Лекция профессора Кирилла Ларина (Университет Хьюстона)

В рамках программы Фонда Дмитрия Зимина «Династия»
«Краткосрочные визиты иностранных ученых в российские научные центры»
19 сентября 2015г. – 28 сентября 2015 г.

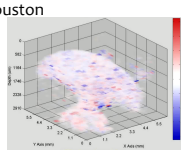
Экспериментальные исследования с помощью ОКТ систем

Optical coherence tomography in Developmental Biology

Kirill V. Larin

Department of Biomedical Engineering
College of Optometry

University of Houston

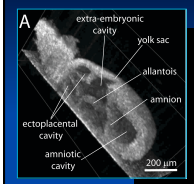


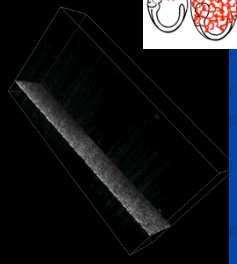
In collaboration with:

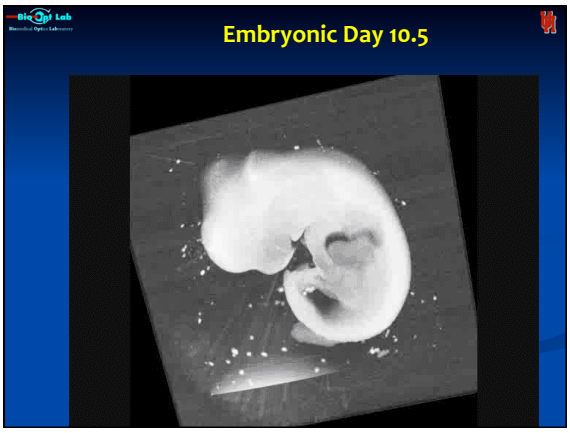
Irina Larina, Ph.D.
Assistant Professor, Department of Molecular Physiology & Biophysics
Baylor College of Medicine

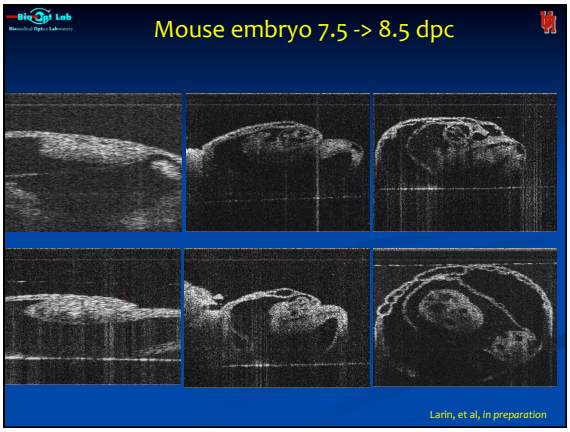
Mary Dickinson, Ph.D.
Professor, Department of Molecular Physiology & Biophysics
Baylor College of Medicine

