DWI assessment of ischemic changes in the fetal brain

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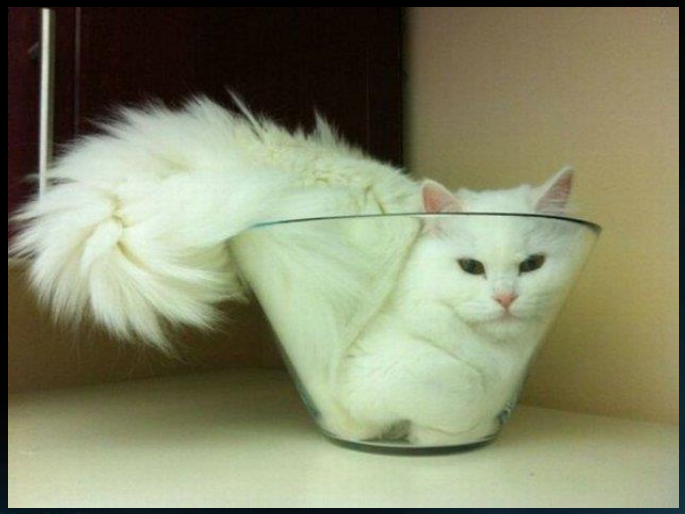
Diffusion

Molecular diffusion, or Brownian motion, was first formally described by Einstein.

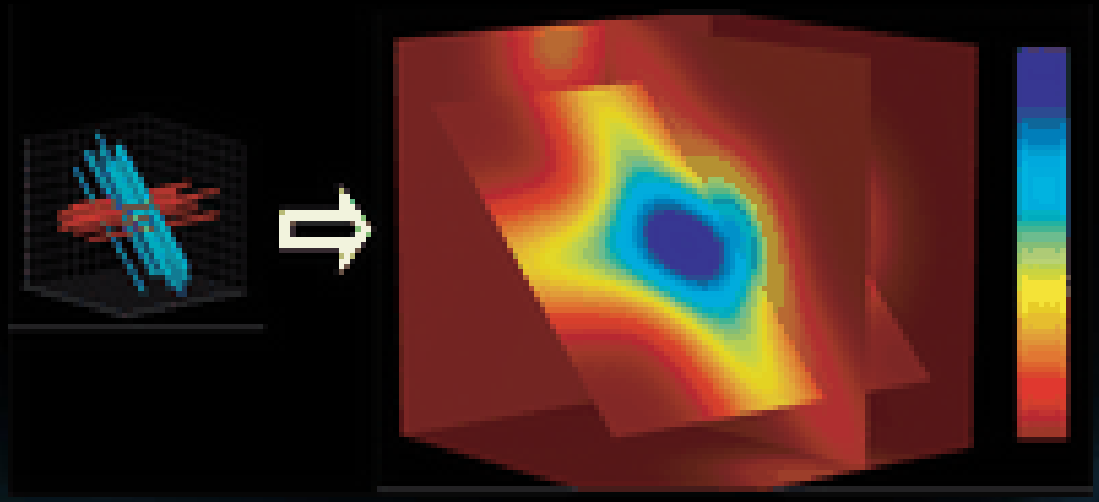
In a glass of water, the motion of the water molecules is completely random and is limited only by the boundaries of the container.



In a tubular structure the motion is directed by the boundaries (pipe, axon)

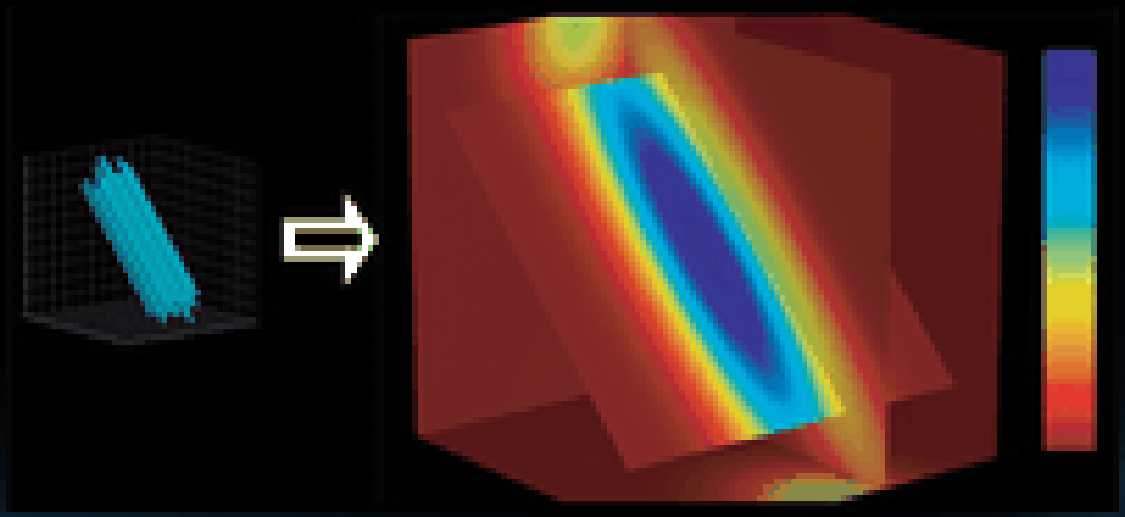
Direction of Diffusion

In a voxel that contains spherical cells or randomly oriented tubular structures that intersect, the motion of the water molecules is random and is not constricted to one direction = Isotropic.



Direction of Diffusion

In a voxel that contains longitudinal cells or tubular structures without intersections, such as axons , the motion of the water molecules is confined by the adjacent elements, and becomes directional = Anisotropic.

