International Symposium on the FETAL BRAIN

September 15-16, 2016

Children's National
Fetal Medicine Institute
Part of the Children's National Health System
Harnessing the Power of Quantitative MRI to Advance Understanding of the Fetal Brain

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I have no financial relationship or off-label usage to disclose.
Fetal Origins of Lifelong Disorders

WHAT HAPPENS IN THE Womb SHAPES THE LIFESPAN

Autism
Heart disease
Hypertension
Attention deficit disorder
Schizophrenia
Diabetes
Stroke
Cerebral palsy
Non-Invasive Fetal Monitoring & Imaging
Fail to pick up ‘signals’ of distress
Rescue & ‘damage control’
Prevention will always beat cure
PROTECT the developing brain
Challenges in Fetal MRI

- Fetal and maternal motion
- High water content of the immature brain
- Decreased tissue contrast
- Decreased spatial resolution
Fetal Brain Tissue Segmentation Pipeline

Gholipour et al., Med Image Comput 2014
Automated Fetal Brain Tissue Segmentation

Gholipour et al., Med Image Comput 2014
Healthy Pregnancies

>300 pregnancies
Brain Volume [CC] vs Gestational Age [wks]

- 95th Percentile
- 90th Percentile
- 75th Percentile
- 25th Percentile
- 10th Percentile
- 5th Percentile

Advanced Fetal Brain Diagnostics - Clinical Excellence
Normative Fetal CSF Reference Curves

Andescavage et al., Under Review
Isolated Mild Ventriculomegaly

Atrial Diameter >10

Scott et al., Human Brain Mapping 2013
In vivo Fetal Subplate Growth Patterns

*Subplate*  
*Cortical Plate*  
*Intermediate Zone*  

*T2 contrast*
Unsupervised fetal cortical parcellation

Cortical signature computation:
1) Local gyrification index
2) Cortical thickness
3) Cortical depth

Dahdouh & Limperopoulos, SPIE 2016
Defining Individual Cortical ‘Signatures’
Fetal Brain Connectivity

Fornix

Cortico-spinal corticopontine tracks

Mitter et al PLOS one 2015
Fetal Brain Connectivity

Resting-state fMRI measures fetal cortical activity at rest using BOLD

Quantify emerging functional networks in 34 week fetus
**Fetal Brain Metabolism**

Understanding the role of the placenta in supporting the fetal brain
In Vivo Placental Structural Features Extraction

Placental Thickness

Textural Regularity

Global Entropy

Fetal Entropy

Maternal Entropy
Maternal Hyperoxia BOLD fMRI Studies

You et al., JMRI 2016
Fetal Brain and Placenta Pre-Processing Pipelines

**Fetal brain**
- Motion correction
- ROI averaging
- Band-pass filtering
- Compute Phase Sync

**Placenta**
- ROIsplitting
- Motion correction
- ROI averaging
- Band-pass filtering

Raw EPI → ROI splitting → Defining ROI masks
Placental Perfusion MRI Techniques

Non-invasive imaging by labeling water molecules in the blood (ASL)

Zun et al., ISMRM 2016
Placental Perfusion using VS-ASL

Zun et al., ISMRM 2016
In Vivo Placental Diffusion Imaging

- DWI signals
  - Bias Field correction
  - Non-rigid intra/inter registration
    - QA
      - Parameter estimation
      - Reject
      - QA
  - ADC
  - IVIM
  - DKI
- Fetal part
- Maternal part
- Manual cluster merging
- Hierarchical clustering
- Self-organizing Map (SOM)
- Self-organizing maps and Hierarchical clusters

T2
ADC
K
How do we Harness the Power of this Technology?
Hazards of premature extra-uterine life
Impaired 3rd Trimester Brain Growth in Preterm Infants

Intensive care *helps* vs *harms* the developing brain
Advanced Fetal MRI: Impact in NICU

- Increasing ability to identify the effects of an unsupportive or hostile intrauterine environment
- Advancing understanding of discrepancies between *in utero* and *ex utero* development during third trimester
- Translating this into management of the premature infant *in utero* and *ex utero*
  - unfavorable intrauterine factors trigger both premature delivery *and* brain injury?
  - intrauterine brain insults trigger premature delivery?
  - immaturity compromise acute transition?
Congenital Heart Defects
# 1 Birth Defect 1 in 100 Babies
Brain Growth in Fetuses with CHD and Controls

![Graph showing brain growth in fetuses with CHD and controls over gestational age.](image)
Differences in Cortical Depth in HLHS vs. Control Fetuses

Independent predictors
- Cerebral placental ratio <1.0
- Absent antegrade arch flow

Clouchoux et al., Cerebral Cortex, 2012
Altered Functional Brain Connectivity in CHD Fetuses

Decreased Functional Connectivity
Association Regions = Higher-order integrative cortical areas
Paralimbic Regions = Emotional processing, behavior, memory

Cruz et al., ASNR 2016
Placental Volume Predicts Birthweight in CHD Fetuses

*Impaired placental growth in CHD is associated with GA and birth weight at delivery

Andescavage et al. Placenta 2015
Maternal Hyperoxia BOLD fMRI Studies

You et al., JMRI 2016
Altered Brain BOLD Response in CHD Fetuses

Fetal Brain

Percent Signal Change in the Brain

- Control
- CHD

Early hyperoxia (HO)
Late HO
Early return normoxia (NO)
Late return NO

p=0.042

You et al., AHA 2015

Placenta

Percent Signal Change in the Placenta

- Control
- CHD

Beginning hyperoxia (HO)
Late HO
Early return normoxia (NO)
Late return NO
Altered Brain BOLD Response in HLHS Fetuses

- **Percent Signal Change in the Brain**
  - **Control**, **2v**, **1v**

- **Early hyperoxia (HO)**
- **Late HO**
- **Early return normoxia (NO)**
- **Late return NO**

- **p = 0.01**
- **p = 0.03**

You et al., AHA 2015
Cerebral lactate is present in 24% CHD fetuses.
Should this Fetus Go Through Labor?

Frequency (ppm)

Amplitude
Summary and Future Directions

Safeguard the development brain

- Providing **early biomarkers** of brain/placenta failure
- Assessing and monitoring **periods of risk**
- Assisting in determining the optimal **time of delivery**
- Assisting in determining the optimal **mode of delivery**
- Anticipating level of care during the **transition** (delivery) period
- Enormous potential for advancing the field of **neuroprotection**
  - Selecting & monitoring candidates for **prenatal clinical trials**
  - Treatment guidance and therapeutic response assessment
Looking Ahead

- Elevate the standard of care from damage control to prevention
- Fetal **precision** imaging to capture most subtle but pervasive indicators of abnormal brain development
- Fetal brain **plasticity** and **resilience**
- Rapid automation of qMRI tools to support **real-time assessment** of fetal brain health
Team Fetal

“Stronger Is: Turning discovery into transformative care, one baby at a time”.

[Image of a group of people]