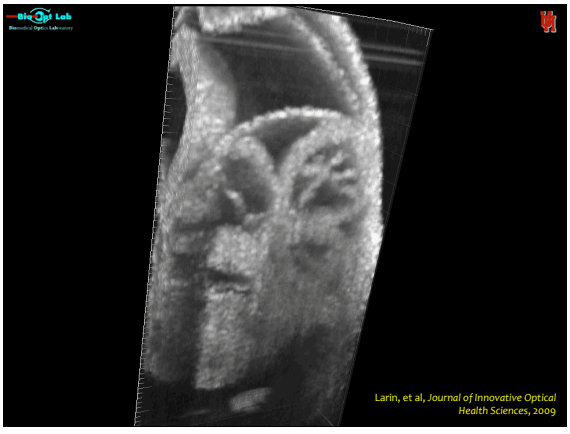
Embryonic Day 7.5



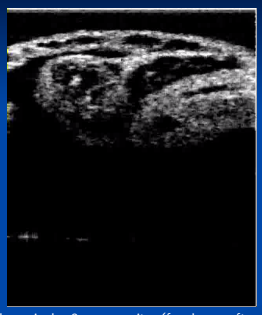


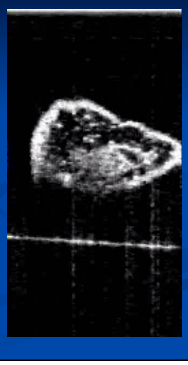

Embryonic Day 10.5


Mouse embryo 7.5 -> 8.5 dpc
Larin, et al, in preparation


Larin, et al, Journal of Innovative Optical Health Sciences, 2009

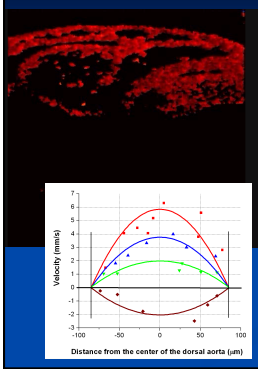
Imaging at RBC level!



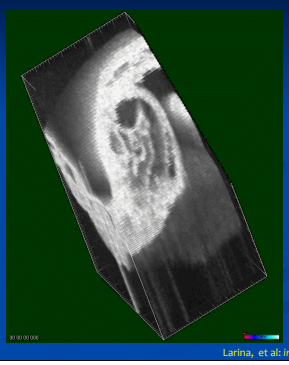


embryonic day 8.5, 10 somites (few hours after beginning of blood cell circulation)
48 fps

Doppler imaging of circulating RBCs



Mlc2a

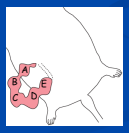


Larina, et al: *in preparation*

In Utero Experimental Methods

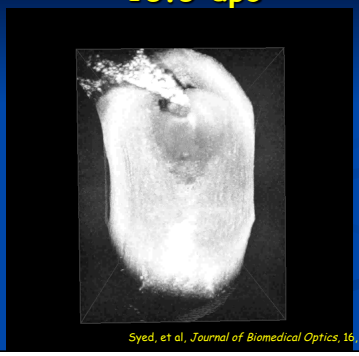
Following development in the same embryos (survival surgeries)

- Pregnant females were anesthetized with isoflurane and kept on the heating pad during the whole procedure.
- The uterine horn was exposed for imaging through an abdominal incision (about 1 to 2 cm long).
- After the imaging, the incision was stitched back.
- The procedure was repeated after 48 and 96 hours. The animal was sacrificed after the third imaging session.



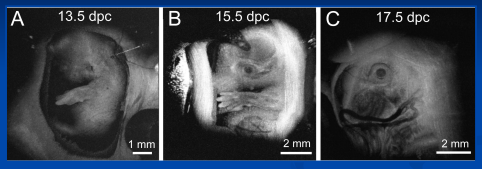
All procedures implemented were performed according to the protocol approved by IACUC (Animal Care Committee) at University of Houston

Live mouse embryo at 15.5 dpc



Syed, et al, *Journal of Biomedical Optics*, 16, 2011.

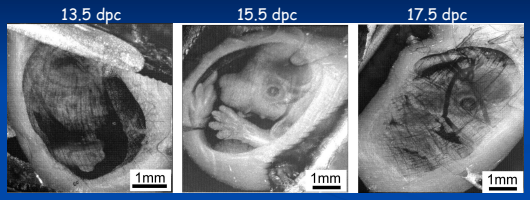
External Embryonic Morphology



These results suggest that OCT is a potentially useful to study growth abnormalities and craniofacial defects.

Syed, et al, *Journal of Biomedical Optics*, 16, 2011.

Embryonic Morphology



Morphological development and growth of the same embryo mapped with OCT.

Syed, et al, *Journal of Biomedical Optics*, 16, 2011.

Embryonic Limb Development

Limb Abnormalities

Holt-Oram Syndrome (HOS) caused by mutation of Tbx5 gene

Syndactyly causes webbing of digits

Amniotic band Syndrome can cause amputation of digits or limbs.

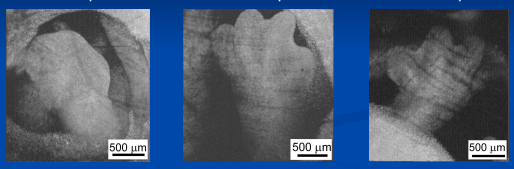
Syed, et al, *Journal of Biomedical Optics*, 16, 2011.

