Optical Imaging for Neuroscience and Developmental Biology

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Electrical and Computer Engineering

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Outline

- **Introduction**
  - Biomedical Imaging Modalities
  - Why Optical Imaging?
  - Optical Biopsy with Optical Coherence Tomography (OCT) and Microscopy (OCM)
- **Applications in Neuroscience and Developmental Biology**
  - 3D imaging of brain slices
  - Evaluate heart function in fruit flies
- **Summary**

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BIOMEDICAL IMAGING MODALITIES

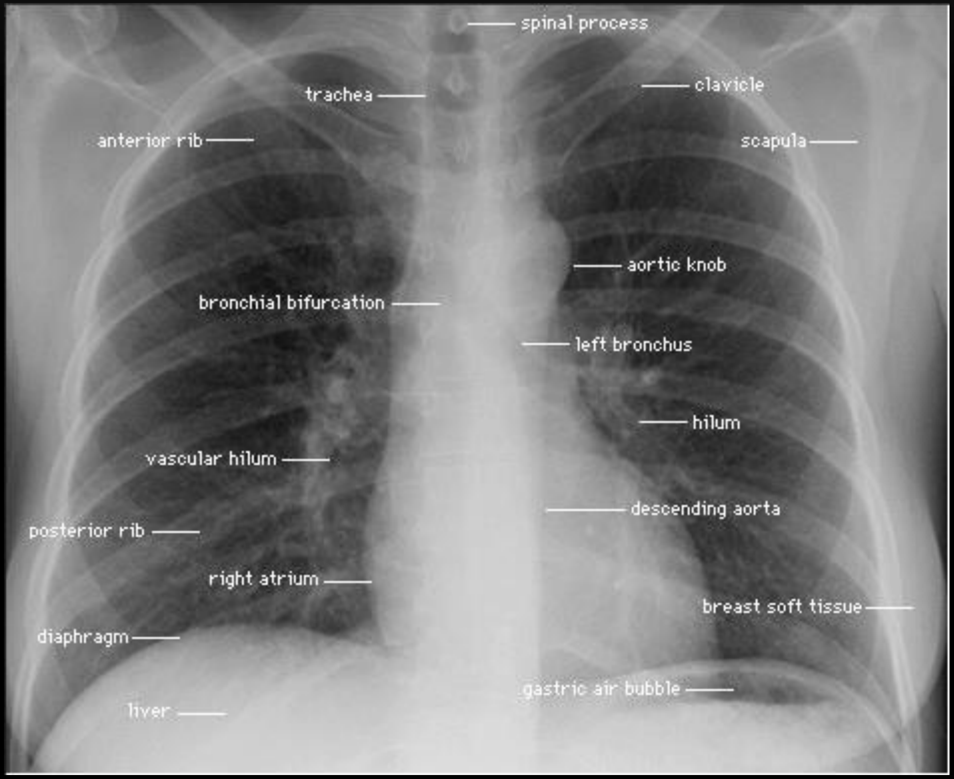
- ✓ X-Ray
- ✓ Computed Tomography (CT)
- ✓ Positron Emission Tomography (PET)
- ✓ Magnetic Resonance Imaging (MRI)
- ✓ Ultrasonography (US)
- ✓ Optical Imaging

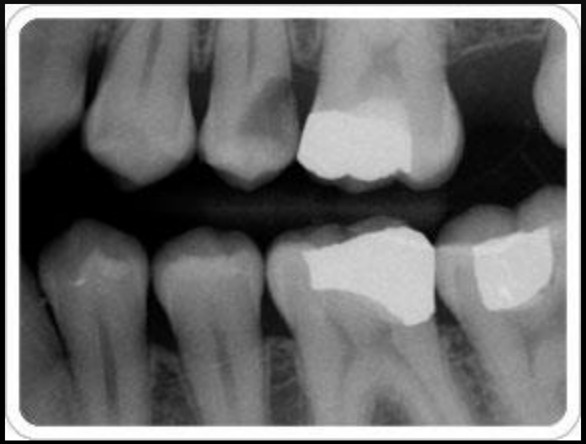
X-RAY

- ✓ Discovered in 1895 by Wilhelm Conrad Röntgen, who received the first Nobel Prize in Physics in 1901.

X-RAY

X-RAY



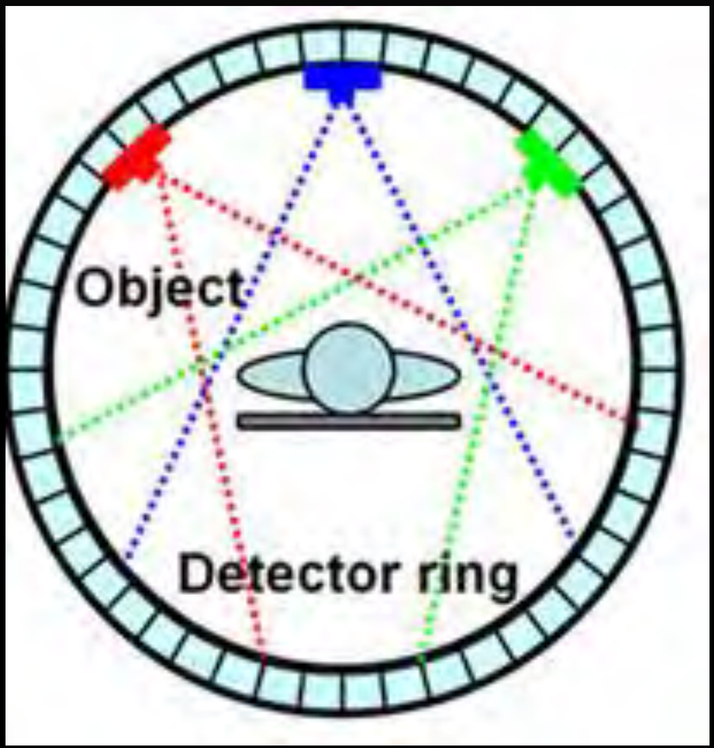


Ionizing radiation

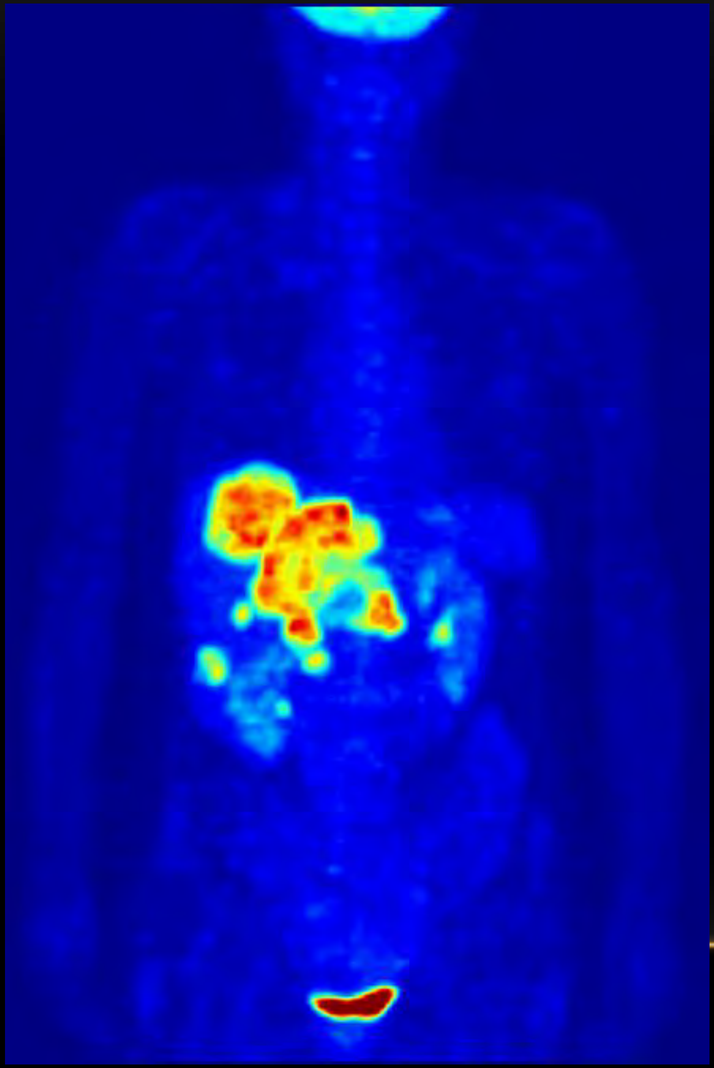
COMPUTED TOMOGRAPHY (CT)

- Invented in 1971 by Allan Cormack and Godfrey Hounsfield, who shared the 1979 Nobel Prize for Physiology or Medicine

COMPUTED TOMOGRAPHY (CT)

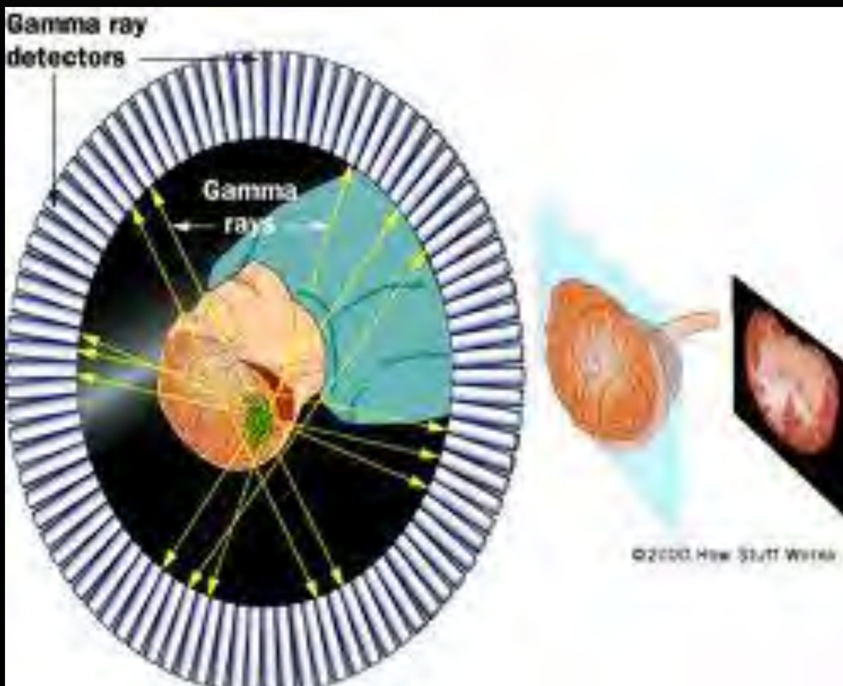


POSITRON EMISSION TOMOGRAPHY (PET)



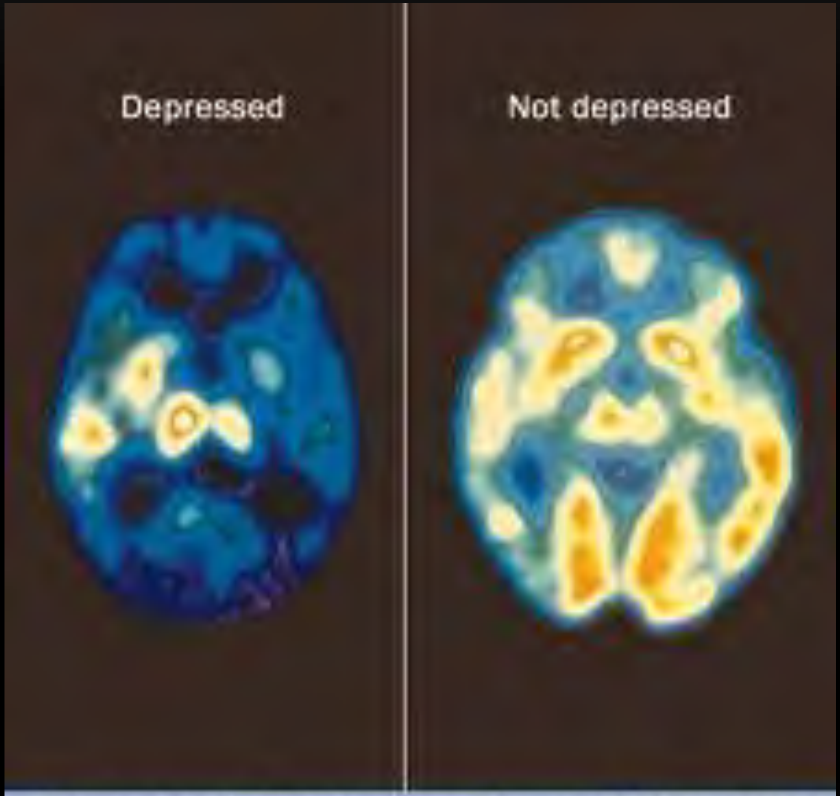
- ✓ Concept was introduced by David E. Kuhl, Luke Chapman and Roy Edwards in the late 1950s.
- ✓ Was further developed by Michel Ter-Pogossian, Michael E. Phelps and others.

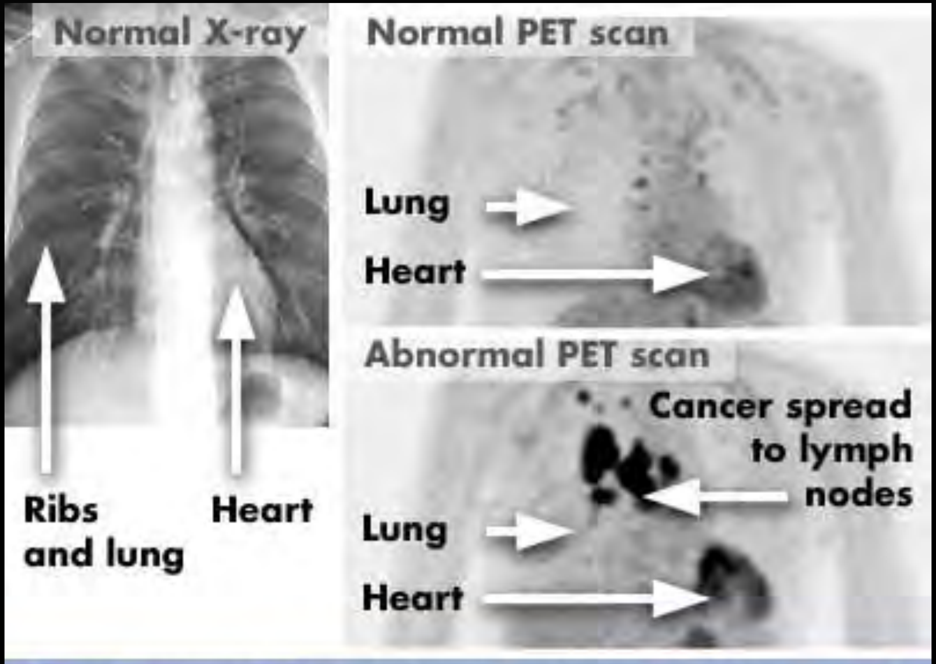
POSITRON EMISSION TOMOGRAPHY (PET)



- Inject radioactive tracer, Fluorodeoxy-D-glucose (FDG), an analogue of glucose.
- Pairs of gamma rays emitted by the tracer were detected.
- The concentrations of tracer give tissue metabolic activity proportional to tissue glucose uptake.