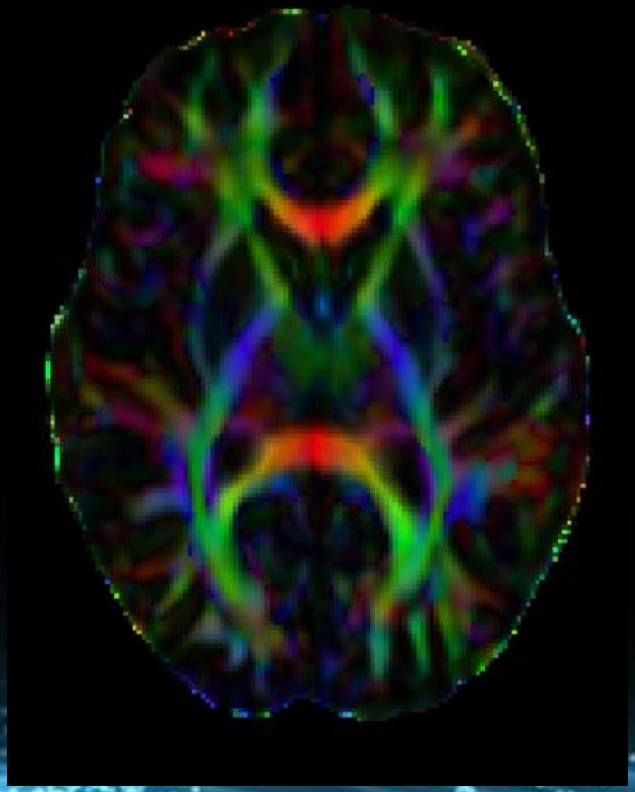


Diffusion Tensor Imaging (DTI)

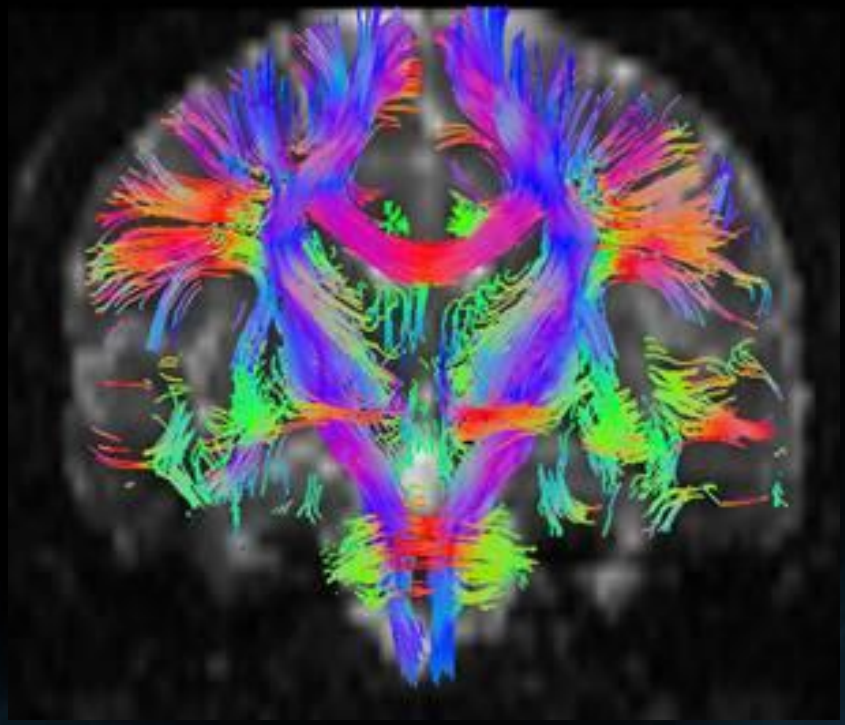
For every brain position an orientation distribution function is plotted to characterize the local diffusion probability density function → tracking the bundles of axons in the brain in 2D or 3D

Diffusion Tensor Imaging (DTI)

DTI color map



Tractography

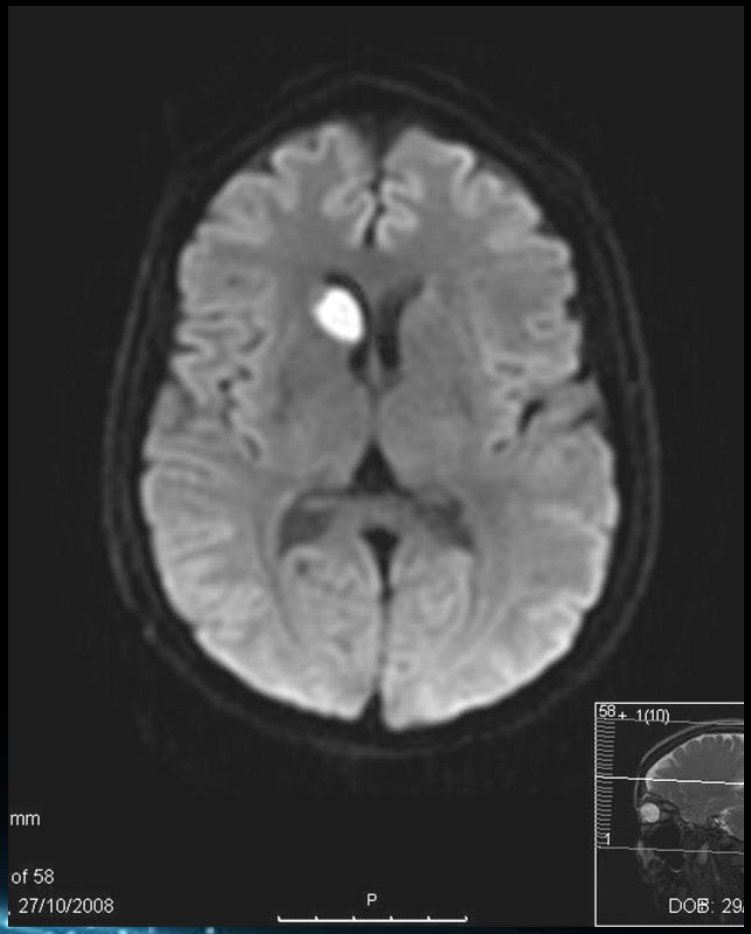


Diffusion Weighted Imaging (DWI)