3D Reconstruction at 15.5 dpc

Syed, et al, *Journal of Biomedical Optics*, 16, 2011.

Limb Development

12.5 dpc | 13.5 dpc | 14.5 dpc

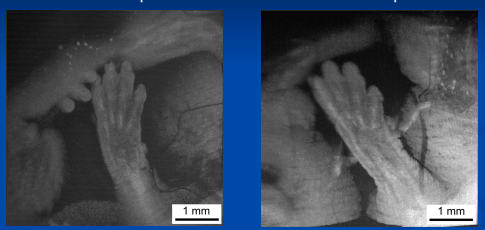


The digits start to get indented in the digital interzones and the programmed cell death in the digital interzones separate the digits.

Syed, et al, *Journal of Biomedical Optics*, 16, 2011.

Limb Development

15.5 dpc | 16.5 dpc

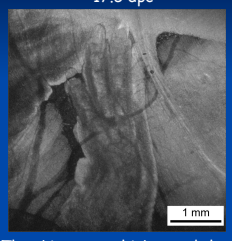


The digits have completely separated and the first evidence of nail (claw) primordia is visible. The digits also grow more parallel to each other.

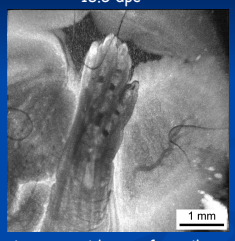
Syed, et al, *Journal of Biomedical Optics*, 16, 2011.

Limb Development

17.5 dpc



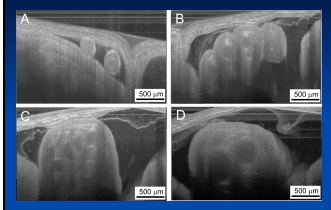
18.5 dpc

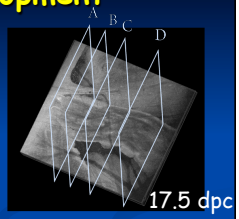


The skin grows thicker and there is more evidence of cartilage primordia in digits.

Syed, et al, *Journal of Biomedical Optics*, 16, 2011.

Limb Development





Cartilage primordia of digits, metacarpal bones, radius bone and ulna bone are clearly visible

These results suggest that our methodology can potentially be used to visualize formation and development of digits, cartilage and bones in the limb of normal and mutant embryos.

Syed, et al, *Journal of Biomedical Optics*, 16, 2011.

LV2229 Pcgf3 mouse mutant at E15.5

Hindlimb imaging with OCT

mutant

normal

Larina, et al, *in preparation*.

Brain Development

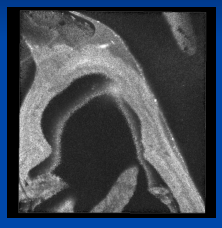
Brain Development

- Numerous mouse models of brain disorders are available.
- Mother's health and life style can affect the brain development of the fetus.
- Pharmacological and toxicological studies in the mouse model can help understand these defects.

Syed, et al, *Journal of Biomedical Optics*, 16, 2011.

In utero Images of The Brain

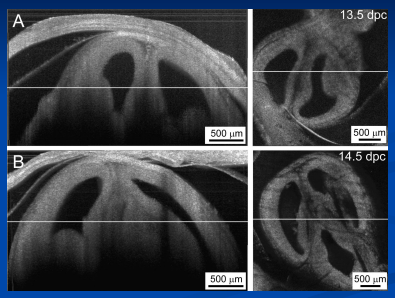
13.5 dpc



14.5 dpc

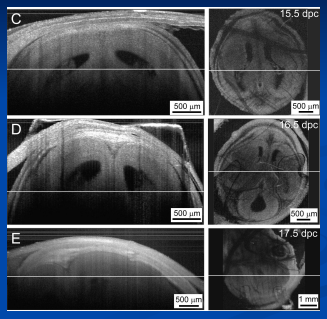
Syed, et al, *Journal of Biomedical Optics*, 16, 2011.