POSITRON EMISSION TOMOGRAPHY (PET)

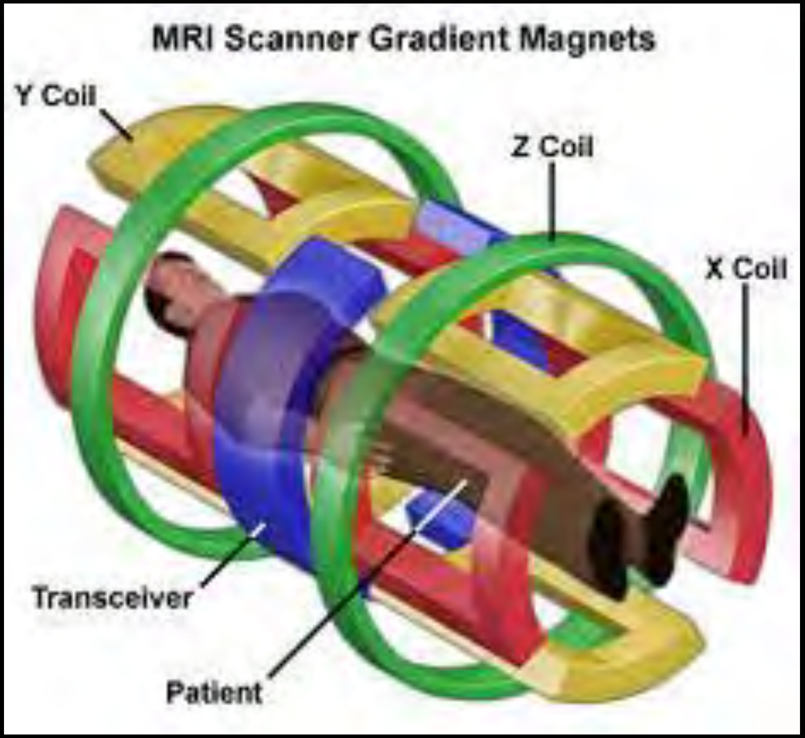


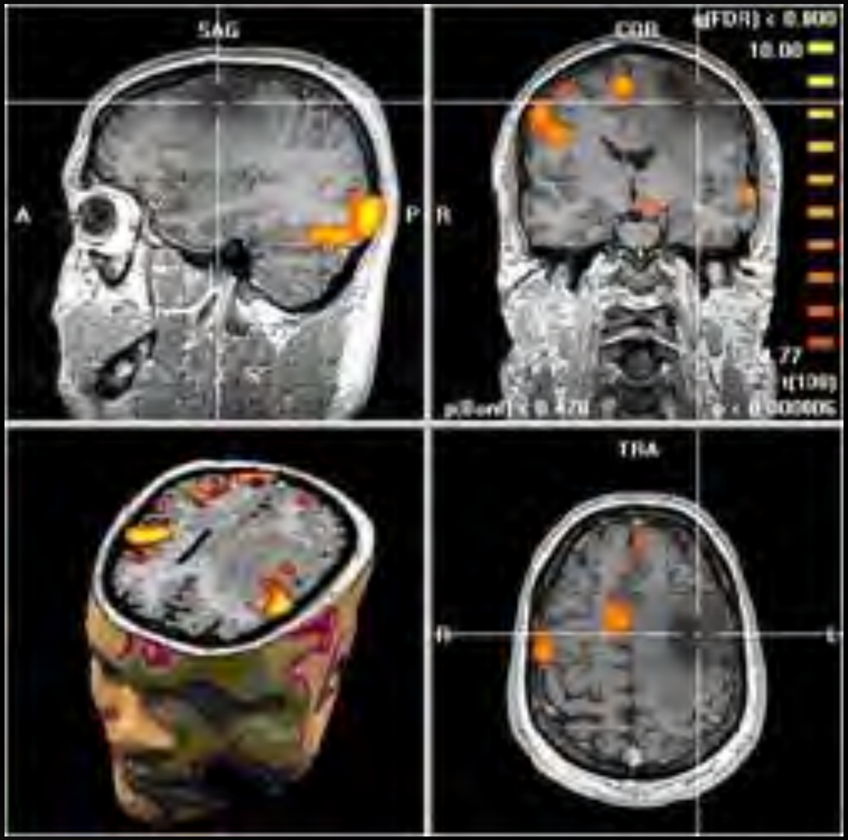


MAGNETIC RESONANCE IMAGING (MRI)

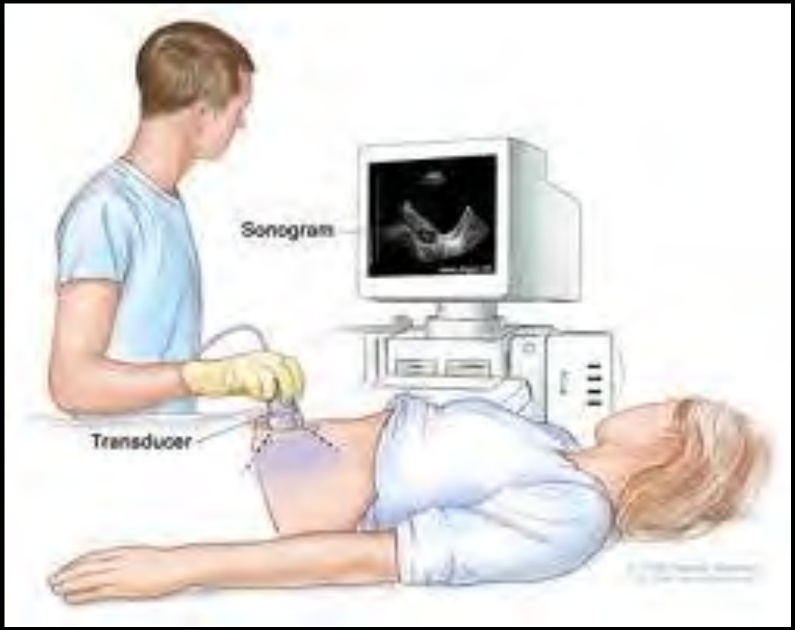
- ✓ Paul Lauterbur (University of Illinois) demonstrated first MRI image in living mouse in 1974.
- ✓ Peter Mansfield (University of Nottingham) demonstrated first MRI image in human in 1977.
- ✓ They won the Nobel Prize for Physiology or Medicine in 2003.

MAGNETIC RESONANCE IMAGING (MRI)



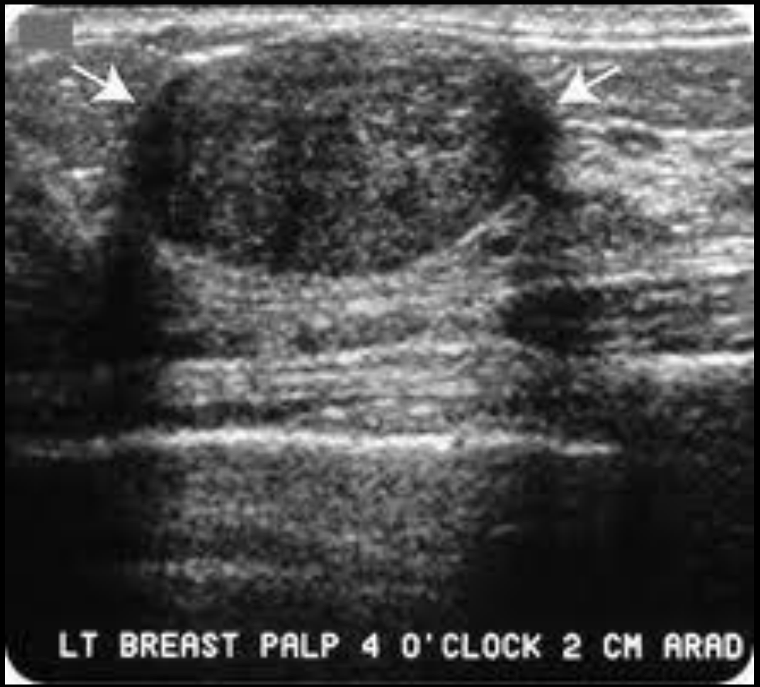


ULTRASONOGRAPHY (US)



- ✓ First applied to the human body by Dr. George Ludwig at the Naval Medical Research Institute in 1940s.
- ✓ Typically, 2 to 18 megahertz, though frequencies up to 50–100 megahertz have been used experimentally.

ULTRASONOGRAPHY (US)



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WHY OPTICAL IMAGING?

Characteristics	X-Ray	CT	PET	MRI	US	Optical Imaging
Ionizing Radiation	Yes	Yes	Yes	No	No	No
Spatial Resolution	mm-cm	mm-cm	cm	mm	100um - mm	Um to sub-um
Temporal Resolution	second	min	Tens of min	min	Sub-second	Sub-second
Contrast	Tissue density	Tissue density	Contrast agents	Tissue parametrical property	Tissue mechanical properties	Intrinsic contrast / contrast agents
Imaging Depth	Deep	Deep	Deep	Deep	Deep	Shallow
3D capability	No	Yes	Yes	Yes	Yes	Yes
Cost	$	$$$	$$$	$$$	$$	$

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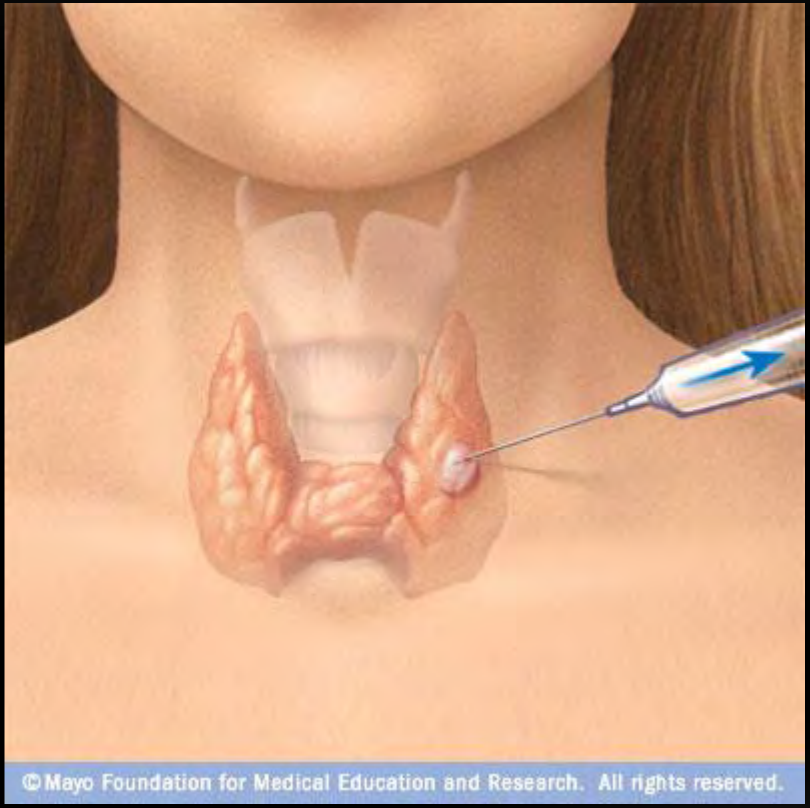
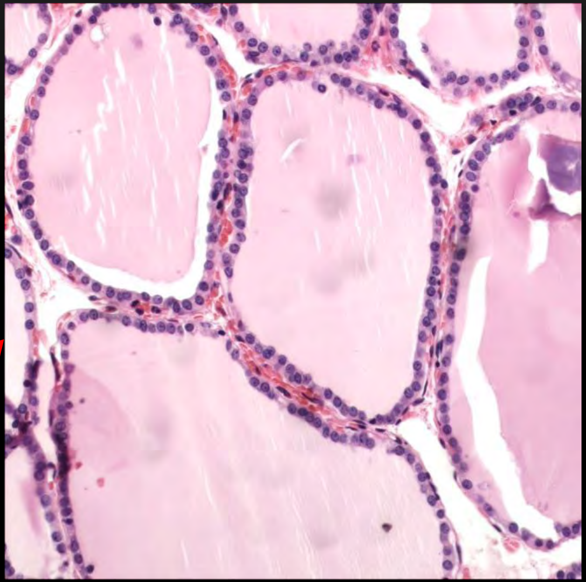
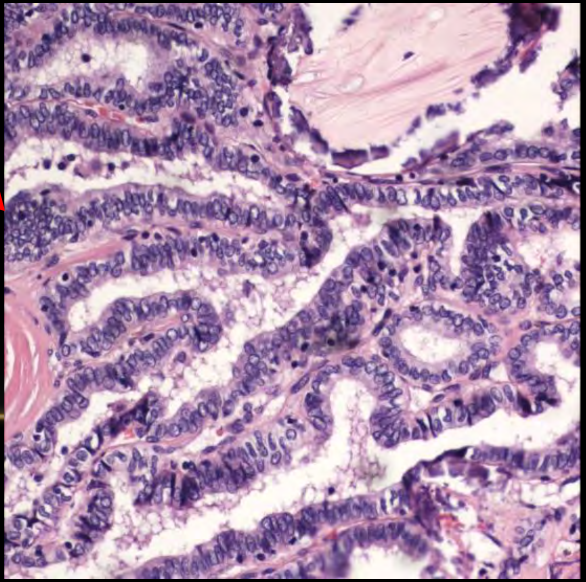
BIOPSY



Benign





Tumor

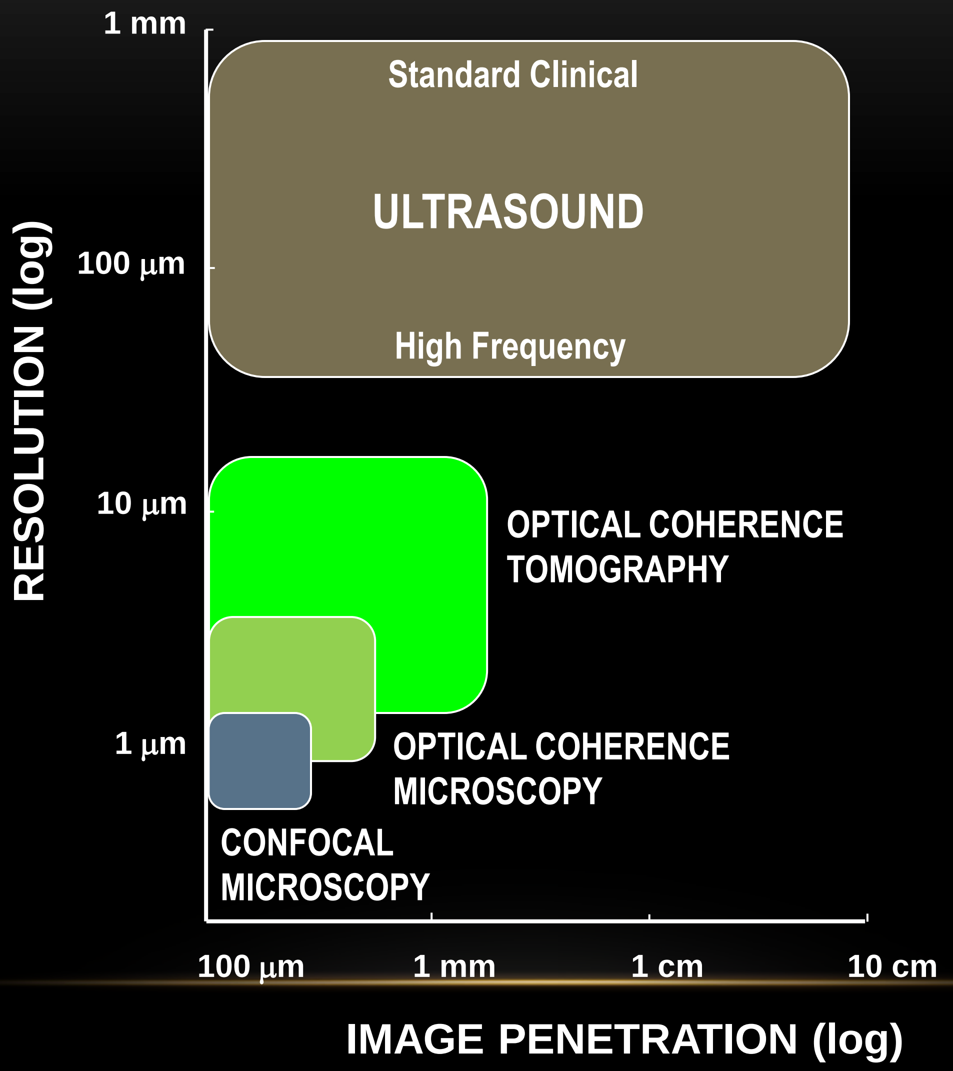
Several days to weeks!!!

