Health Consequences of Maternal Obesity on F1 Offspring

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- **Previous Works**
  - Maternal nutrient restriction alters gene expression in the ovine fetal heart
  - Maternal nutrient restriction predisposes ventricular remodeling in adult sheep offspring
  - Evidence for similar changes in offspring phenotype following either maternal undernutrition or overnutrition: potential impact on fetal epigenetic mechanisms

Maternal nutrient restriction alters gene expression in the ovine fetal heart

Fetal heart weight (g)				Organ wt/fetus wt (%)		
Item	Control $n = 9$	Restricted $n = 8$	*P*	Control $n = 9$	Restricted $n = 8$	$^{*}P$
Fetus	319.1 ± 10.78	221.2 ± 11.96	0.0002	—	—	—
LV	0.94 ± 0.07	0.94 ± 0.07	NS	0.29 ± 0.02	0.42 ± 0.02	0.0041
RV	0.66 ± 0.04	0.61 ± 0.05	NS	0.21 ± 0.02	0.27 ± 0.02	0.0245
Septum	0.43 ± 0.04	0.39 ± 0.04	NS	0.14 ± 0.01	0.17 ± 0.01	0.0773

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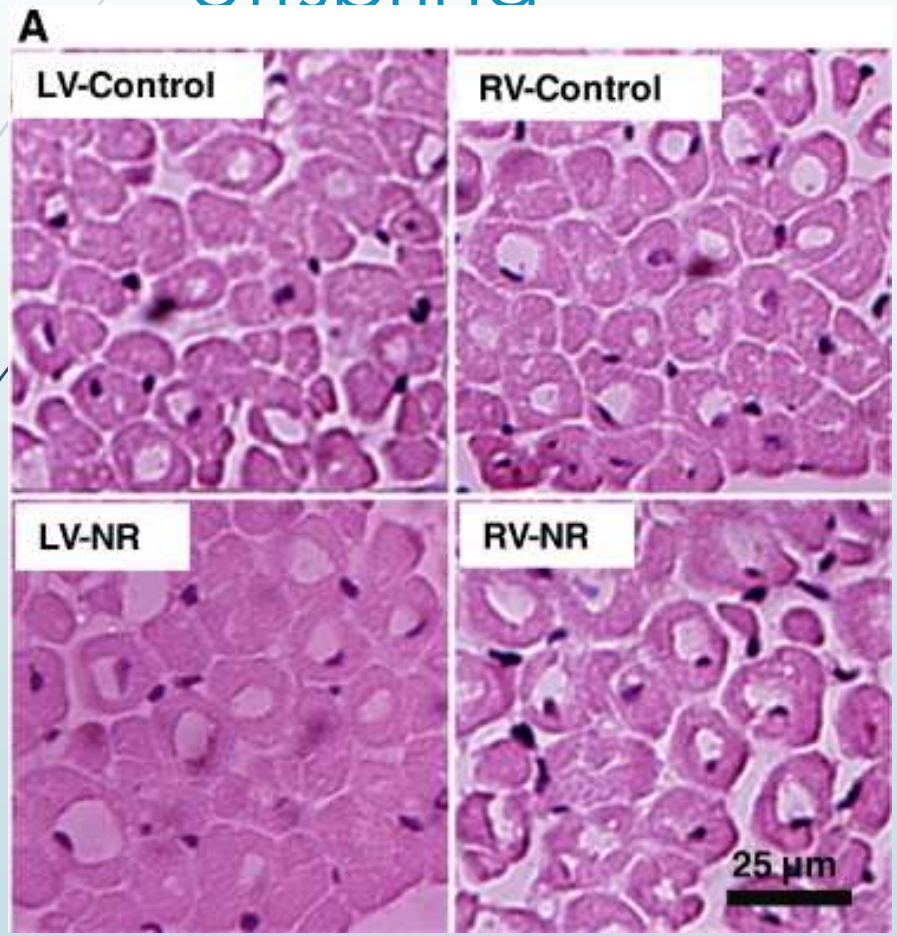
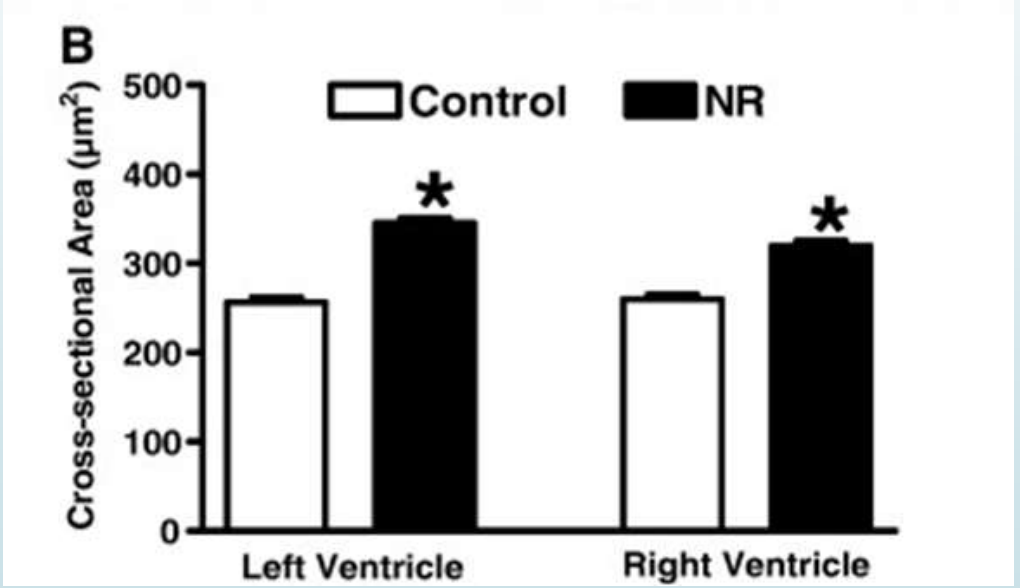
Maternal nutrient restriction predisposes ventricular remodeling in adult sheep offspring