Brain Development



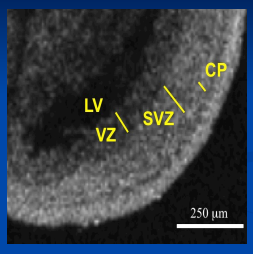
Syed, et al, *Journal of Biomedical Optics*, 16, 2011.

Brain Development



Syed, et al, *Journal of Biomedical Optics*, 16, 2011.

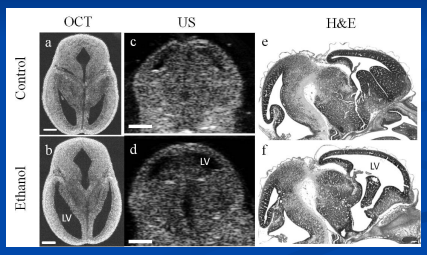
In utero Images of The Brain



OCT image of mouse brain showing Cortical Plate (CP) Sub Ventricular Zone (SVZ), Ventricular Zone (VZ), and Left Ventricle (VL),. These layers are indistinguishable from HFUS images

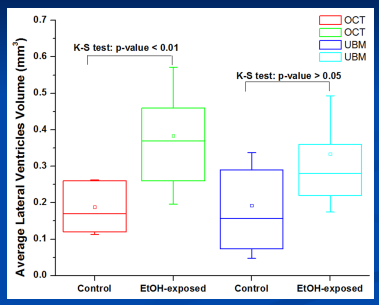
Effect of Alcohol and Nicotine Exposure on Fetal Brain Development

Effect of ethanol on mouse fetal brain development at E14.5.



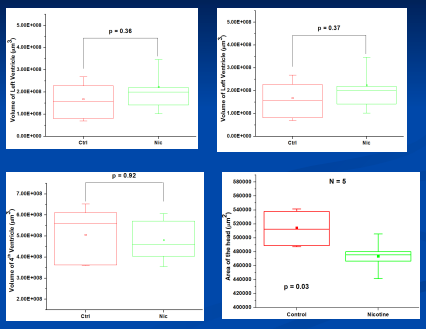
N. Sudheendranet al., *Journal of Biomedical Optics*, 2013

Control vs EtOH-exposed OCT vs UBM



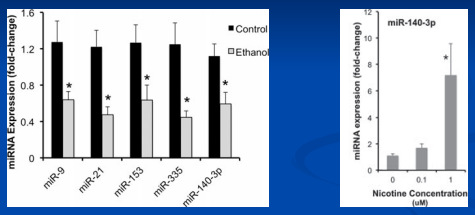
N. Sudheendranet al., *Journal of Biomedical Optics*, 2013

Effect of NIC exposure on mouse fetal brain development at E14.5



While there is no statistically significant difference in volume of the ventricles, there is a significant difference on the head area

EtOH and NIC exert mutually antagonistic effect?



Balaraman S, Winzer-Serhan UH, Miranda RC. Opposing actions of ethanol and nicotine on microRNAs are mediated by nicotinic acetylcholine receptors in fetal cerebral cortical-derived neural progenitor cells. Alcoholism, clinical and experimental research 2012;36(10):1669-77. PMCID: 3390449.

Eye Development

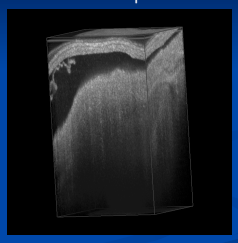
Ocular Defects

- Ocular abnormalities can be affect cornea, retina or lens development and mostly related to mutations.
- Types of Ocular abnormalities
  - congenital cataract
  - microphthalmia
  - anophthalmia
  - coloboma
  - corneal opacity
  - congenital glaucoma

3D OCT Images of Embryonic Eye

15.5 dpc

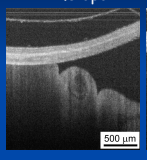
17.5 dpc



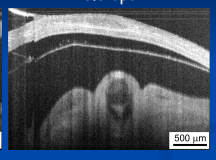
Narendran, et al, *in preparation.*

Eye Development

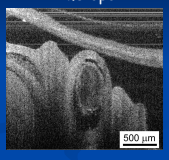
12.5 dpc



13.5 dpc



14.5 dpc

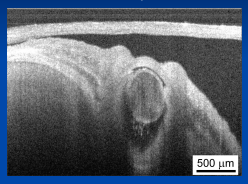


The lens grows in volume along with whole eye. The cornea is separated from the lens and the upper and lower eyelid differentiate and grow.