OBJECTIVE: OPTICAL BIOPSY

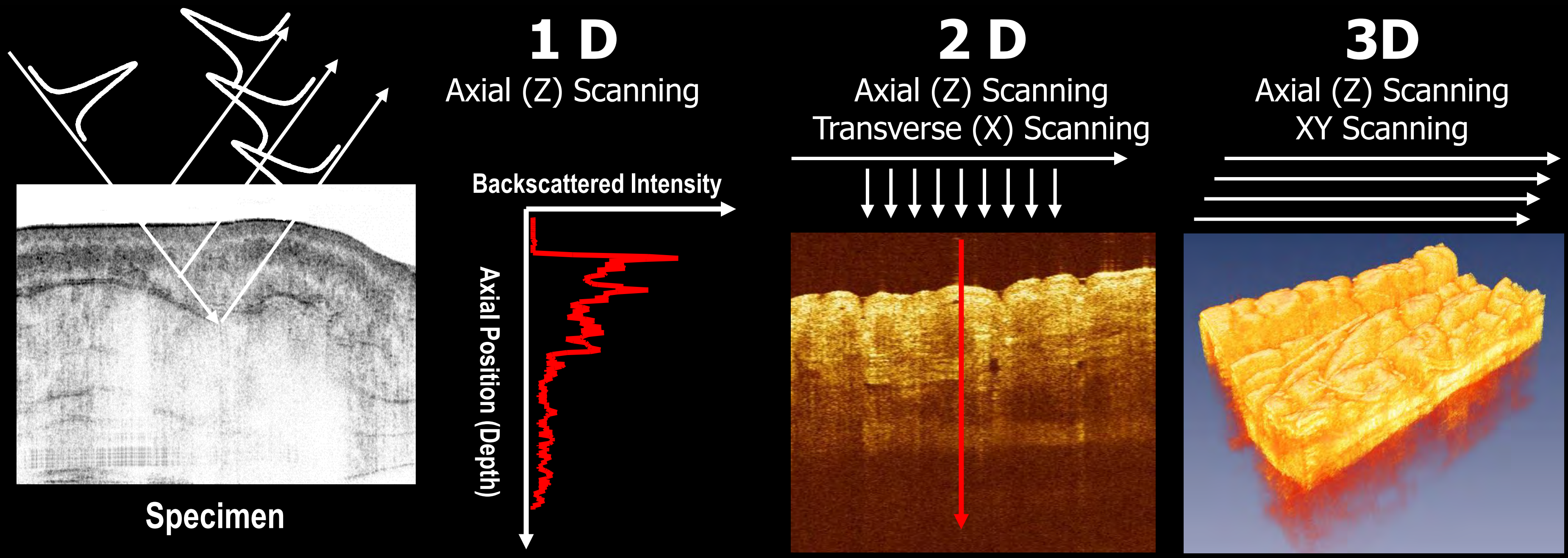
- ✓ ***In situ*, real-time imaging of tissue microstructure with a resolution approaching that of histology, without the need for tissue excision and processing.**

- ✓ Especially important in situations where excisional biopsy is either hazardous or impossible, *e.g.*, in ophthalmic or cardiovascular applications, neuroscience and developmental biology.

HIGH RESOLUTION SUBSURFACE IMAGING

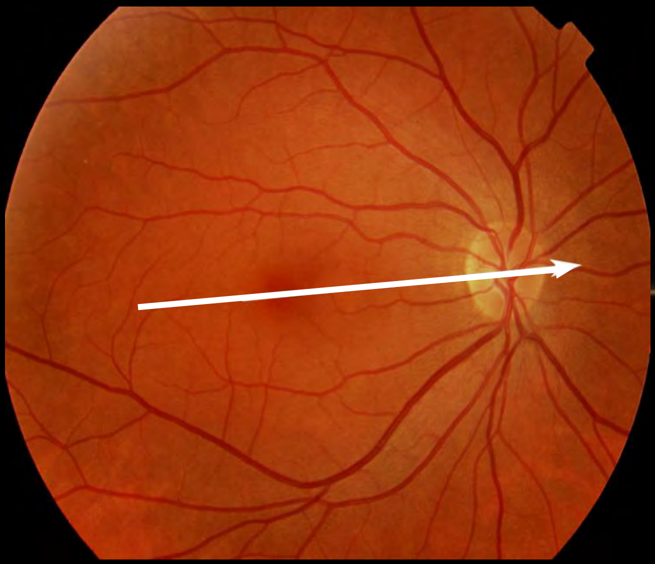


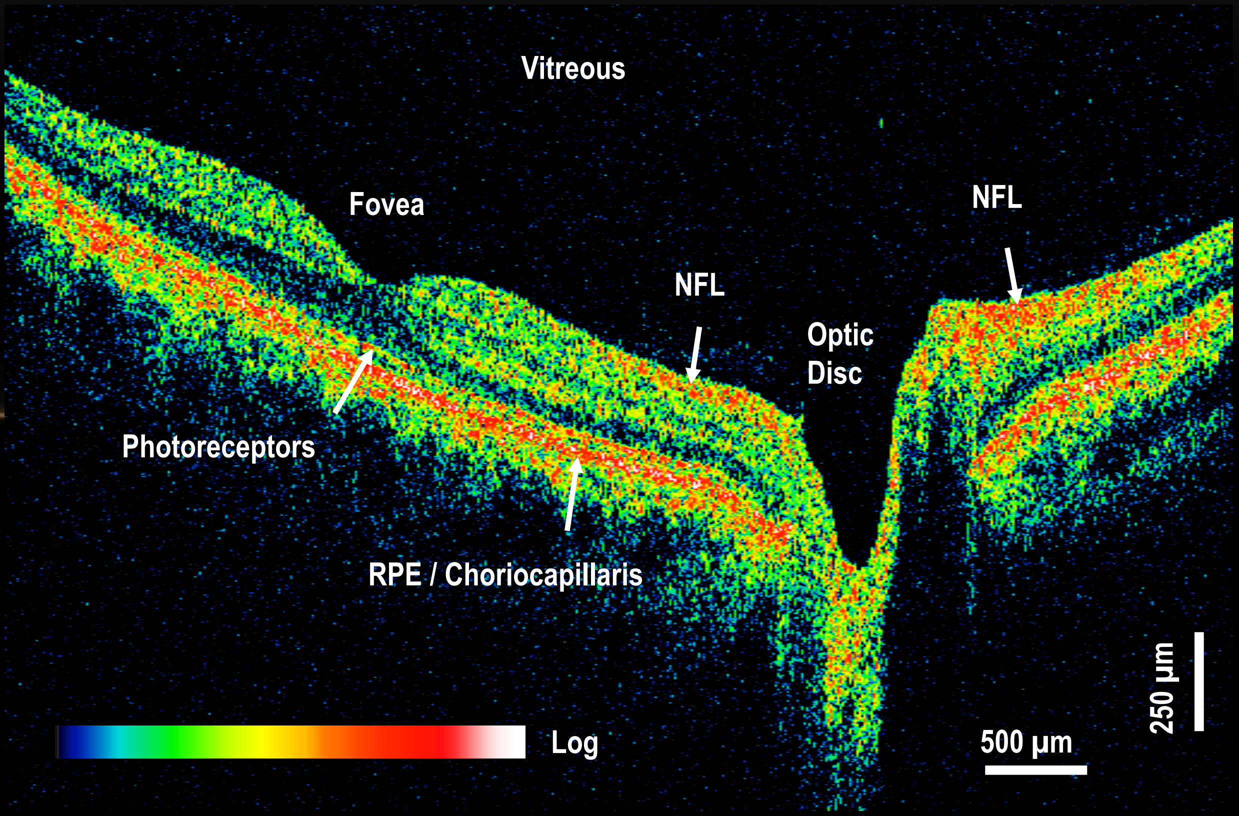
OPTICAL COHERENCE TOMOGRAPHY (OCT)



Huang, *et al*, *Science*, 254, 1178-1181,1991

OCT IN OPHTHALMOLOGY





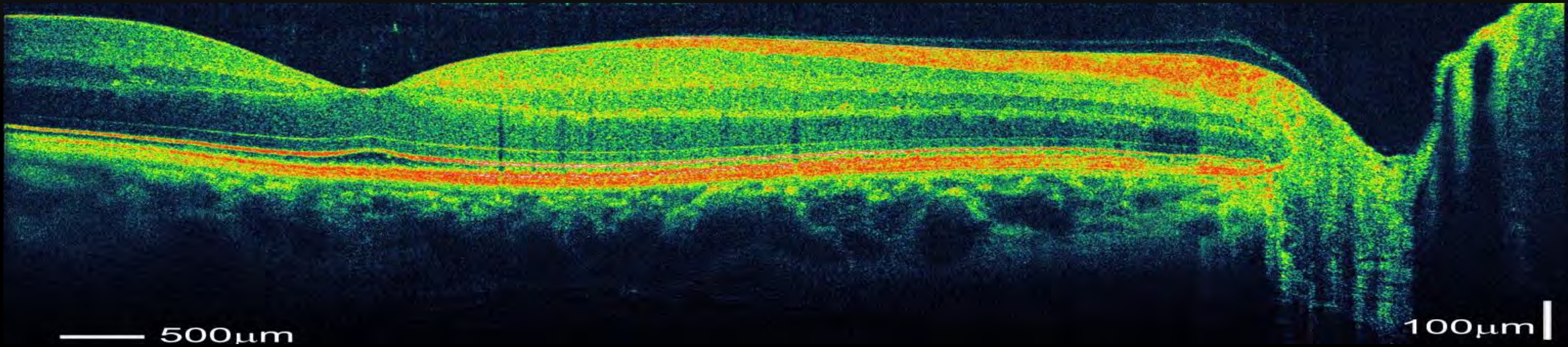
Fovea to optic disc

Huang, *et al, Science*, 254, 1178-1181,1991

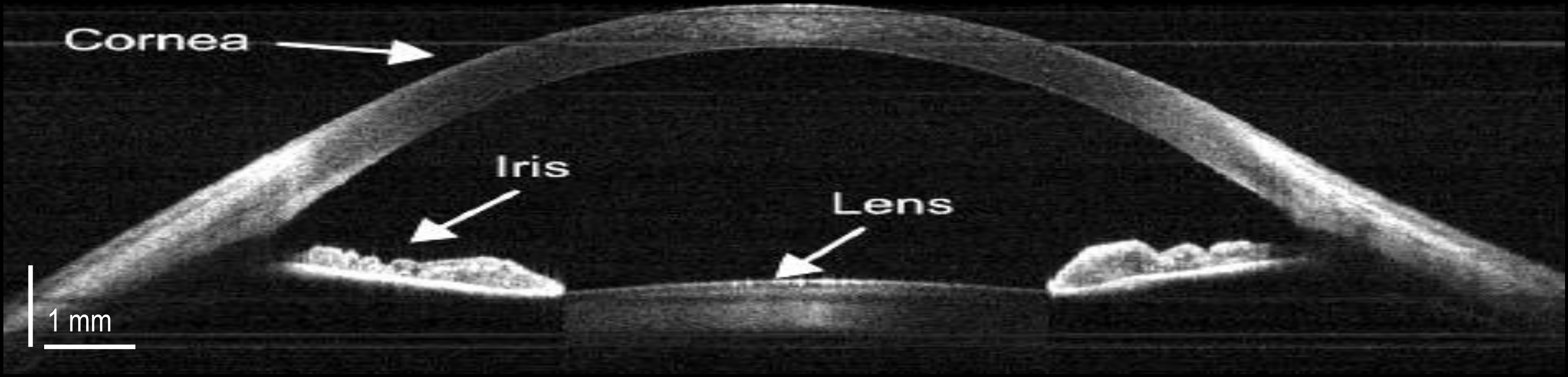
HIGH SPEED, ULTRAHIGH RESOLUTION OCT

(250,000 – 400,000 A-lines/s)