In DWI constructed images, each image voxel has an image intensity that reflects a single best measurement of the rate of water diffusion at that location.

This measurement is more sensitive to early changes after an injury than more traditional MRI measurements.

Acute Infarct - DWI



Apparent Diffusion Coefficient (ADC)

ADC is the diffusion index, in which DWI results are displayed – it's units are mm^2/s, as it represents spatial motion.

Low ADC value ⟶ high level of organization

High ADC value ⟶ low level of organization

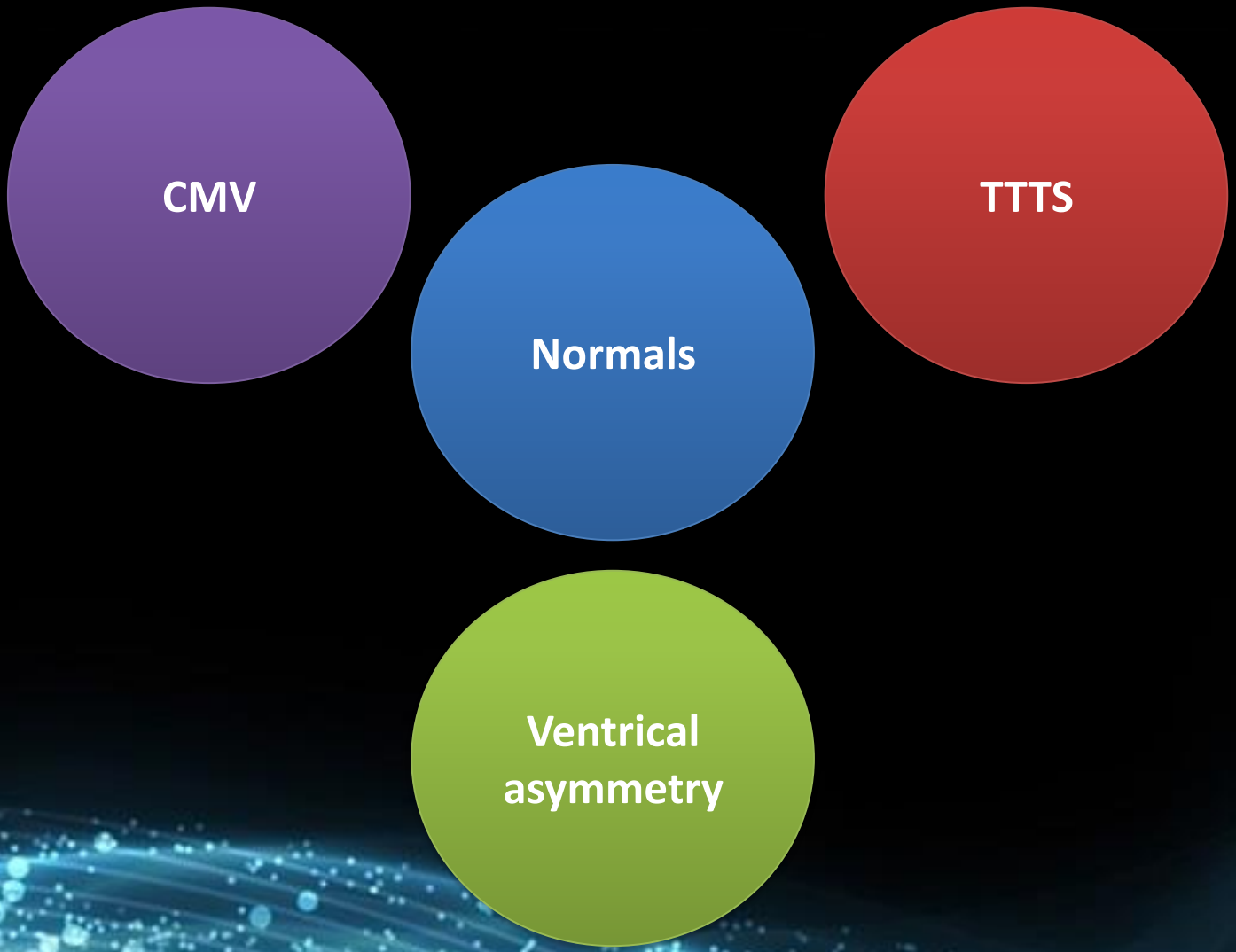
Fetal MRI

- The use of fetal MR imaging for the in utero evaluation of pathological conditions of the CNS is widely accepted as an adjunct to fetal ultrasonography studies.
- Magnetic resonance imaging is thought to characterize CNS anomalies better, and to provide a more exact diagnosis and accurate prognosis

Peruzzi P, Corbitt RJ, Raffel C. Magnetic resonance imaging versus ultrasonography for the in utero evaluation of central nervous system anomalies. J Neurosurg Pediatr. 2010 Oct;6(4):340-5

So, what have we been up to?