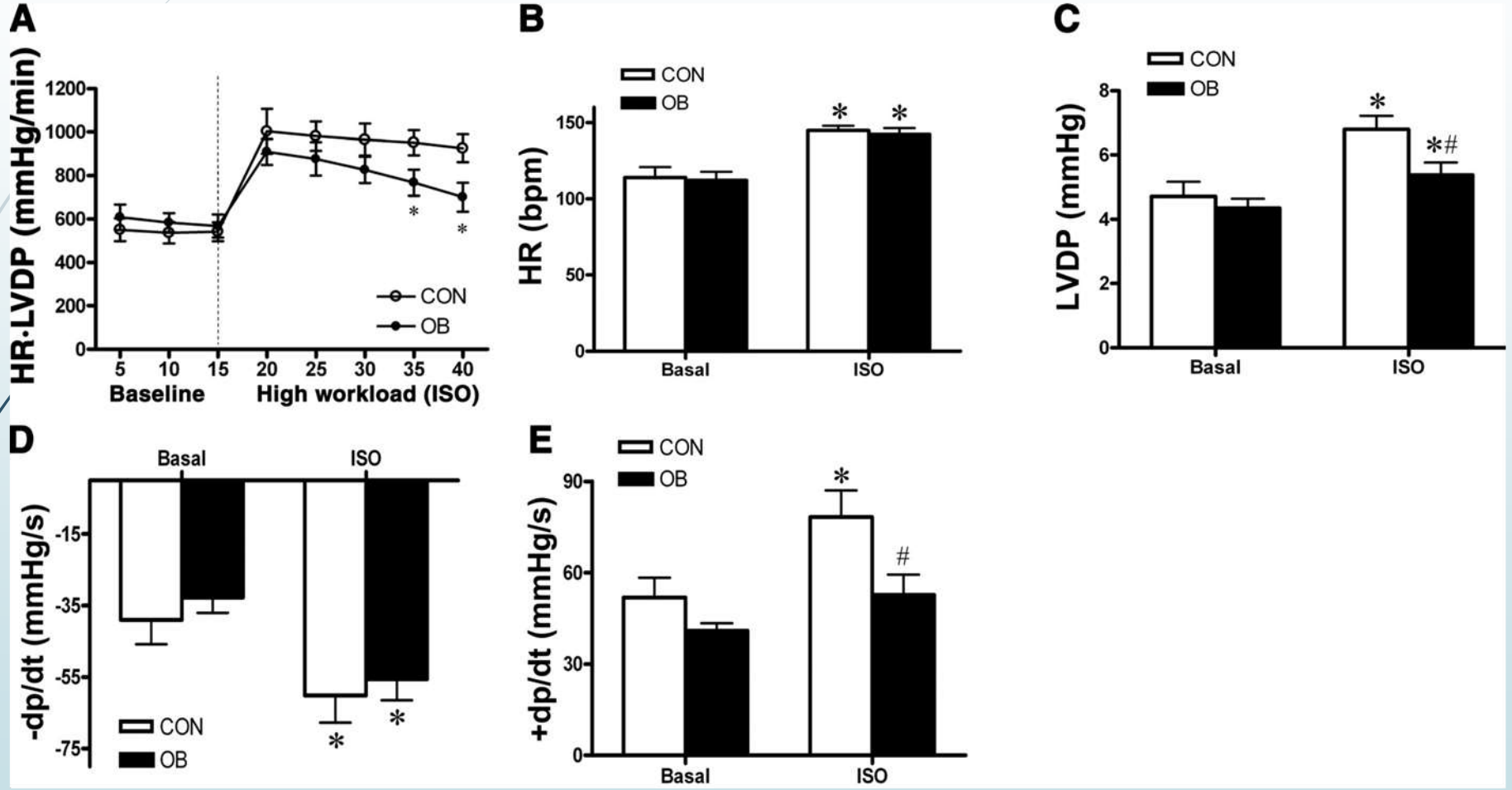


Evidence for similar changes in offspring phenotype following either maternal undernutrition or overnutrition: potential impact on fetal epigenetic mechanisms

	NR	OB
Mid-gestation (Day 78) fetus		
Fetal weight	–	+
Crown rump length	–	+
Liver weight	–	+
Pancreatic β-cell numbers	+	+
Cardiac ventricular weight/fetal weight	+	+
Plasma glucose	–	+
Plasma insulin	ND	+
Late gestation (Day 135) fetus		
Fetal weight	ND	ND
Fetal crown rump length	ND	ND
Liver weight	ND	ND
Pancreatic β-cell numbers	–	–
Cardiac ventricular weight/fetal weight	+	+
Newborn lambs, unsuckled		
Birth weight	ND	ND
Crown rump length	ND	ND
Plasma glucose	+	+
Plasma insulin	–	–
Adult offspring		
Growth rate	+	+
Insulin resistance	+	+
Plasma leptin	+	+
Adiposity	+	+
Appetite	+	+

	NR	OB
Mid-gestation (Day 78) fetus		
Fetal weight	–	+
Crown rump length	–	+
Liver weight	–	+
Pancreatic β-cell numbers	+	+
Cardiac ventricular weight/fetal weight	+	+
Plasma glucose	–	+
Plasma insulin	ND	+
Late gestation (Day 135) fetus		
Fetal weight	ND	ND
Fetal crown rump length	ND	ND
Liver weight	ND	ND
Pancreatic β-cell numbers	–	–
Cardiac ventricular weight/fetal weight	+	+
Newborn lambs, unsuckled		
Birth weight	ND	ND
Crown rump length	ND	ND
Plasma glucose	+	+
Plasma insulin	–	–
Adult offspring		
Growth rate	+	+
Insulin resistance	+	+
Plasma leptin	+	+
Adiposity	+	+
Appetite	+	+

Figure 4. Fetal cardiac contractile function at d 135 of gestation, assessed by the Langendorff perfusion system.



Jingying Wang et al. FASEB J 2010;24:2066-2076

Summary

- Similarities with gestational over nutrition and under-nutrition
- Maternal obesity decreases cardiac ability
- Under nourishment during gestation leads to altered cardiac gene expression and remodeled ventricular structure