High Speed, Ultrahigh Resolution OCT of Human Retina



High Speed OCT of Human Anterior Segment



Potsaid, *et al*, Opt. Express, 18(19), 20029-20048, 2010

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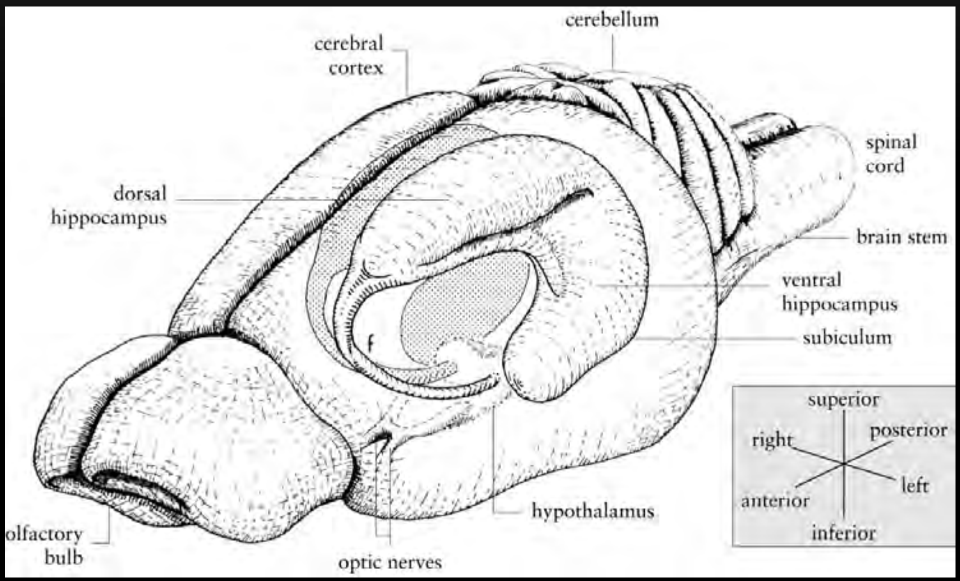
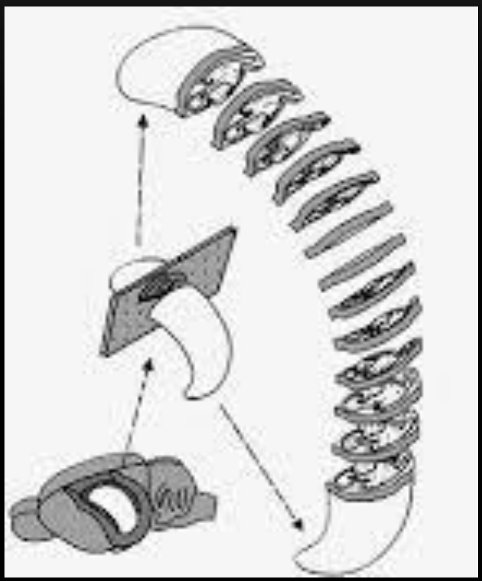
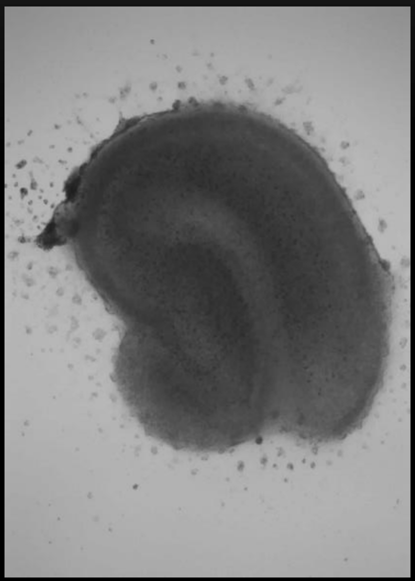
Organotypic Hippocampal Slice Cultures







Cheung and Cardinal *BMC Neuroscience* 2005

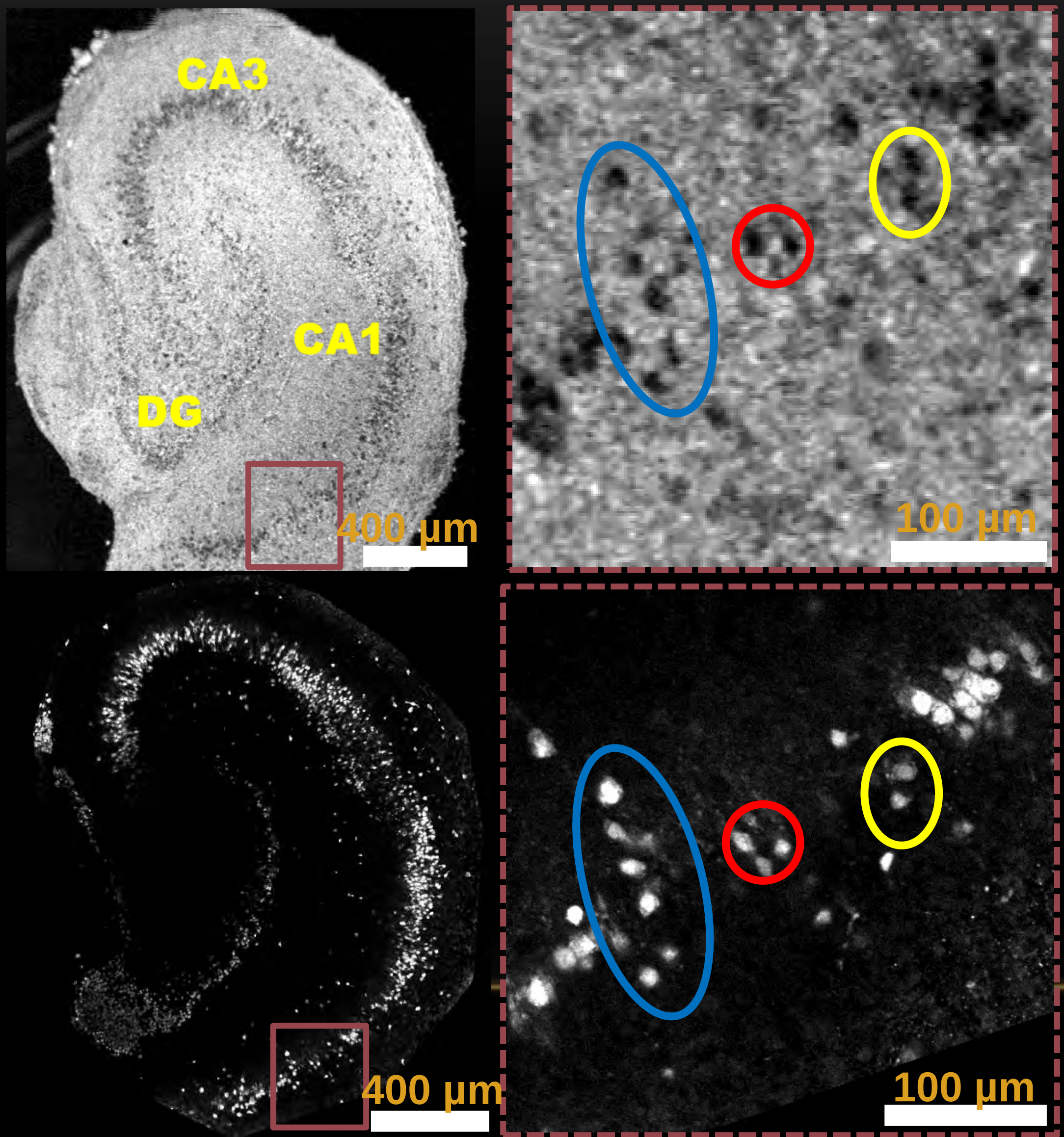
Characteristics:

a. ***Hippocampus of 7-day old Sprague-Dawley rats***

b. ***~300µm thick***

Collaboration with Dr. Yevgeny Berdichevsky at Lehigh

Comparison of OCM and Confocal Images



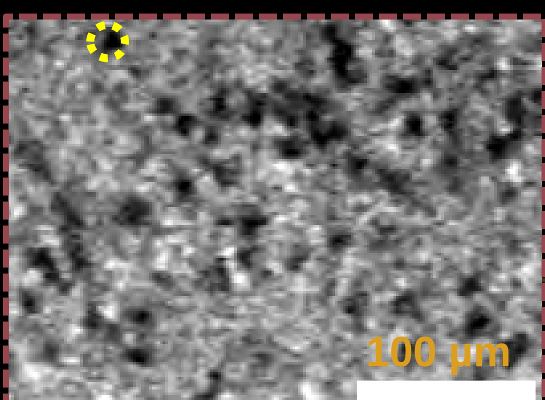
Nuclei: anti-NeuN

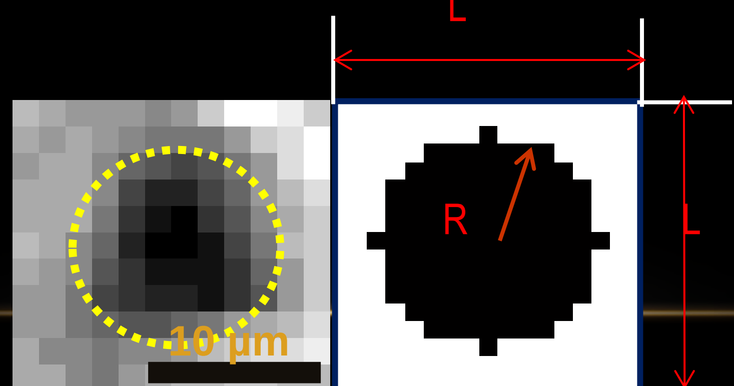
F. Li, *et al*, Neurophotonics, 2014

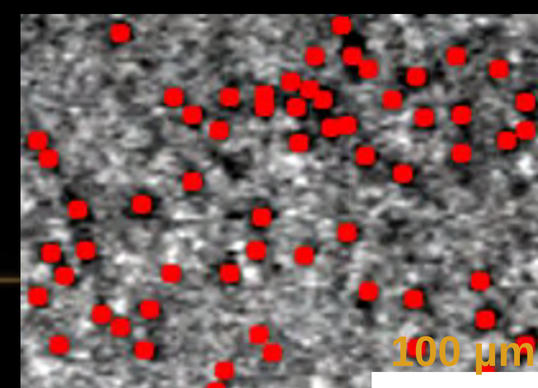
Quantify Neurons in 3D

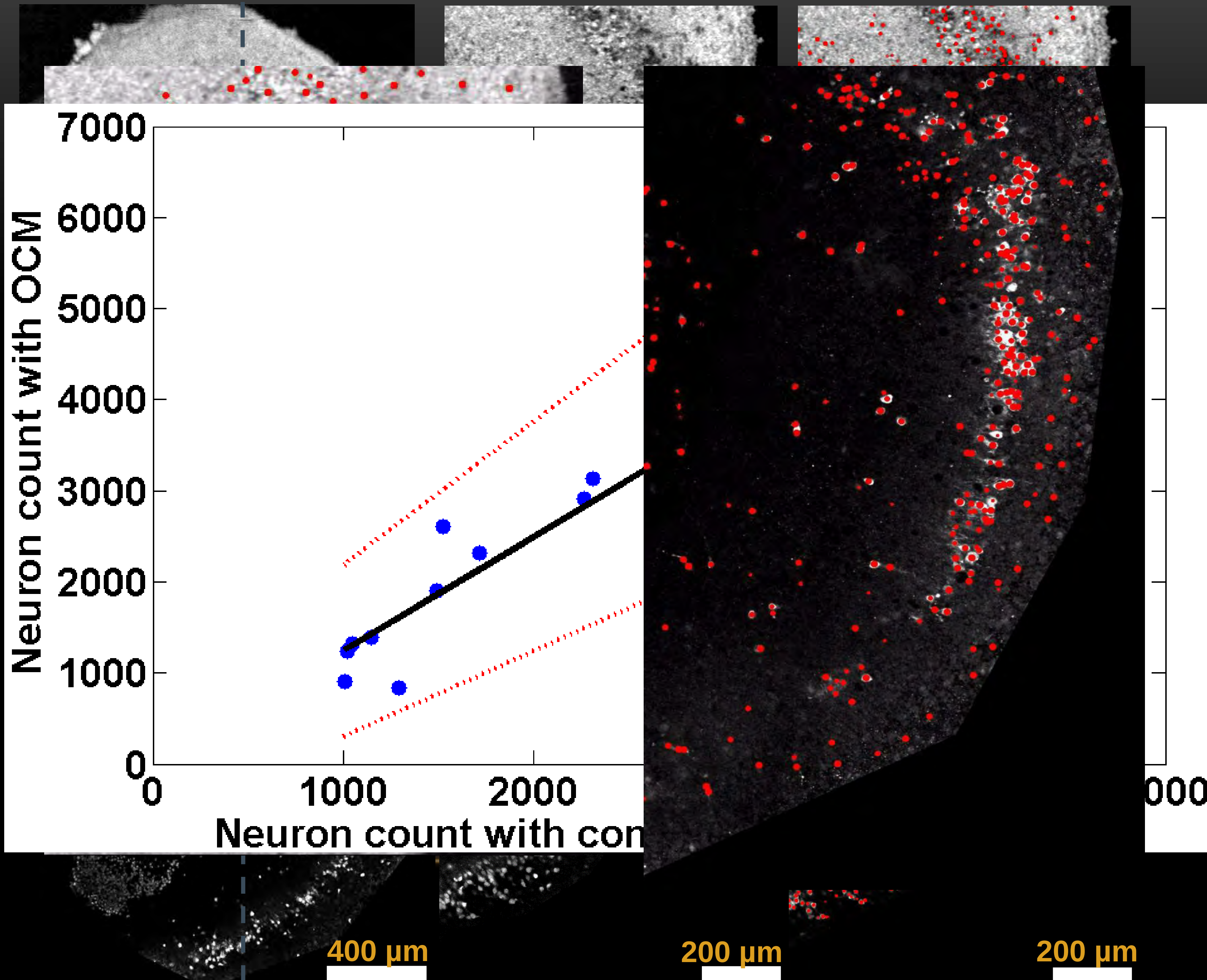
CA3: Cornuammonis III
CA1: Cornuammonis I
DG: Dentate gyrus