Studies

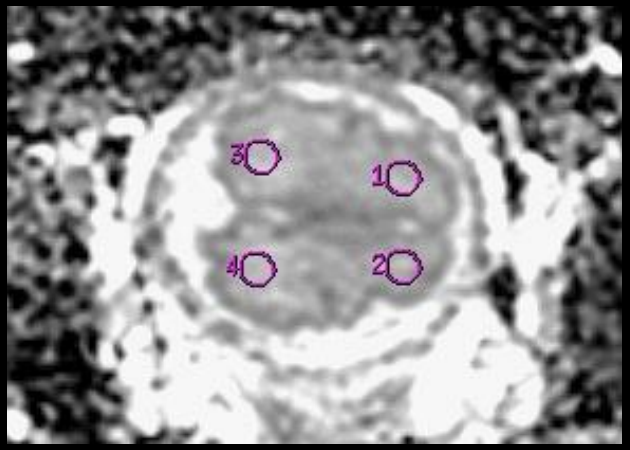


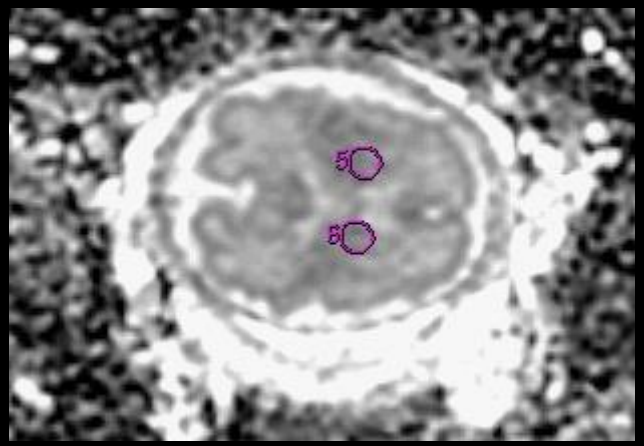
Methods

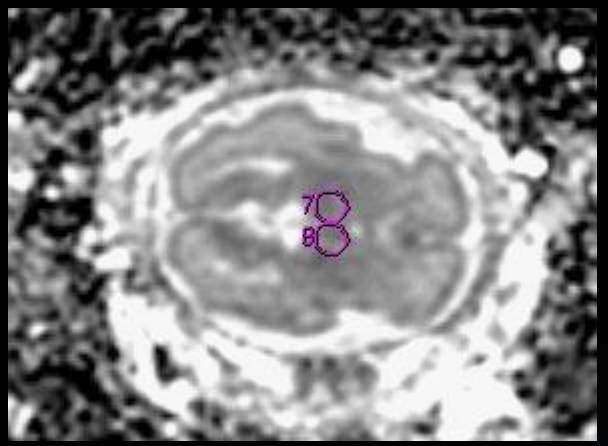
ADC measurement in 8 Regions of interest (ROIs) in each of the fetal brains (frontal WM, parietal WM, temporal WM, occipital WM, basal ganglia, thalamus, cerebellum and pons).

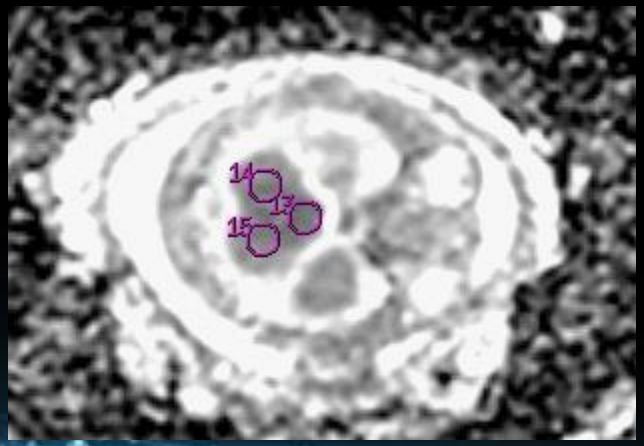
Plotting the changes of it in relation to the gestational age.