My Work

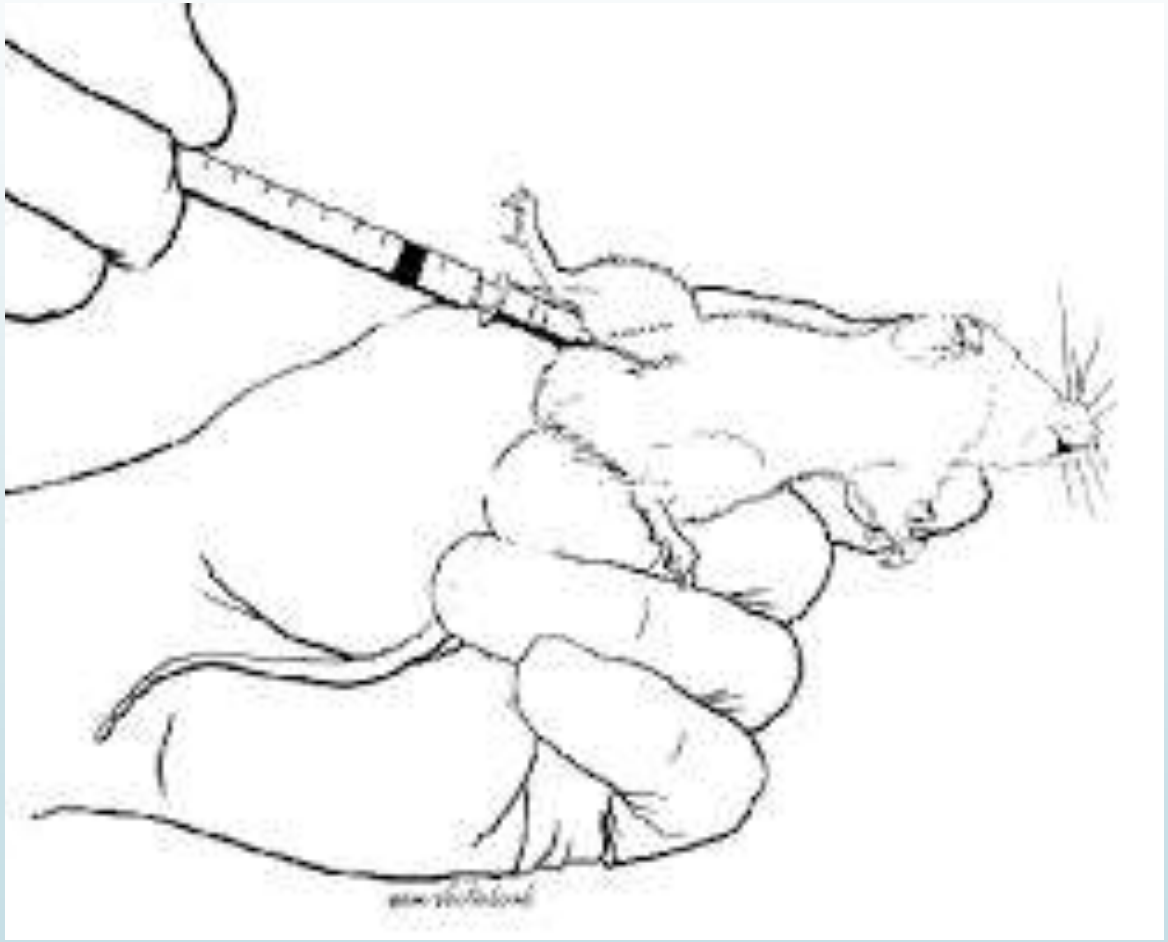
- Preliminary study with mice
  - Cardiomyocyte Isolation
  - IonOptix SoftEdge system
  - Measured individual cardiomyocytes contractile properties
    - Contractile Force
    - Sarcomere Length
    - Ca^{2+} Activity

Cardiomyocyte Isolation

- Anesthetize the mouse
- Surgically remove the heart
- Catheterize the aorta
- Feed buffer solution through catheter
- Add Digestive enzymes to buffer
- Dice digested tissue with scissors
- Add Ca^{++} and digestive enzymes
- Finalize solution in O_2