Chu *et al*, Journal of Molecular Histology, 2007



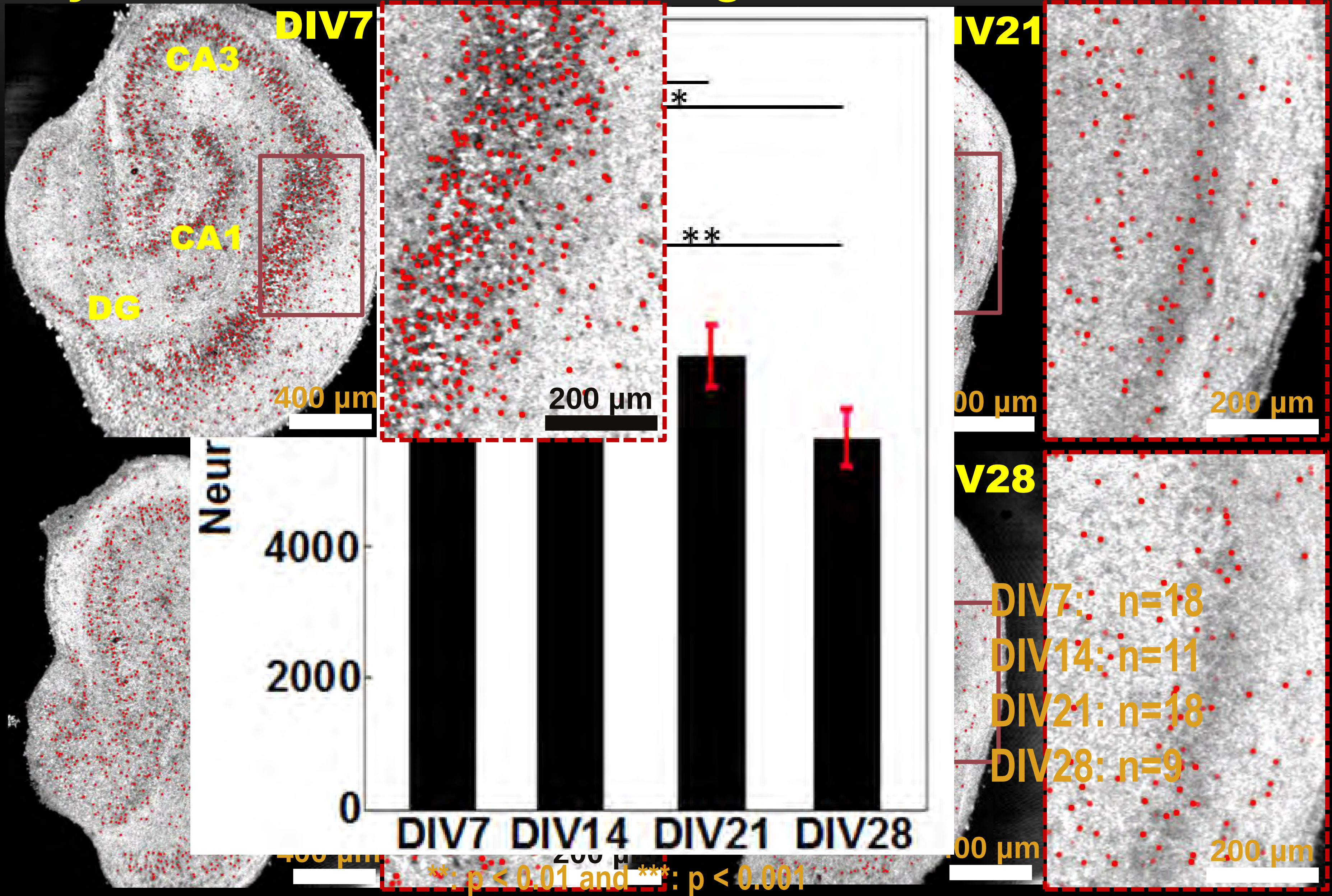




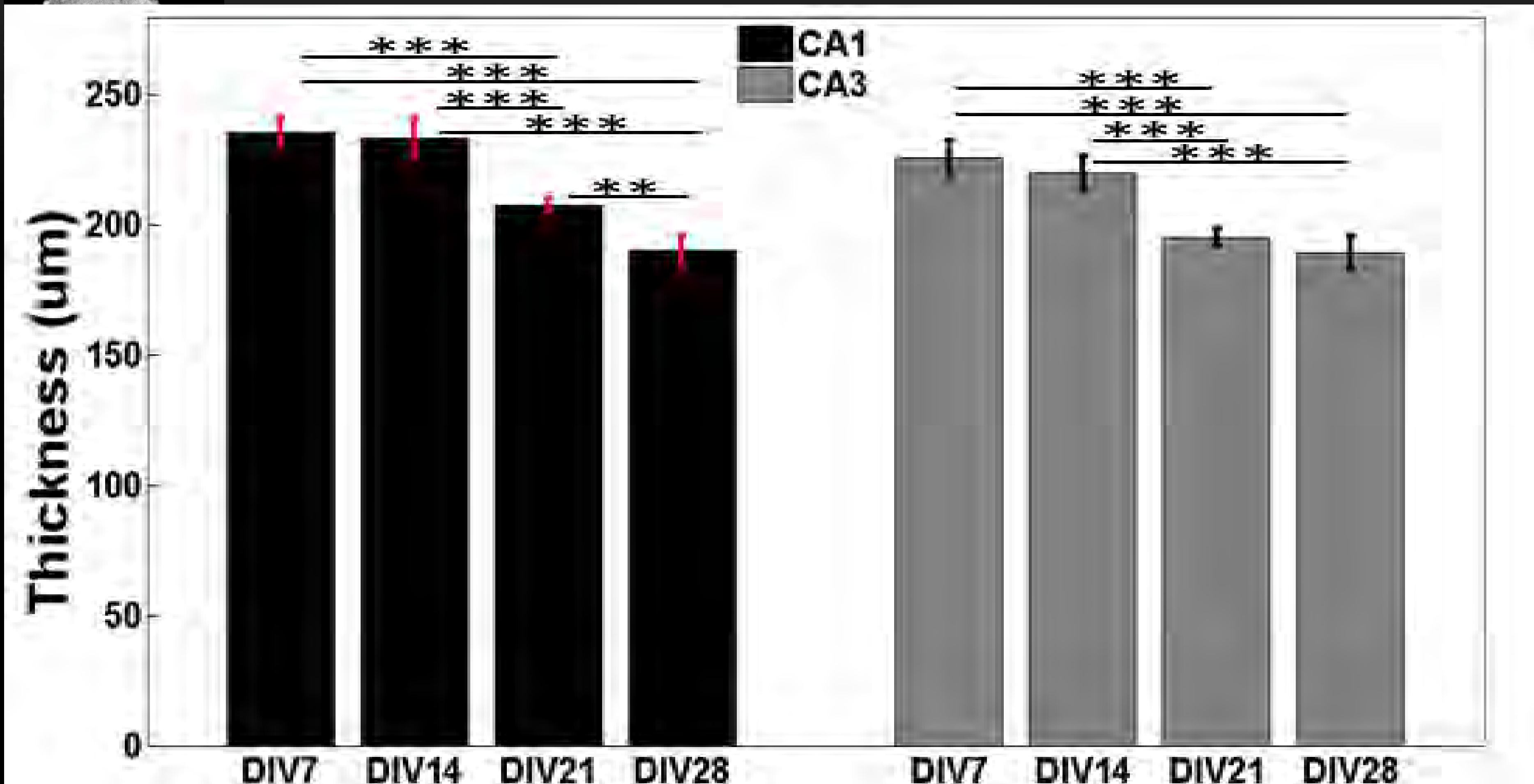


7000
6000
5000
4000
3000
2000
1000
0
0
1000
2000
000
Neuron count with OCM
Neuron count with con
400 µm
200 µm
200 µm

Evaluation of seizures-induced neuronal injury as days *in vitro* increased using OCM



Slice thickness measurement as days *in vitro* increased using OCM

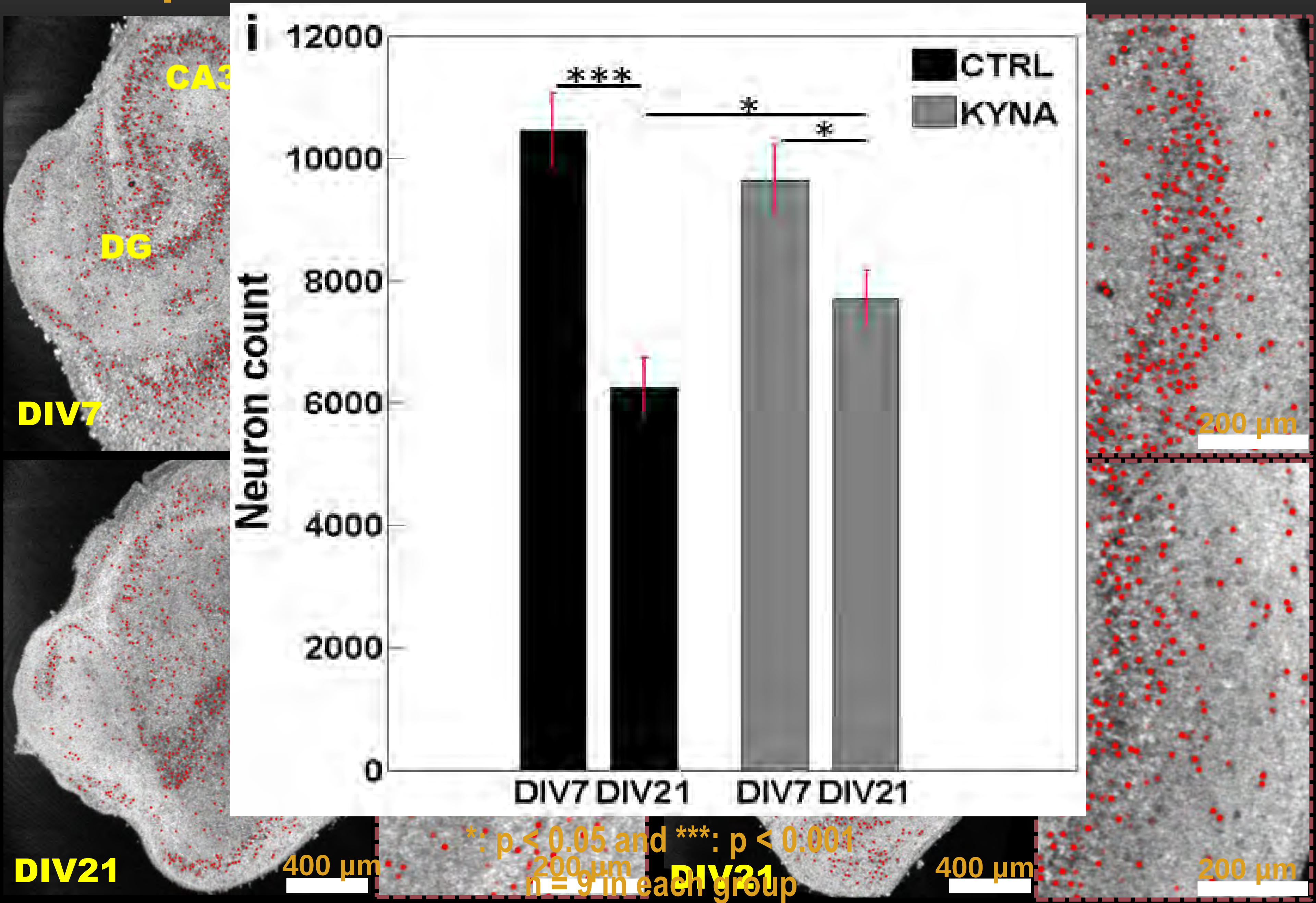


**: $p < 0.01$ and ***: $p < 0.001$

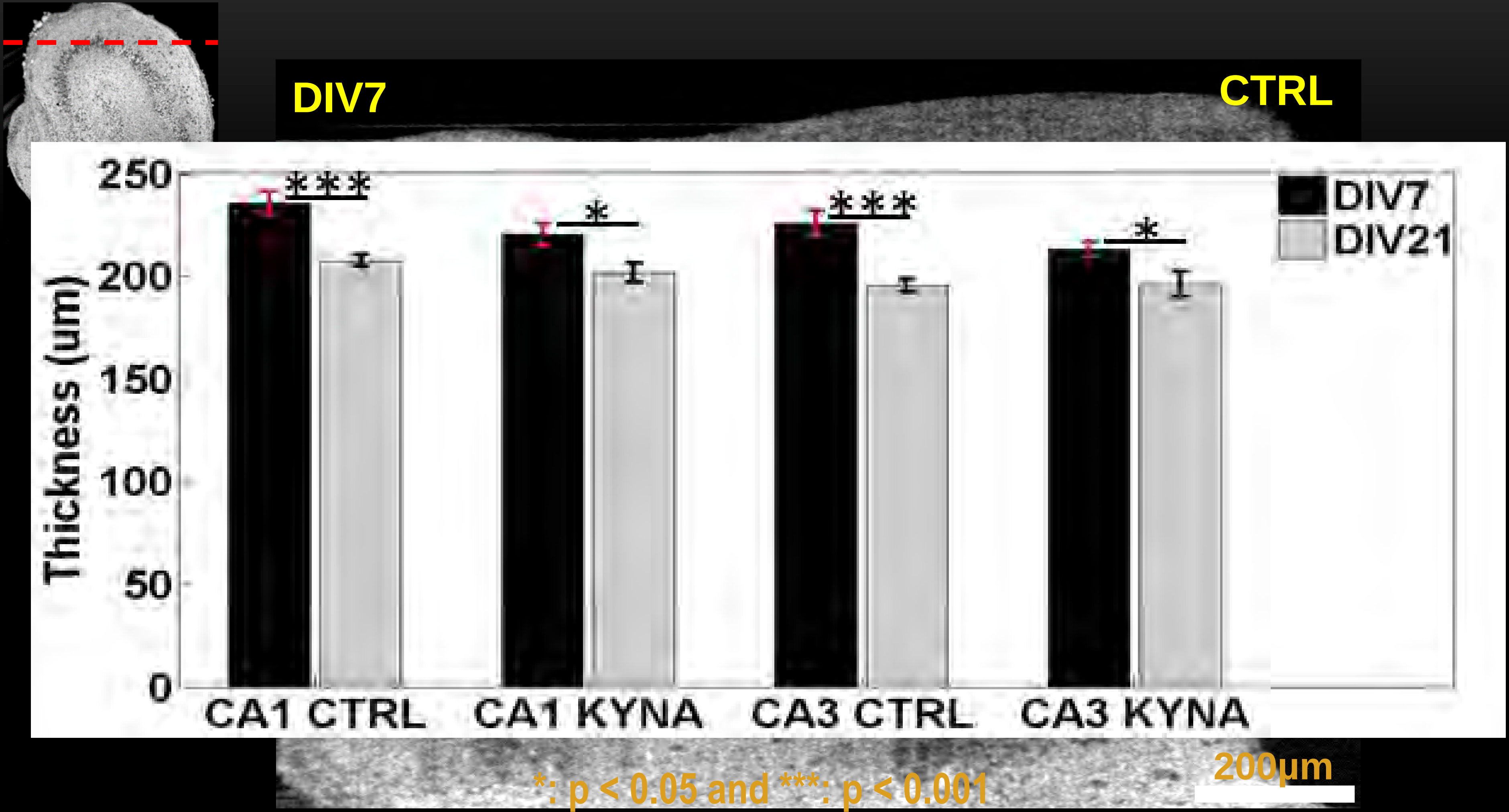
DIV7: n=18; DIV14: n=11; DIV21: n=18; DIV28: n=9

