the statistic

- **Output:** voxel-wise probability of the existence of differences

DTI Group Comparison

- Objective: Detect groupwise differences between populations
- Cramers test [Whitcher et al., 2007]
  - Use of the full tensor: Log-Euclidean distance on tensors
  - Permutation testing: No assumption on a specific PDF for the statistic

- Output: voxel-wise probability of the existence of differences

Robust DTI Comparison: Continuous STAPLE

• Challenges: several sources of bias in DTI comparison
  • Acquisition problems (DTI distortion, movement artifacts)
  • Registration errors

→ Need for a robust group comparison

• Continuous STAPLE [Commowick et al., 2009]
  • Input: vector images (e.g. tensors in the Log-Euclidean space)
  • EM algorithm to compute at the same time
    – Typical tensor image underlying the dataset
    – Parameters for each image: offset to the typical image and covariance matrix

Local Computations for Continuous STAPLE

• Great interest of continuous STAPLE
  • Produce a robust estimation of typical tensor image
  • Parameters characterize bias in the individual images
  • Adequacy parameters may be used to compare images

• Problem: parameters are computed over the whole image
  • Need for local estimates for voxelwise comparison

• Proposed solution
  • Run STAPLE on a block around each voxel
  • Keep the parameters and reference value at center voxel
  • Allows voxelwise parameters computation
Towards a Robust Group Comparison

• Use of local continuous STAPLE
  • Parameters should be different between groups
  • Take into account erroneous tensors

• Advantage of the Cramers test
  • May be used for any data as long as a distance can be defined

• Integrating local continuous STAPLE
  • Parameters represent multivariate Gaussians
  • Distance between multivariate Gaussians
    – [Calvo & Oller, 1991]: Analytic solution of the geodesic

Road Map

- Introduction
- Material and Methods
  - DTI Atlas for Group Comparison
  - Towards a Robust Group Comparison
- Results
- Conclusion
FGR Database

- DTI Comparison at time point 2 (~ 42 weeks PMA)
  - Structural (T1, T2) acquisition (slice thickness 1.3mm)
  - DTI acquisition (between 6 and 35 directions, slice thickness 2.5mm)
  - Two groups
    - Standard care (11 infants)
    - NIDCAP group (9 infants)
Coordinate System Construction Results

- **DTI Atlas**
  - Created from 20 DTI
    - From the two groups together

- **Comparison**
  - Classical DTI average
  - Typical DTI Image obtained from STAPLE

→ Illustrates STAPLE ability to handle errors

Average coordinate system anatomy

Average DTI Image
Coordinate System Construction Results

- **DTI Atlas**
  - Created from 20 DTI
    - From the two groups together

- **Comparison**
  - Classical DTI average
  - Typical DTI Image obtained from STAPLE

- Illustrates STAPLE ability to handle errors

**Average coordinate system anatomy**

**STAPLE Typical DTI Image**
Group Differences in White Matter Structure

- Evaluation of WM differences
  - Differences in PLIC on both sides
  - Confirms results obtained in previous studies
  - Better detection power: differences detected on both sides

Regions different between controls and NIDCAP (95% confidence level)
Characterization of Detected Differences

- Study of DTI derived scalar parameters
  - FA and MD values
  - ANOVA on average values
  - On detected regions

- Results
  - No difference in FA values
  - Significant difference for MD
    - Decrease in NIDCAP group

MD ANOVA Analysis
Discussion

• Period of accelerated brain maturation
  • Premyelination period
  • Particularly in central nervous system

• Significant MD decrease in PLIC
  • Less water molecules → more structure
  • Increased premyelination in NIDCAP group

• MD decrease associated to better outcome [Krishnan, 2007]
  • Results suggest a positive impact of NIDCAP on brain development
  • Potential better outcome for the infants

Road Map

- Introduction
- Material and Methods
  - DTI Atlas for Group Comparison
  - Towards a Robust Group Comparison
- Results
- Conclusion
Conclusion

• New algorithm for robust group comparison
  • DTI atlas construction
    – Adapted to the study of very young children
  • Local reference standard construction (continuous STAPLE)
    – Robust to bias sources
    – Using the whole tensor information
  • Integration of STAPLE parameters in a statistical test

• Study of white matter development in preterm FGR infants
  • Significant difference in PLIC regions on both sides
    – Decrease in MD values → better maturation in NIDCAP group
  • Potential positive influence of NIDCAP
Perspectives

• Take into account the temporal component
  • Study at different time points
    – Are differences present before intervention?
    – How exactly is NIDCAP influencing the development?

• Complementary studies from other modalities
  • Comparison of structures volumes extracted from T1
  • Gyrification indexes, cortical thickness
  • Tractography studies
    – Whole brain
    – Regions with differences