Anesthesia

Abdominal administration of ketamin HCL

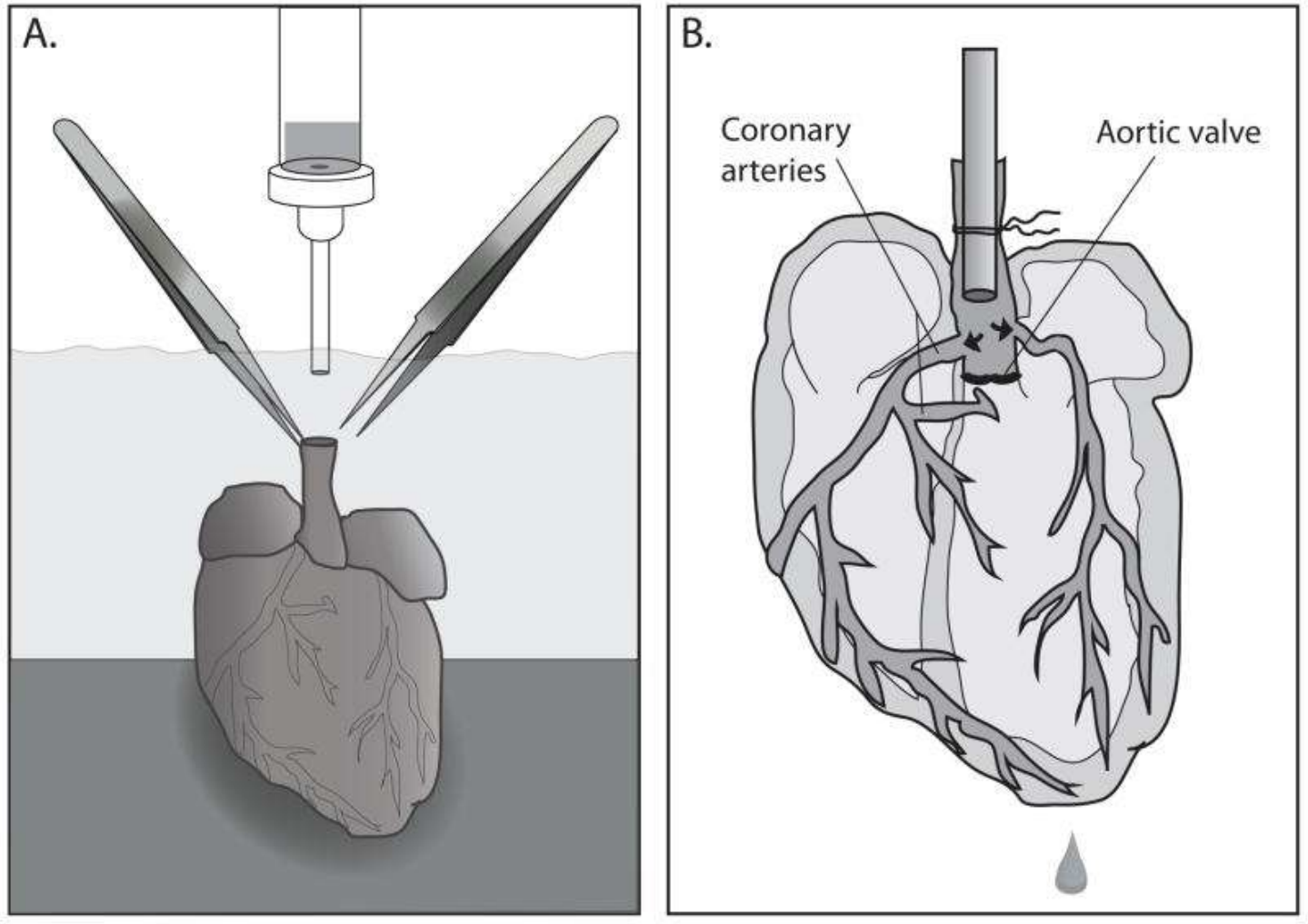


Surgical removal of the heart