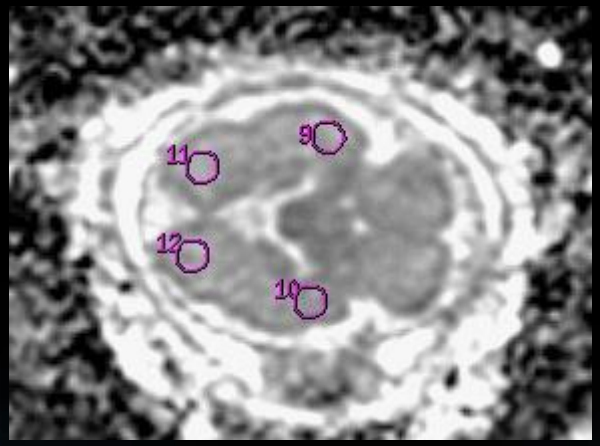
ROIs











Normals

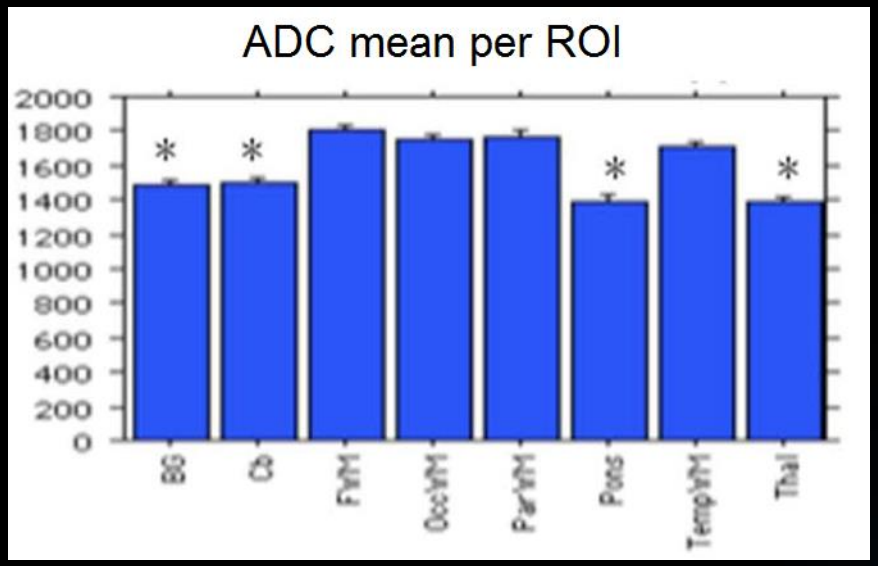
Normal fetuses - cohort

- 46 scans of non-sedated 3rd trimester (26-33 weeks) singleton fetuses, with normal or questionably abnormal results on ultrasound and normal structural MR imaging results.

Normals

Normal fetuses - results

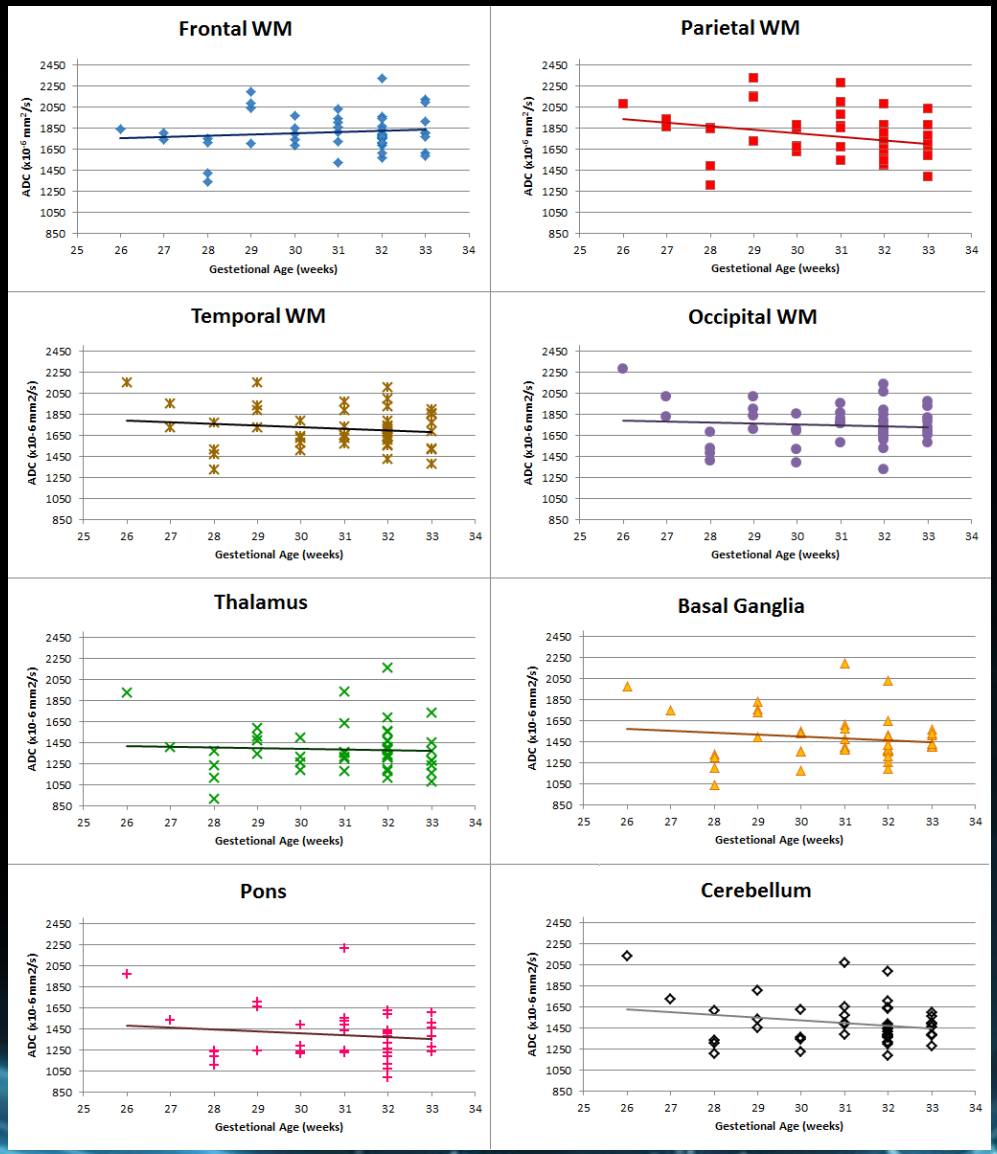
- Maximal ADC values in the white matter, with significantly ($p<0.05$) lower values in basal ganglia and cerebellum and the lowest values in thalamus and pons



Normals

Normal fetuses - results

- Relatively stable ADC values.
- Trend towards a decrease (except in Frontal ROI)