The cross-sectional images are from CA3 region

Neuroprotective Effects of KYNA



Slice thickness in control and KYNA group



*: $p < 0.05$ and ***: $p < 0.001$

n = 9 in each group

The cross-sectional images are from CA3 region

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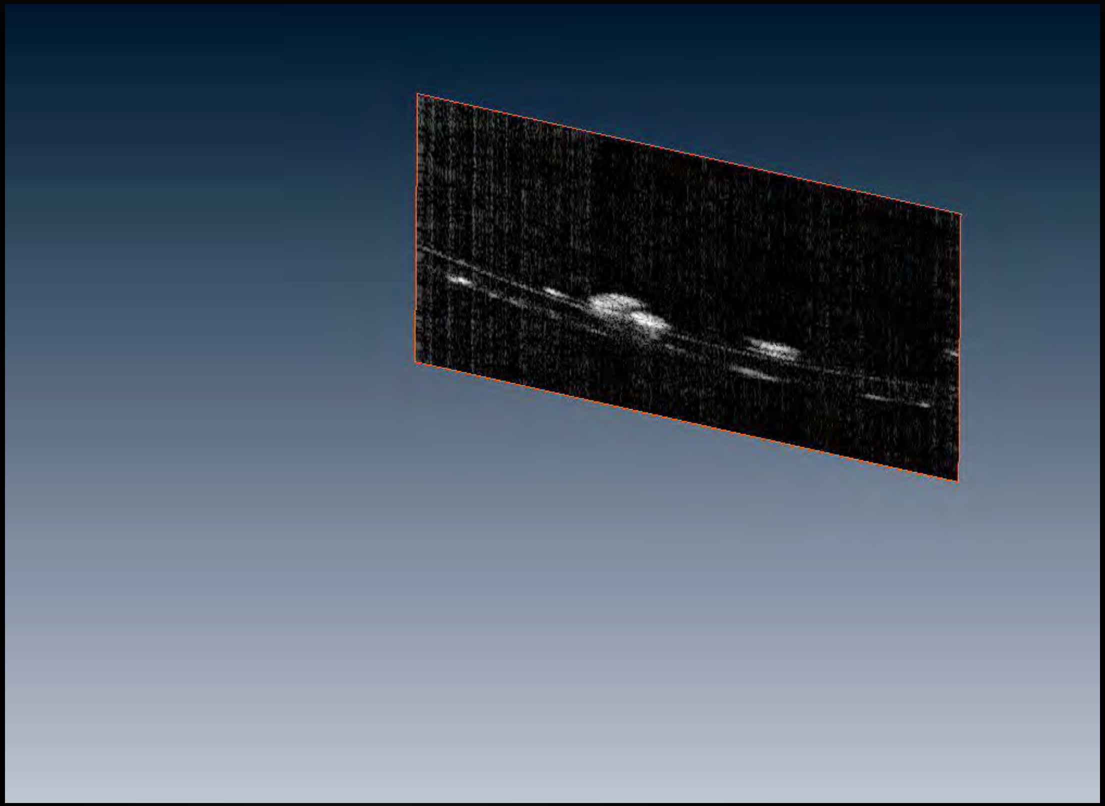
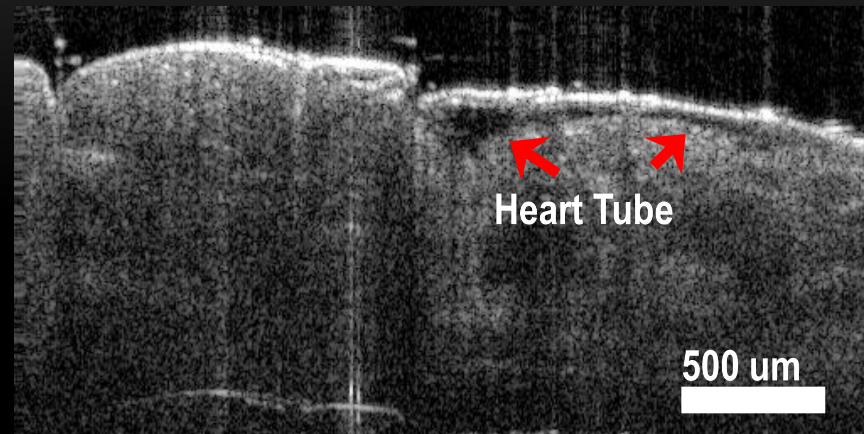
OCT IMAGING OF THE DROSOPHILA HEART



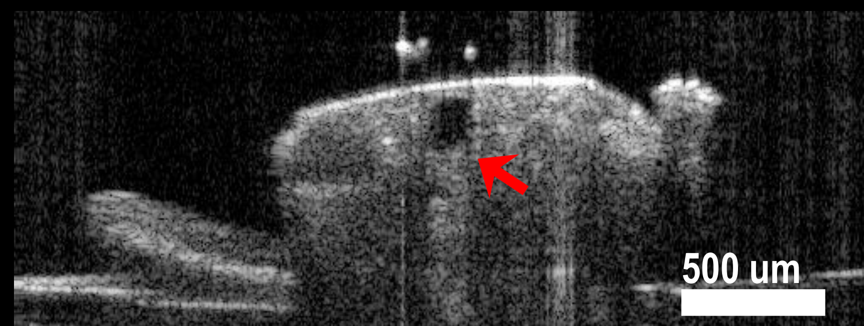
Collaboration with Drs. Rudolph Tanzi and Airong Li at MGH

OCT IMAGING OF THE DROSOPHILA HEART

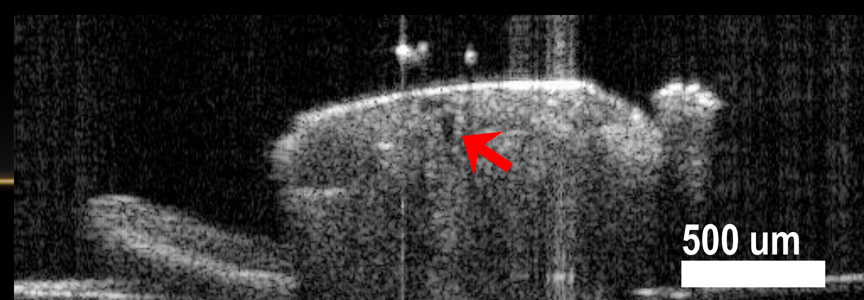
Longitudinal View



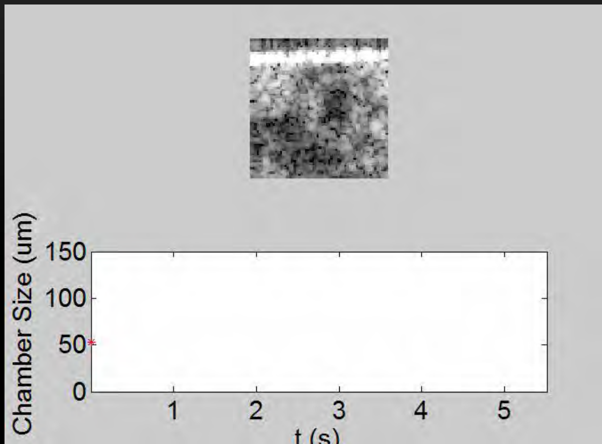
Cross-sectional View
- Diastolic Phase



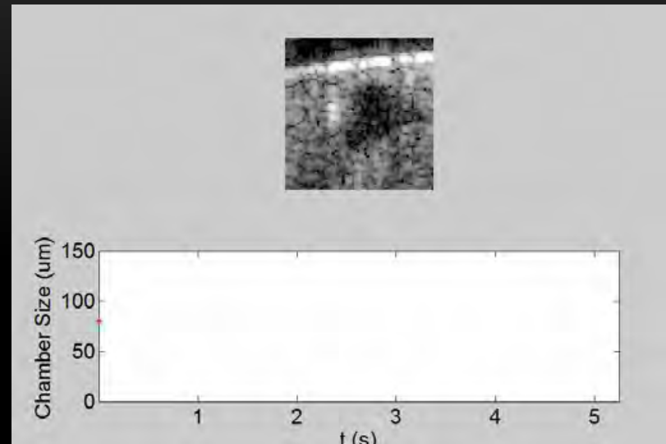
Cross-sectional View
- Systolic Phase



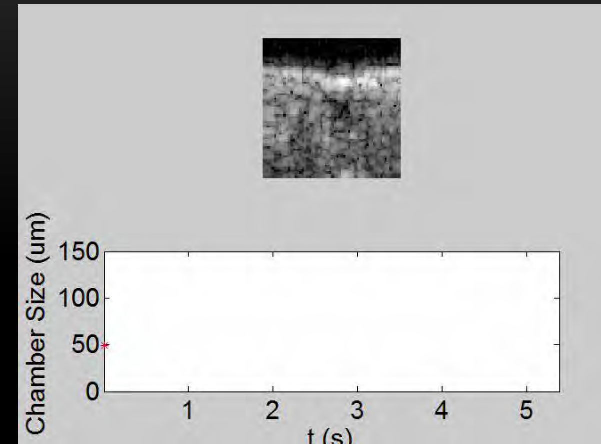
OCT Imaging of the Drosophila Heart



24B-GAL4/+
(Control)



UAS-dPsn; 24B-GAL4
(Over-expression of *dPsn*)



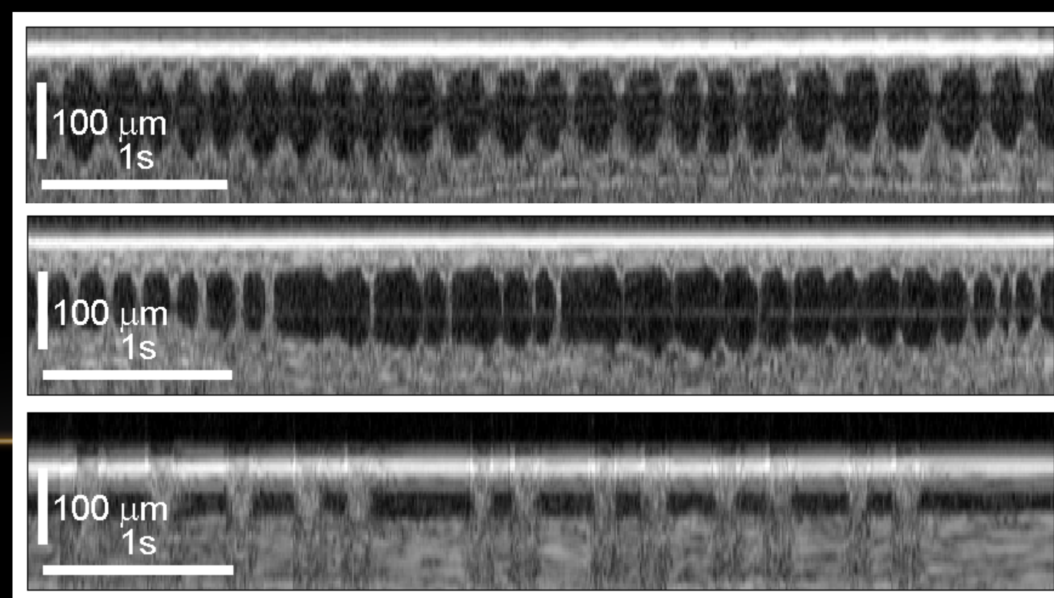
UAS-dPsnRNAi; 24B-GAL4
(Silencing of *dPsn*)

M-Mode Imaging

Control

Over-expression of *dPsn*

Silencing of *dPsn*



GROUP RESULTS

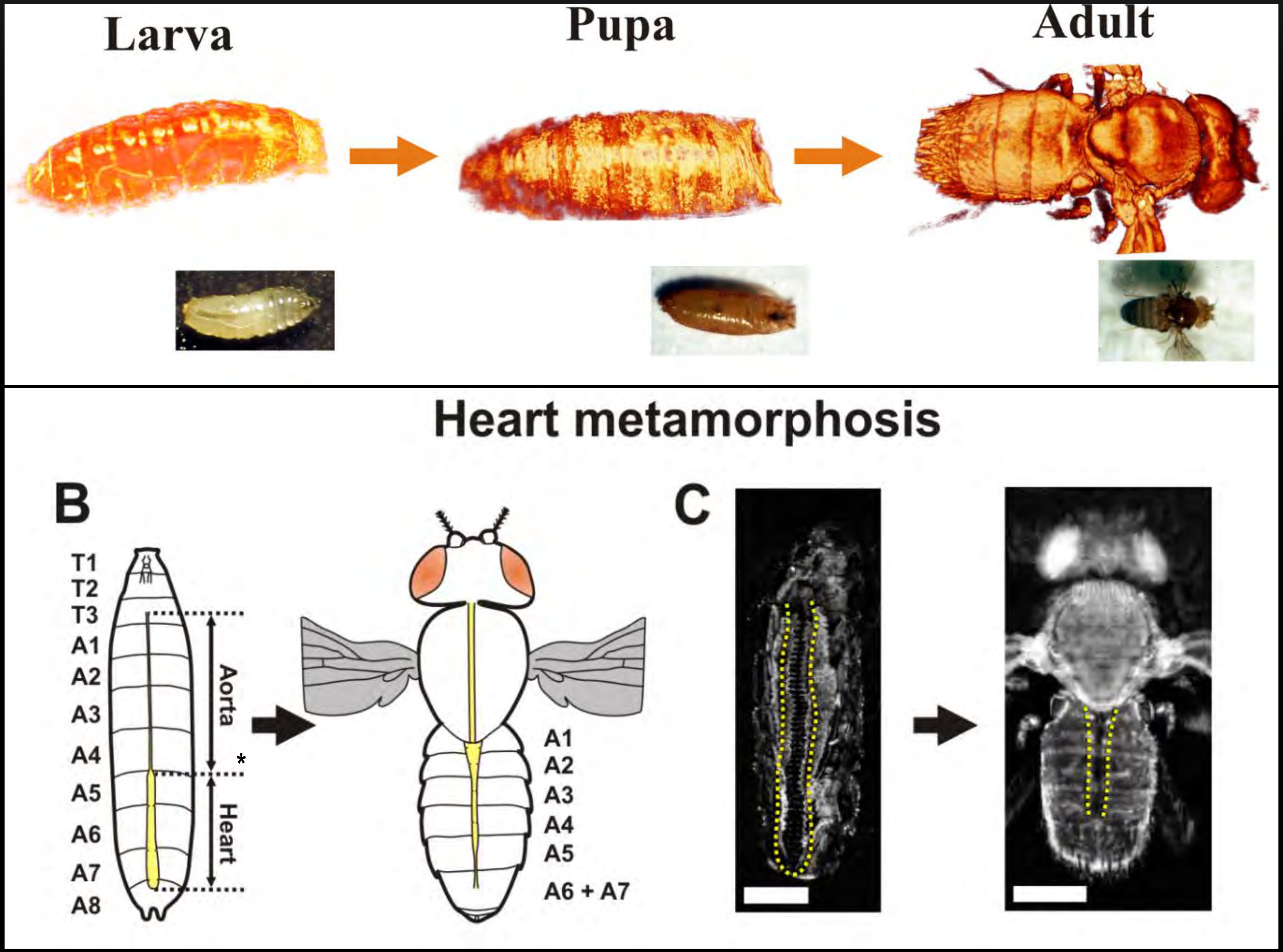
	7 Day old				30 Day old			
Parameters	24B-GAL4/+ (Control) N=31	UAS-dPsn; 24B-GAL4 N=31	UAS-dPsn^{RNAi}; 24B-GAL4 N=24	Total N=86	24B-GAL4/+ (Control) N=30	UAS-dPsn; 24B-GAL4 N=28	UAS-dPsn^{RNAi}; 24B-GAL4 N=28	Total N=86
HR (BPM)	262 ± 10	307 ± 11 *** ↑	231 ± 11 * ↓	269 ± 7	254 ± 10	284 ± 11 * ↑	190 ± 8 ****## ↓	243 ± 7 ##↓
ESD (µm)	20 ± 2	14 ± 2	17 ± 2	17 ± 1	31 ± 4 ##↑	20 ± 4 *↓	14 ± 3 ****↓	22 ± 2 #↑
EDD (µm)	67 ± 2	56 ± 3 *↓	52 ± 4 **↓	59 ± 2	78 ± 4 #↑	66 ± 4 *↓ #↑	73 ± 4 #### ↑	73 ± 2 ####↑
FS (%)	69 ± 4	76 ± 3	67 ± 4	71 ± 2	62 ± 4	69 ± 5	83 ± 4 *** ↑##↑	71 ± 2

HR: Heart rate; EDD: End-diastolic dimension; ESD: End-systolic dimension; FS: Fractional shortening