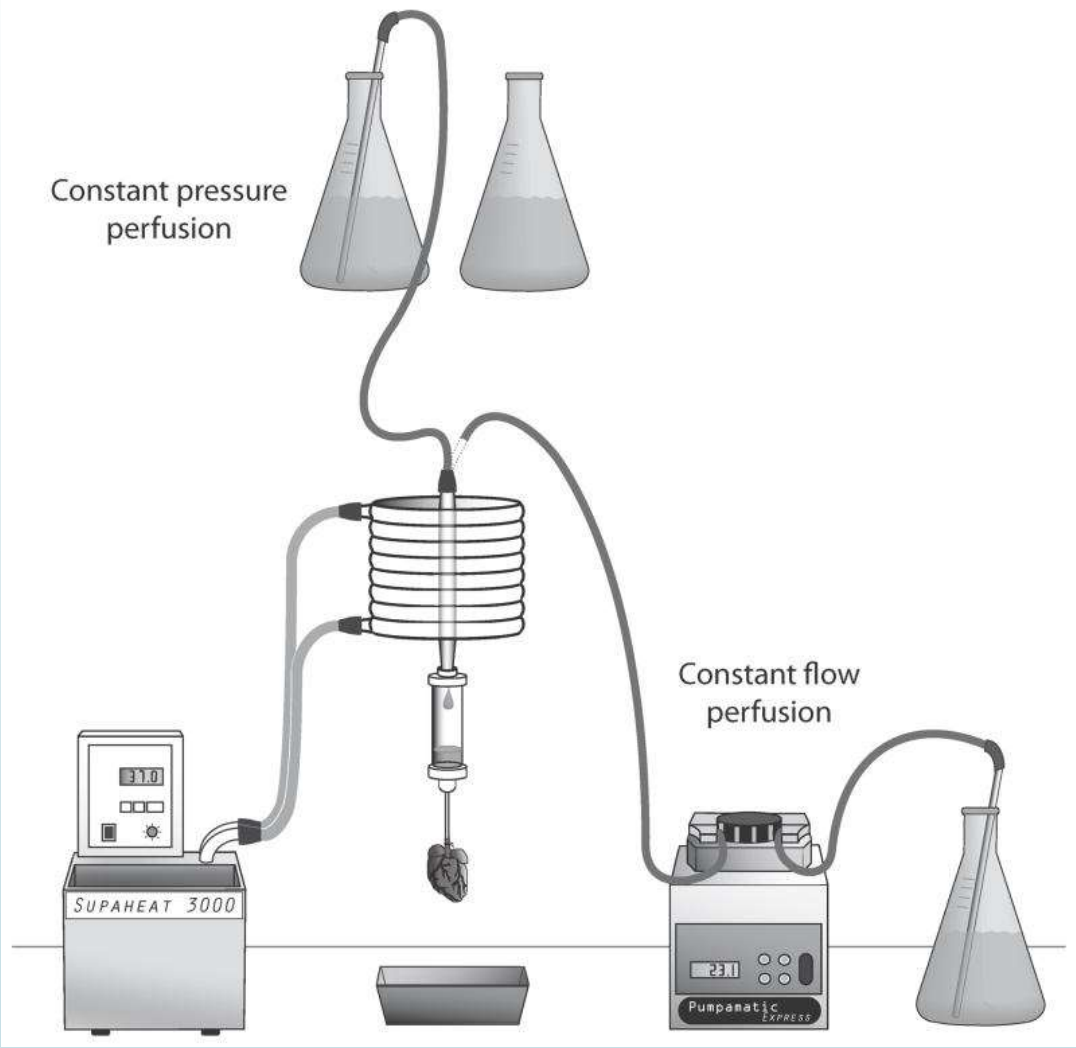
Proper length of the aorta is crucial

Catheterization

Most Important Step!
-Cell death is rapid