TTTS

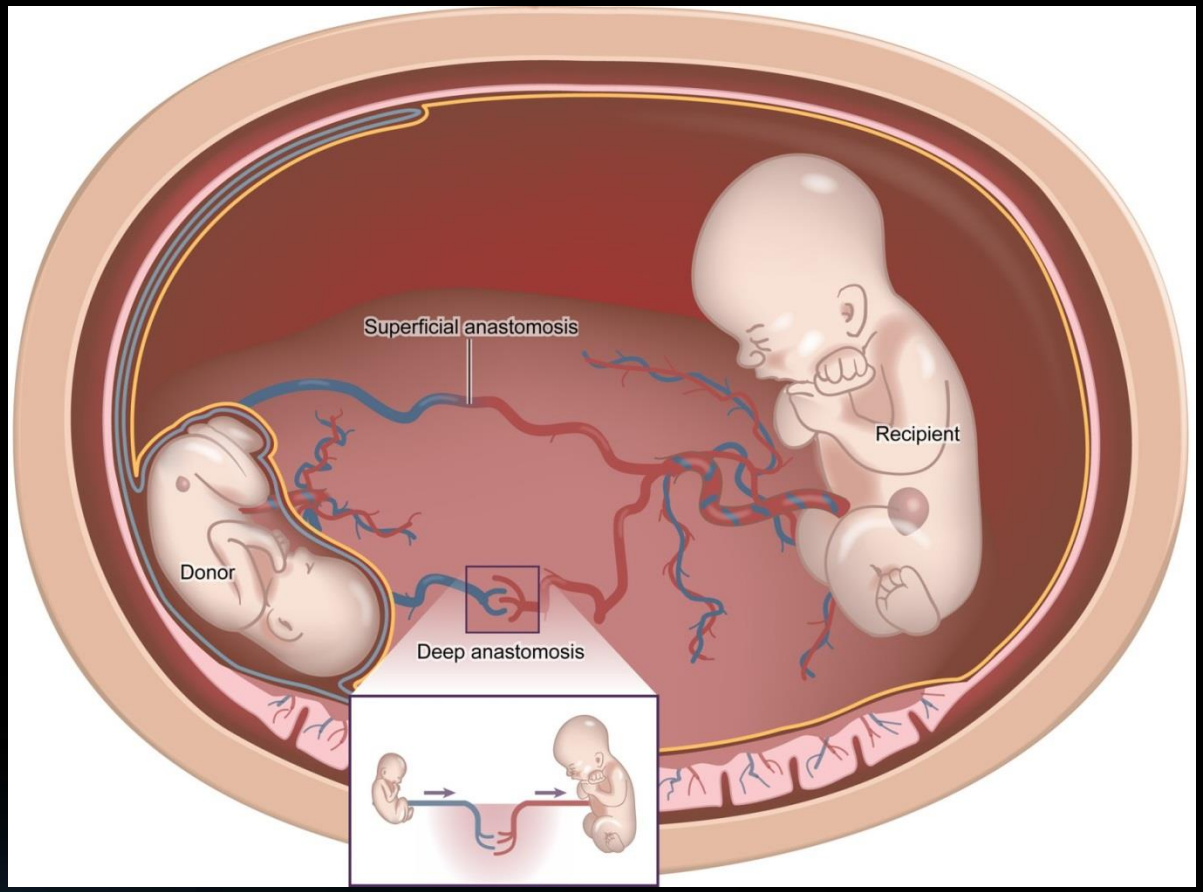
TTTS – what is it?

- Twin-to-Twin Transfusion Syndrome is a condition in which the blood flow through the vascular anastomoses between two identical twins is unequal.

- This creates a situation where the ‘Donor twin’ is large and hyperperfused and the ‘Recipient twin’ is small and hypoperfused.

TTTS

TTTS – what is it?



TTTS

Brain injury in TTTS

- The exact pathogenesis of cerebral injury in TTTS is not fully understood but it appears that donors and recipients are at equal risk for cerebral injury
- If untreated, this condition ends in pregnancy loss by 26 weeks in over 90% of cases.
- Fetoscopic laser surgery caused marked decrease in neonatal morbidity, but neurocognitive morbidity is still a major problem.

TTTS

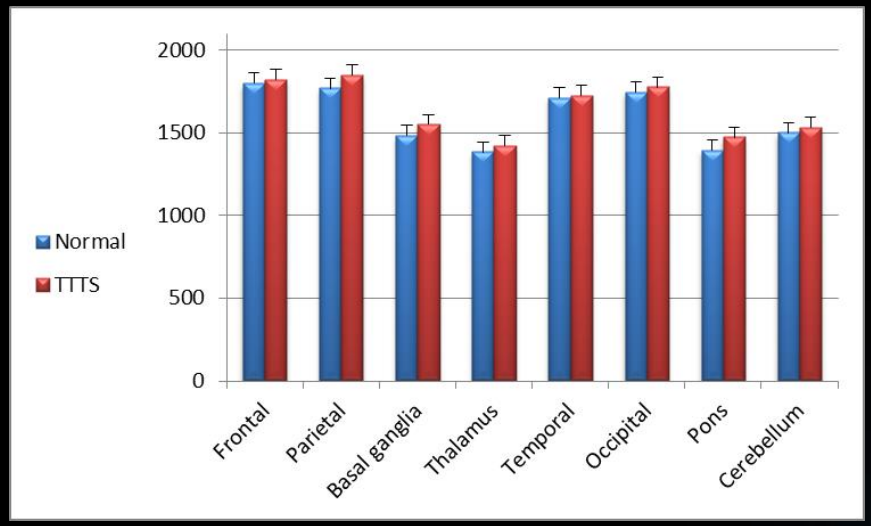
TTTS fetuses - cohort

- 53 diagnostic scans of non-sedated 3rd trimester (26-33 weeks) MCBA twins with a confirmed diagnosis of TTTS.
- Of which:
  - 32 fetuses with a live twin
  - 21 fetuses after the death of a twin (6 after spontaneous death, and 15 after TOP)
- Fetuses from the Normal study were used as controls.