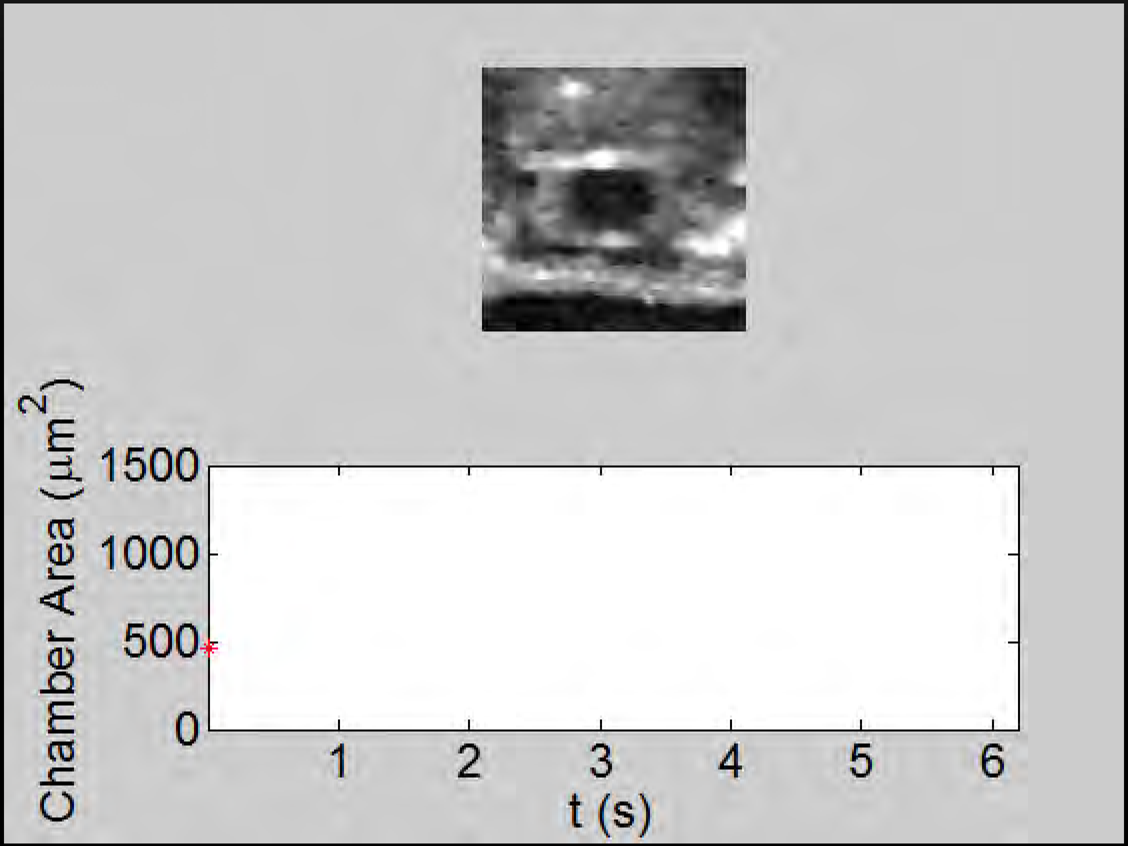
*p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001: vs. Age-matched controls;
#p<0.05, ## p<0.01, ### p<0.001, #### p<0.0001: vs. 7-day old age group
↑ shows significant increase; ↓ shows significant decrease