Cardiomyocyte Isolation

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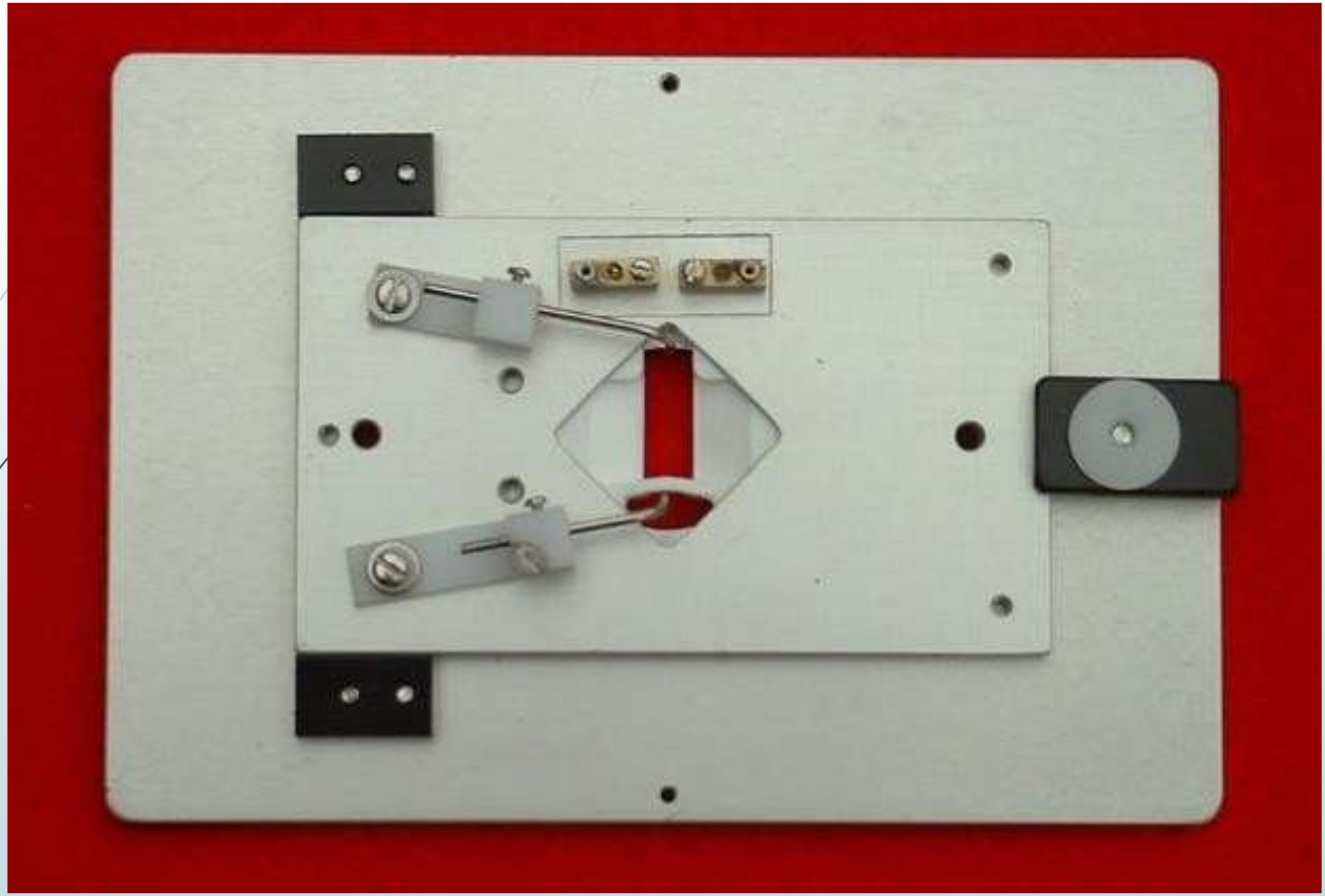