TTTS

TTTS - results

- There were no significant differences in mean ADC values between the TTTS group and the normal controls.

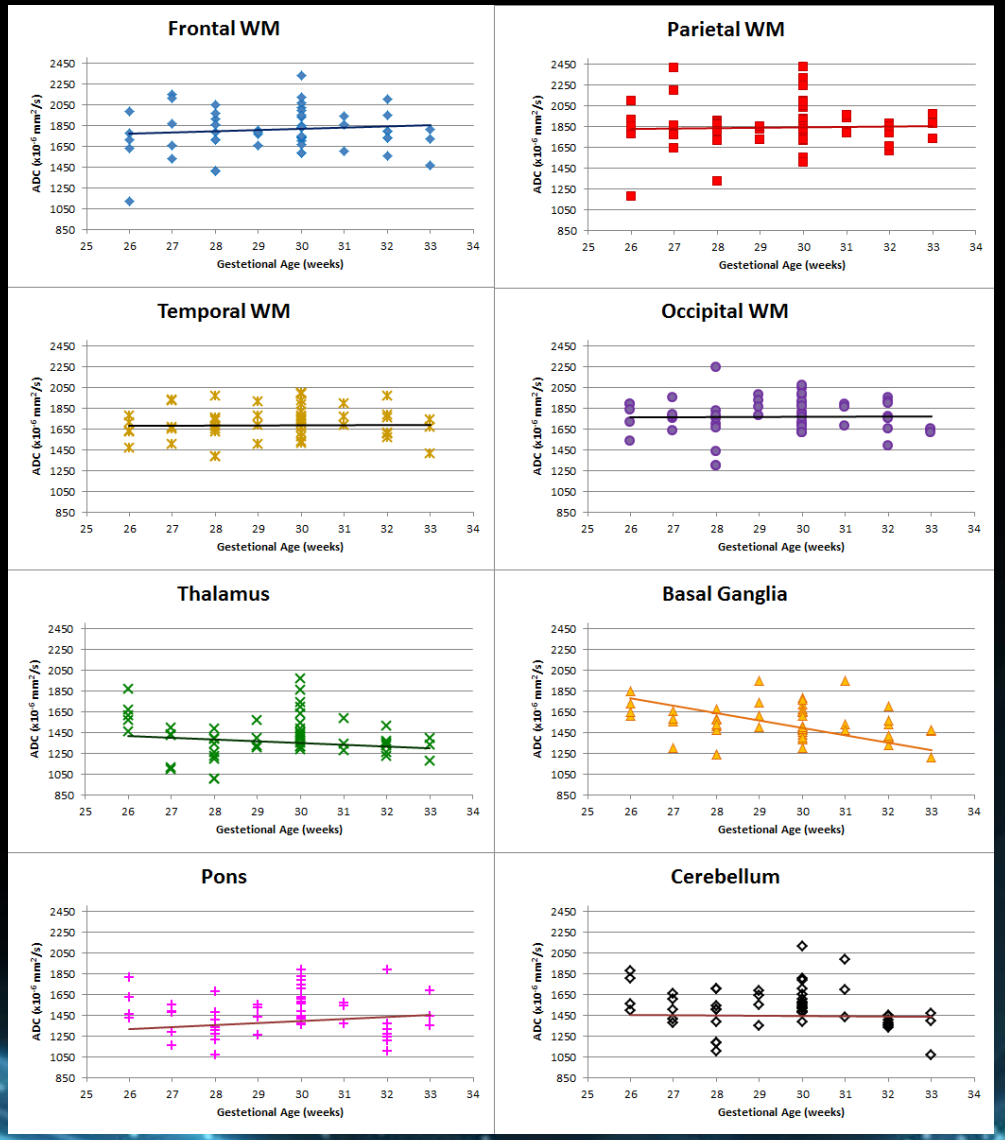


- The occurrence of spontaneous death or TOP, had no significant effect.

TTTS

TTTS - results

- Similarly to the normal baseline, ADC values were relatively stable, with similar mixed trends (except for the Pons ROI)



TTTS

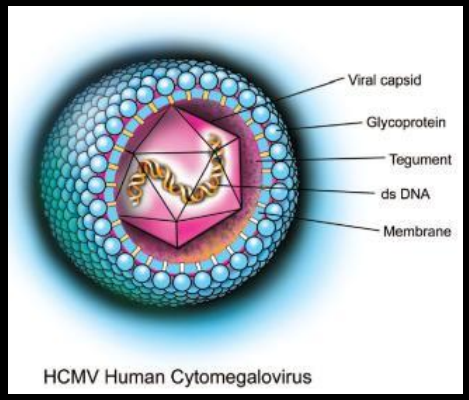
TTTS - results

- When using the non-parametric Mann-Whitney Test between TTTS fetuses with pathological findings on MRI and normal controls, the Pons showed a significant increase in mean ADC ($p<0.01$).
- This finding requires additional investigation.

CMV

CMV – what is it?

- Cytomegalovirus (CMV) is a viral genus of the viral family known as herpesviruses



- CMV is the most common cause of intrauterine infection, affecting 0.3-2% of live-born infants.

- Congenital CMV infection is specifically worrisome when maternal infection occurs during the 1st or 2nd trimester of pregnancy.

CMV

CMV - maternal infection

- 10% of congenitally infected infants are symptomatic at birth:
  About a third of them will die and up to 90% of the survivors will develop long term sequelae, such as hearing impairment or neurological abnormalities

- CMV infection is also considered as a significant risk factor for developing schizophrenia and cognitive deficits later in life.