Li, Zhou, *et al., Curr. Alzheimer Res.*, 8(3):313-322, 2011

DROSOPHILA HEART DEVELOPMENT

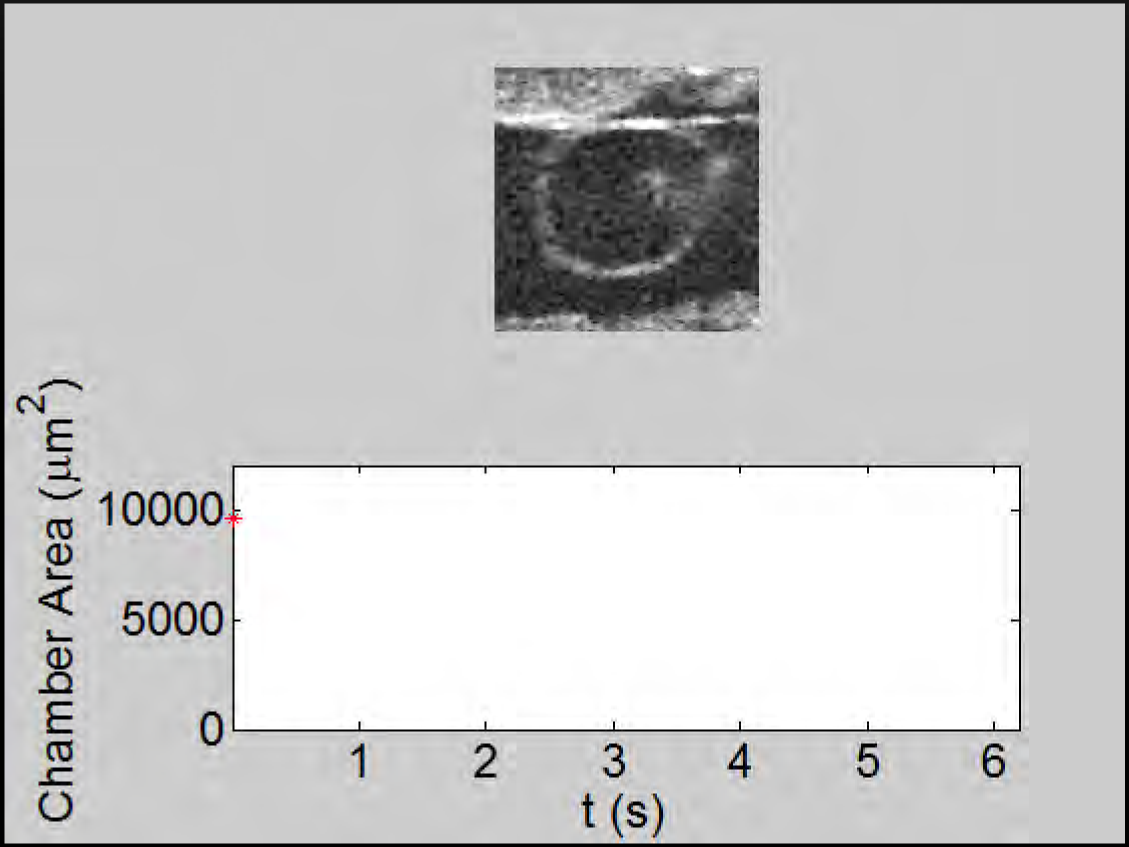


DROSOPHILA HEART DEVELOPMENT



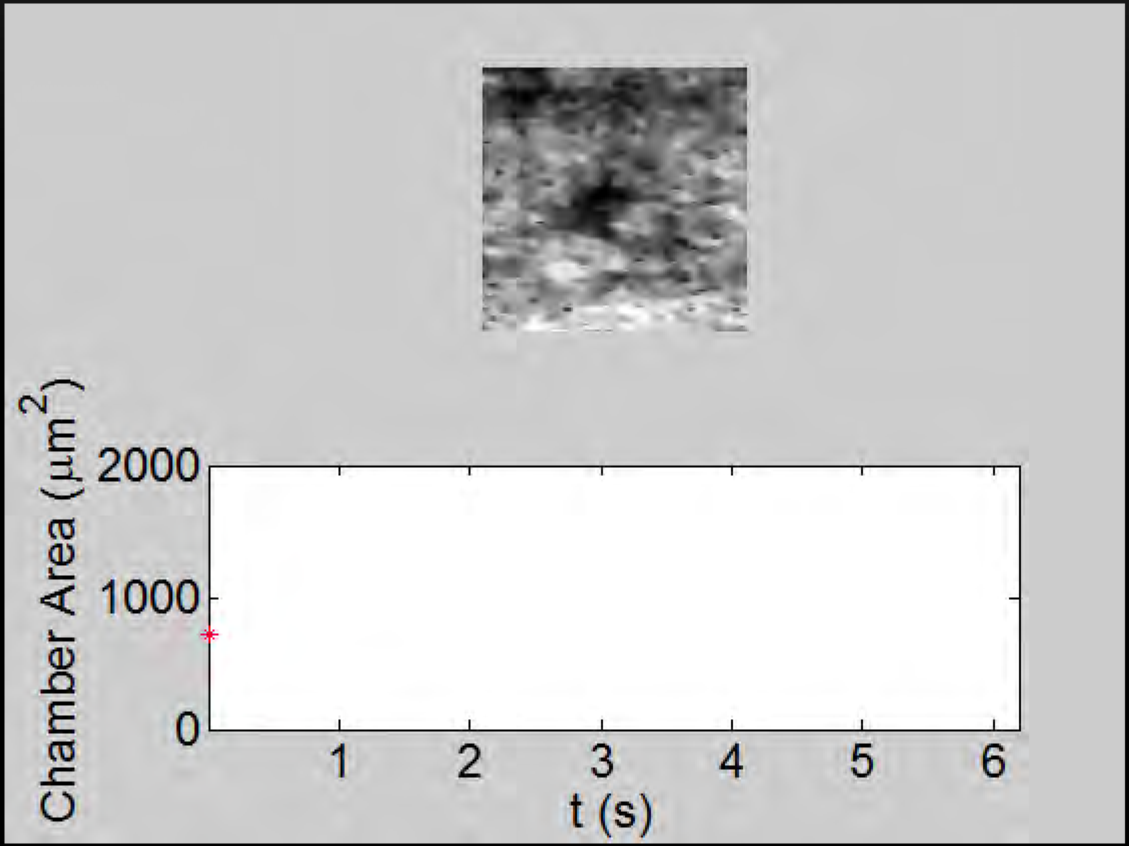
2nd instar larva – L2

DROSOPHILA HEART DEVELOPMENT



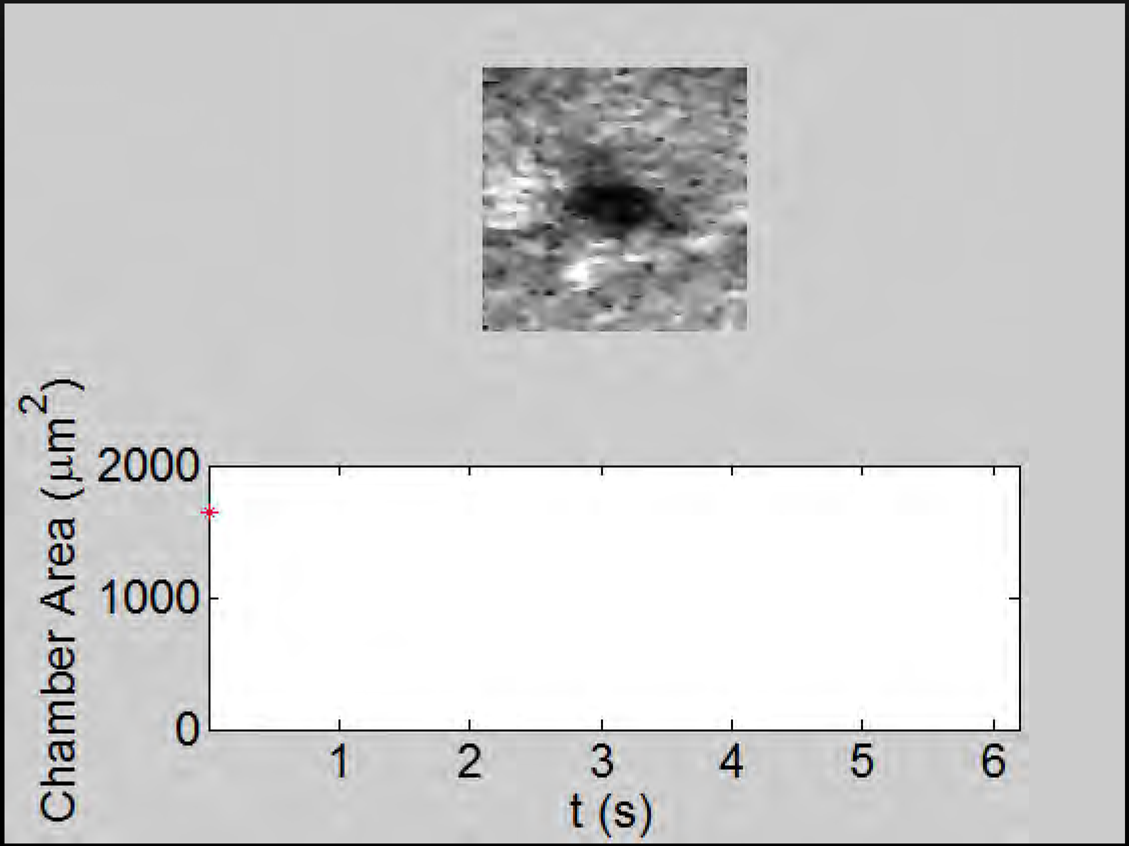
3rd instar larva – L3

DROSOPHILA HEART DEVELOPMENT



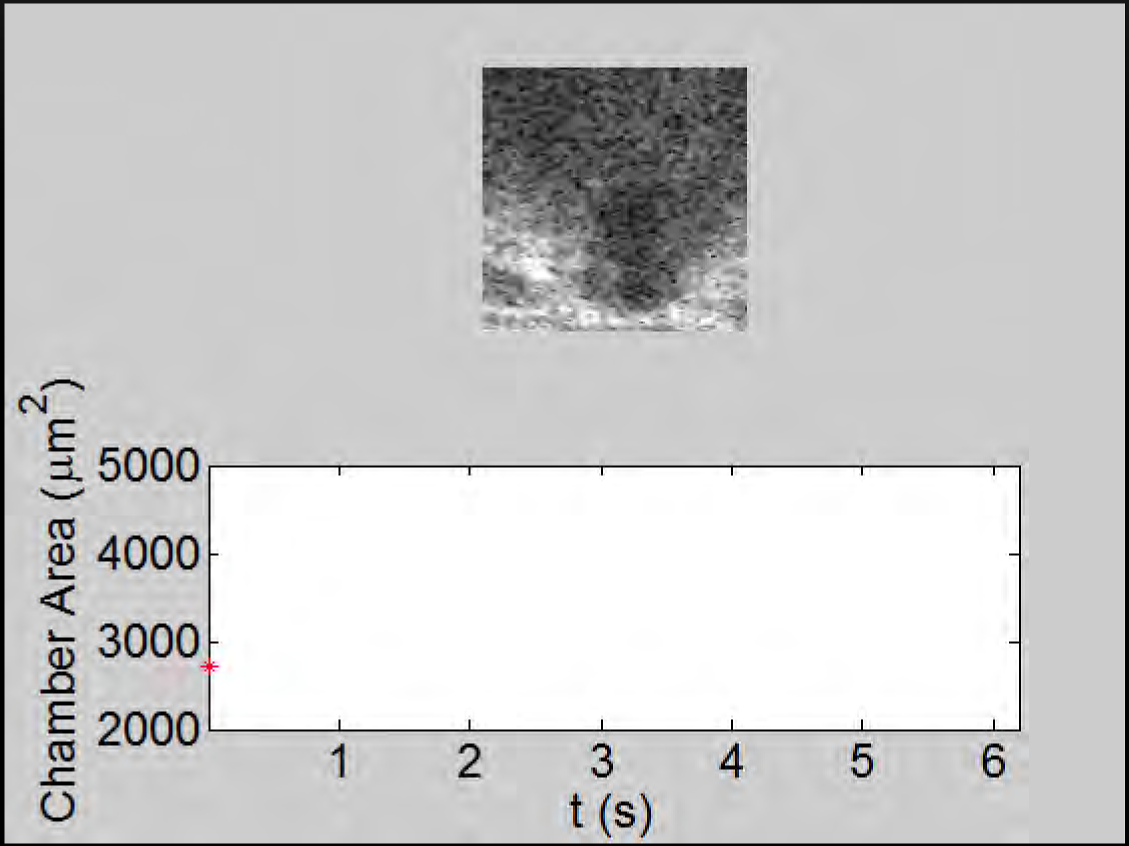
Pupa day 1, 8hr – PD1

DROSOPHILA HEART DEVELOPMENT



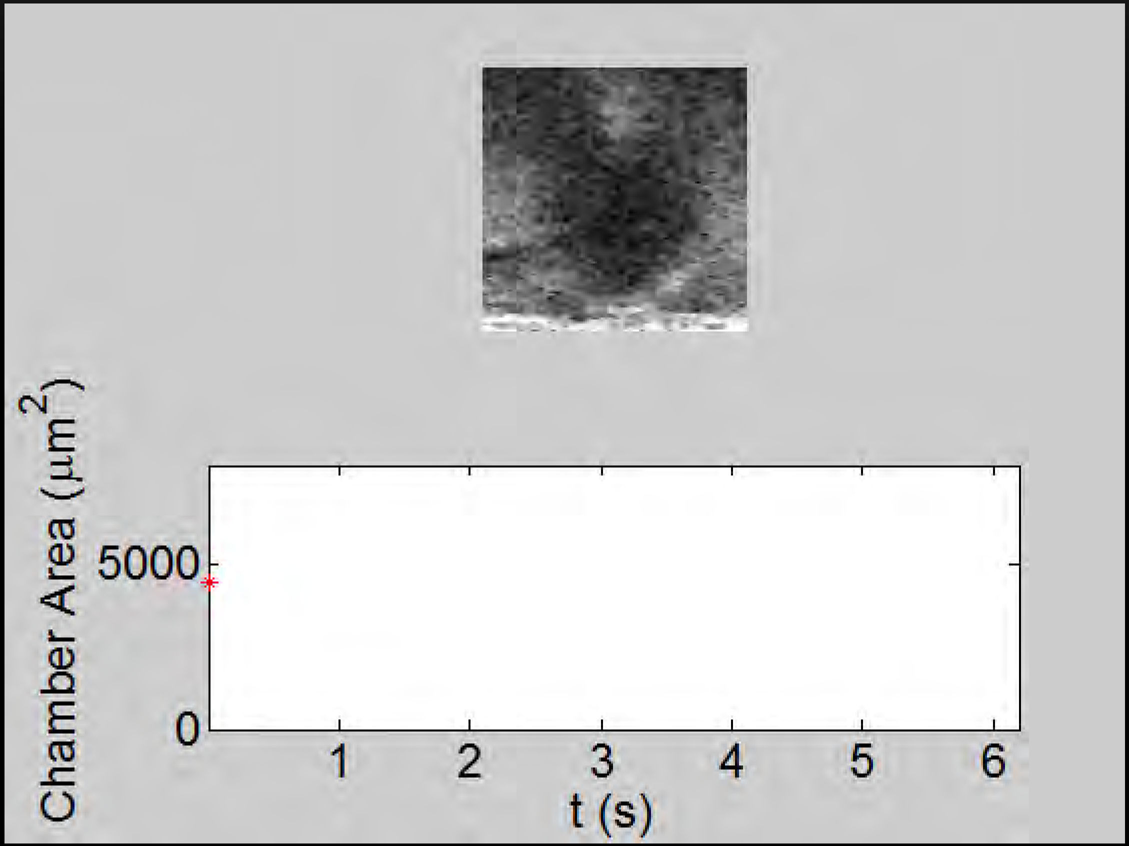
Pupa day 2, 32hr – PD2

DROSOPHILA HEART DEVELOPMENT



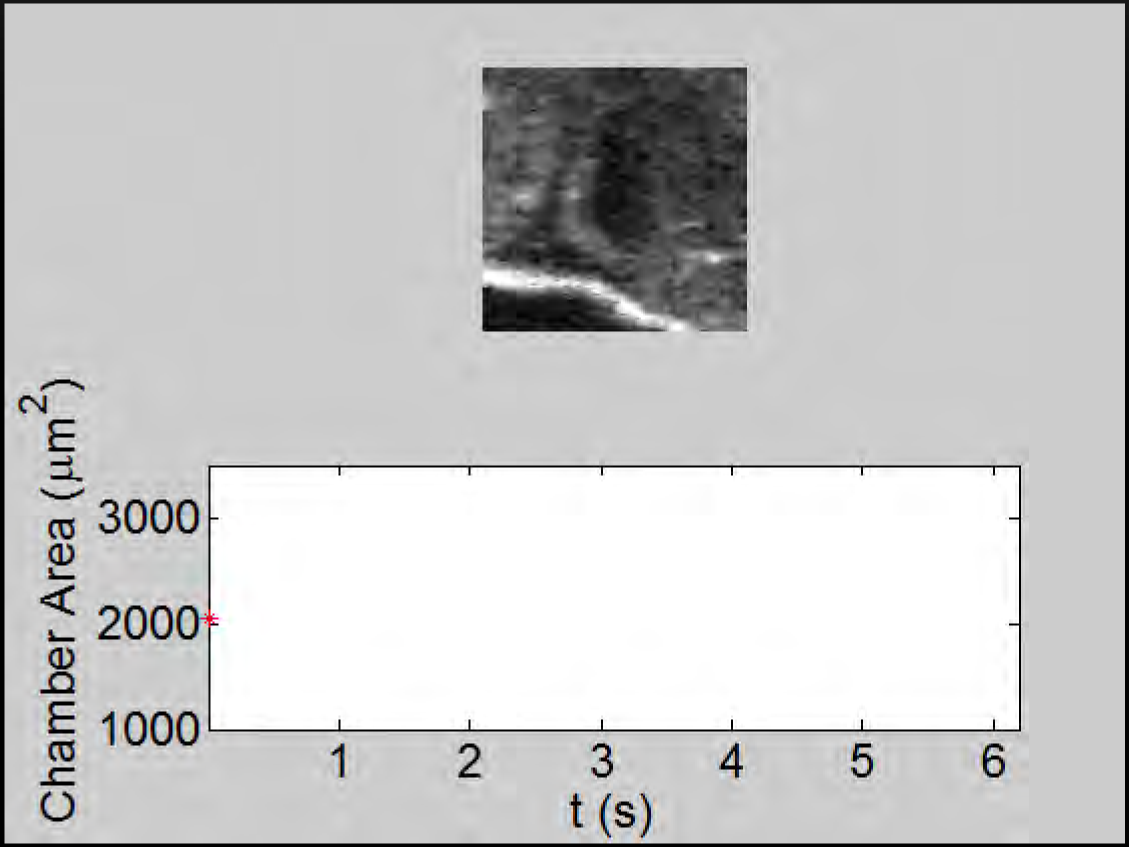
Pupa day 3, 72hr – PD3

DROSOPHILA HEART DEVELOPMENT



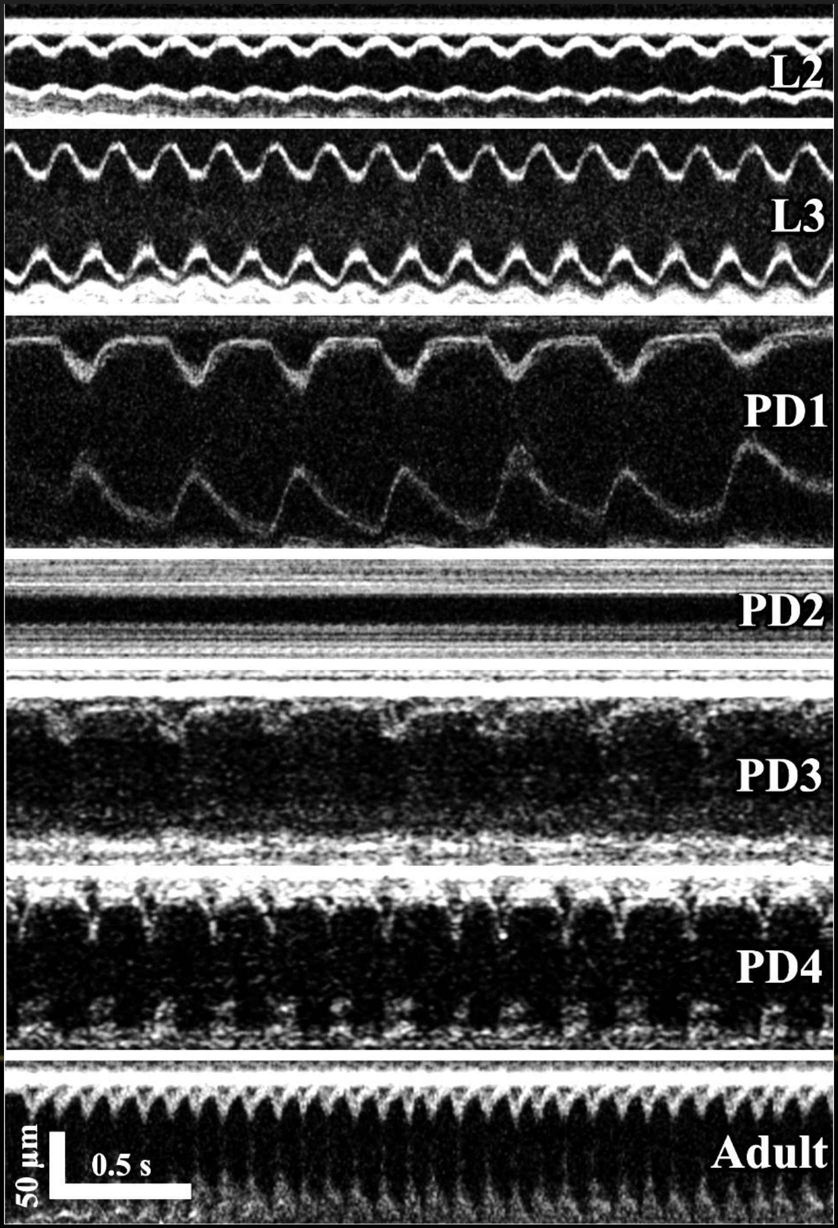
Pupa day 4, 88hr – PD4

DROSOPHILA HEART DEVELOPMENT

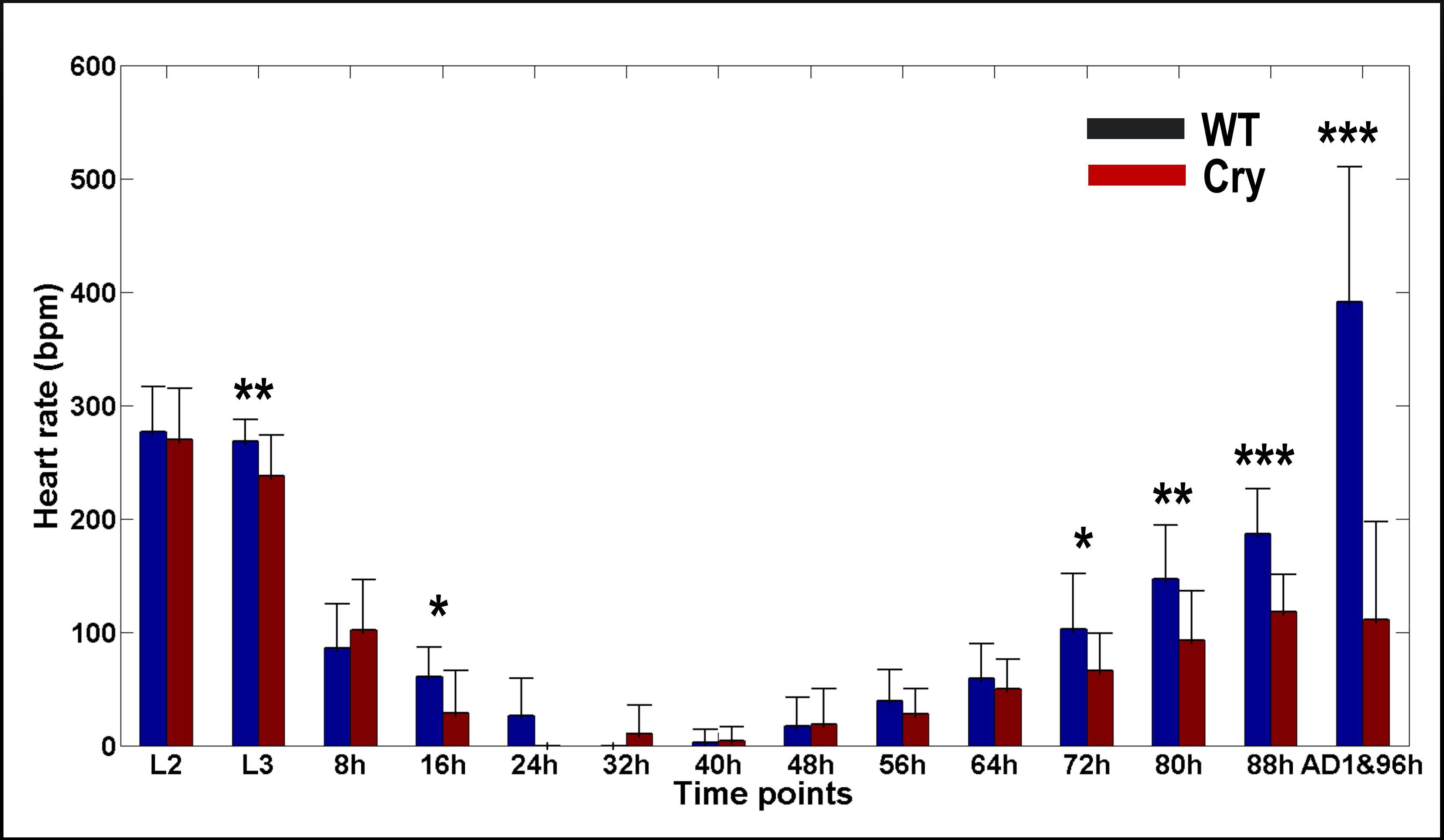


Adult day 1

DROSOPHILA HEART DEVELOPMENT



DROSOPHILA HEART RATE



A. Alex, *et al*, *under review*

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Summary

- Various imaging modalities can be used for clinical and research applications
- Optical imaging provides unique advantages (resolution, contrast, etc.)
- Optical biopsy can be achieved by OCT and OCM
- None-invasive evaluation of epilepsy models in rat brain slices
- None-invasive characterization of heart function in fruit flies

ECE 368/468, BioE 368/468 Introduction to Biophotonics / Optical Biomedical Imaging

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Thank you!