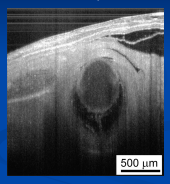
Narendran, et al, *in preparation.*

Eye Development

15.5 dpc



16.5 dpc

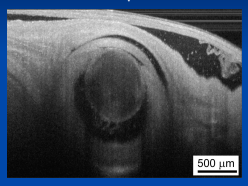


Most important development between these stages is the closing of the eyelid by the fusion of upper and lower eyelid.

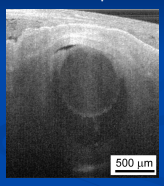
Narendran, et al, *in preparation.*

Eye Development

17.5 dpc



18.5 dpc

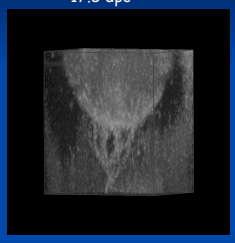


The lens and eye grows bigger in size.

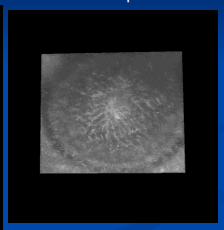
Narendran, et al, *in preparation.*

3D Reconstruction of Hyaloid Vessels

17.5 dpc

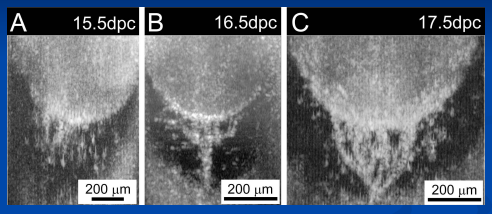


18.5 dpc



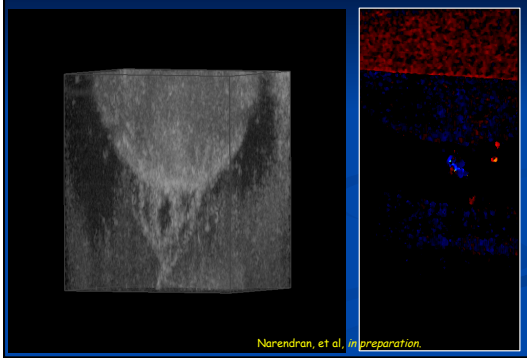
Narendran, et al, *in preparation.*

Hyaloid Vessels



Narendran, et al, *in preparation.*

Hyaloid Vessels - Doppler



Narendran, et al, *in preparation.*

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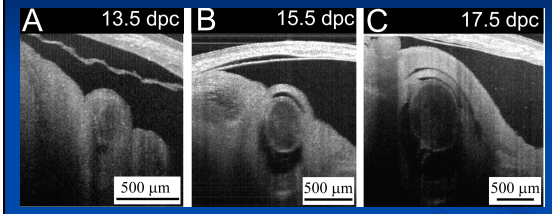
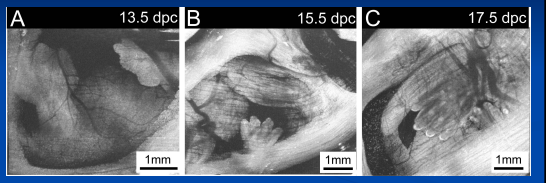
Eye Development



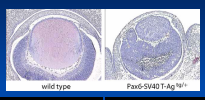
Narendran, et al, *in preparation.*

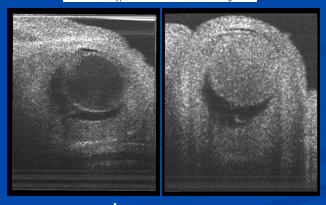
Limb Development



Pax6-SV40 T-antigen mice, a model of embryonic retinoblastoma

This mutant spontaneously forms lesions *in utero*.





normal mutant

Larina, et al, *Journal of Biomedical Optics (in press)*.