CMV

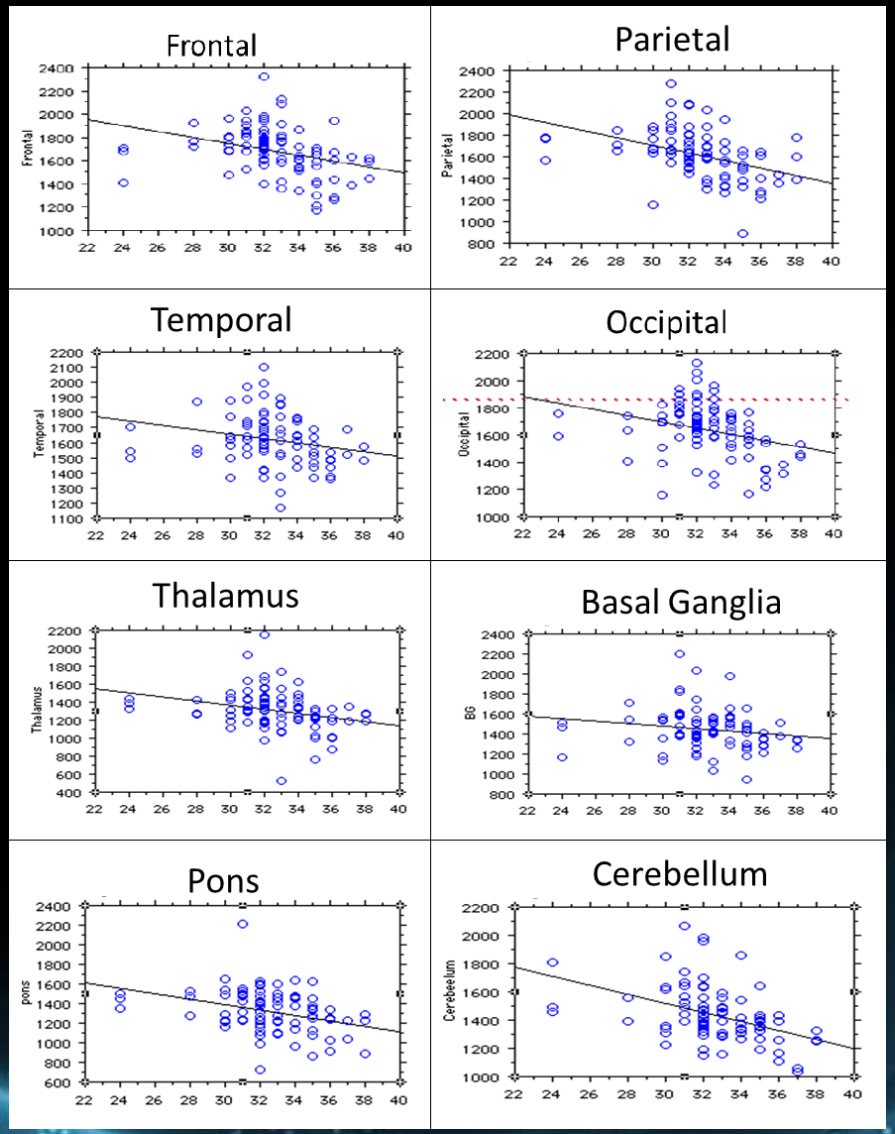
CMV - cohort

- 58 scans of non-sedated 3rd trimester (32.8 ± 3.2 weeks) singleton fetuses, with a PCR-validated (amniotic fluid and/or newborn urine) CMV infection.
- Serological diagnosis of CMV infection of the mother was determined by immunoglobulin G (IgG) and immunoglobulin M antibodies, associated with low IgG avidity, or by seroconversion.

CMV

CMV - results

- ADC values significantly and negatively correlated with GA in all brain regions except the basal ganglia
- The cerebellum had the steepest decline ($r = 0.52$, $P < .0001$)



CMV

CMV - results

- ADC values were significantly reduced in the frontal ($P < .0001$), parietal ($P < .0001$), occipital ($P = .0005$), and temporal ($P = .001$) lobes and thalamus ($P = .006$)
- Maternal age was significantly and positively correlated with ADC values for the frontal lobe of the CMV-infected fetuses ($P < 0.05$).

Ventrical a-sym.

Ventrical asymmetry - what is it?

- Some degree of asymmetry of the lateral ventricles exists in the human fetal brain.
- Ventriculomegaly is defined as an atrial diameter ≥10 mm.
- The etiology and outcome of unilateral and bilateral ventriculomegaly are similar.
- can be caused by a variety of disorders that result in neurological, motor, and/or cognitive impairment

UpToDate
02/2014

Ventrical a-sym.

Ventrical asymmetry - outcome

- There is wide variation in outcome of infants with prenatally diagnosed ventriculomegaly.
- Most children with isolated, mild ventriculomegaly have a normal outcome.

Ventrical a-sym.

Ventrical asymmetry - cohort

- 67 scans of non-sedated 3rd trimester (27-38 weeks) singleton fetuses, with MRI measurements suggesting Cerebral lateral ventricular asymmetry.

Ventrical a-sym.

Ventrical asymmetry - results

Work in progress…

What's next?

- The Vinland adaptive behavior scale, which is a valid and reliable test to measure a person's adaptive level of functioning.
- For each of our studies we aim to perform this evaluation on the children who's MRI scans were used for the study (using questionnaires filled according to interviews with the parents).

Thank you for listening!

Questions?