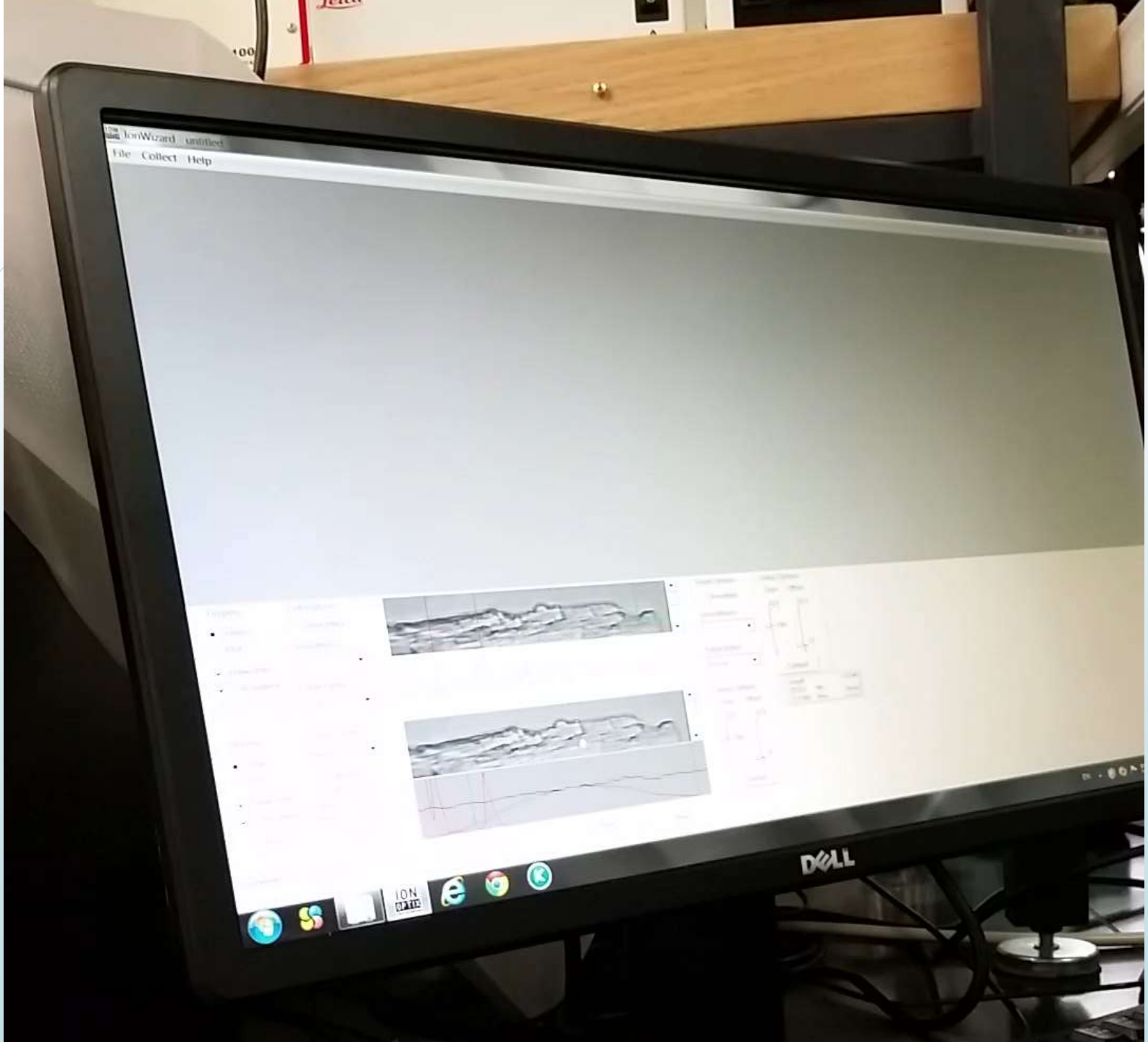
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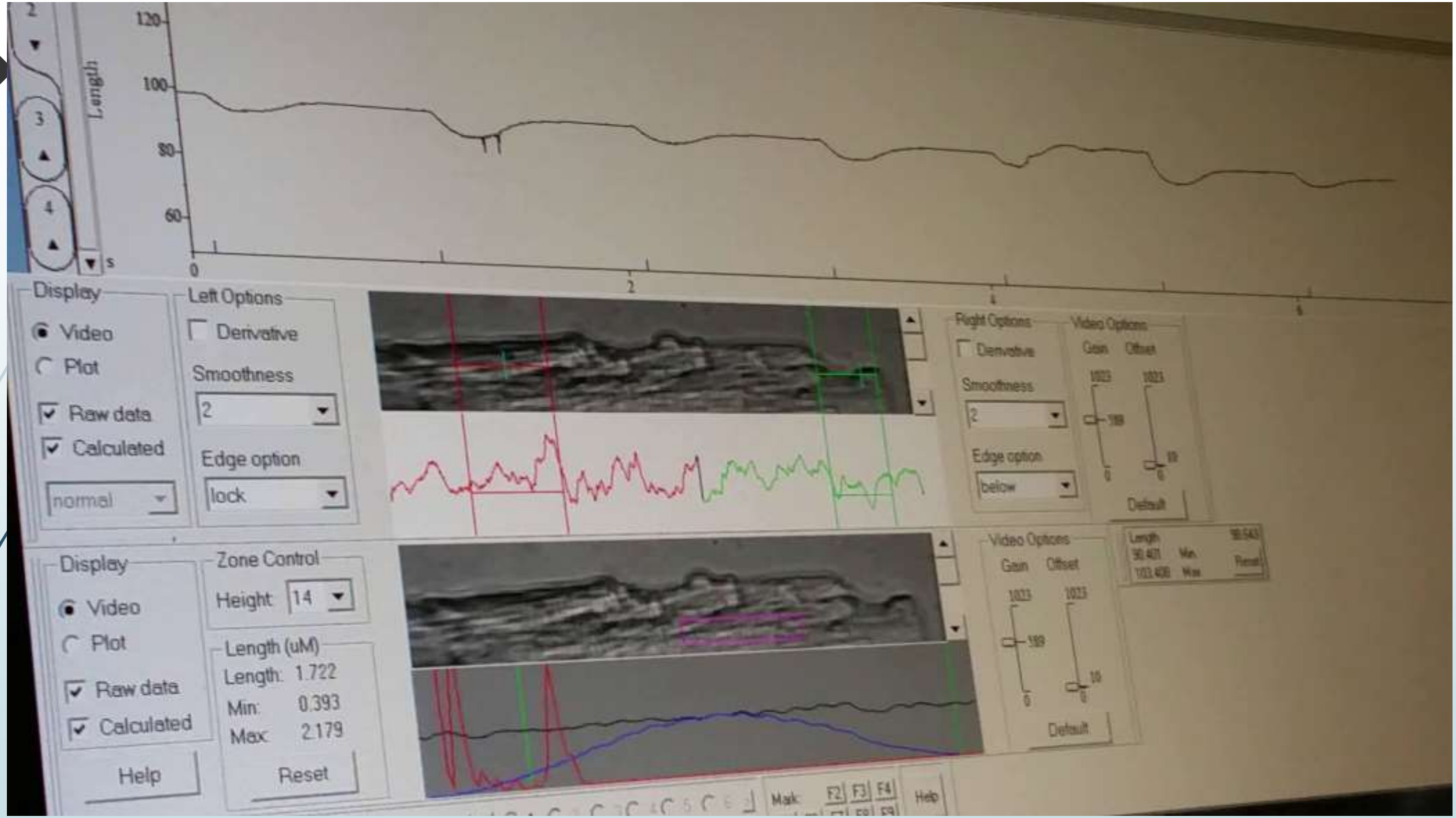
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Data Recorded

- 30-50 myocytes per subject
- 50 readings per myocyte
  - Sarcomere length, cell length, Ca^{++} concentration, contractile force

Works Referenced

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