Pathology and physiology of the coronary circulation in salmonid fish

Who did the work?

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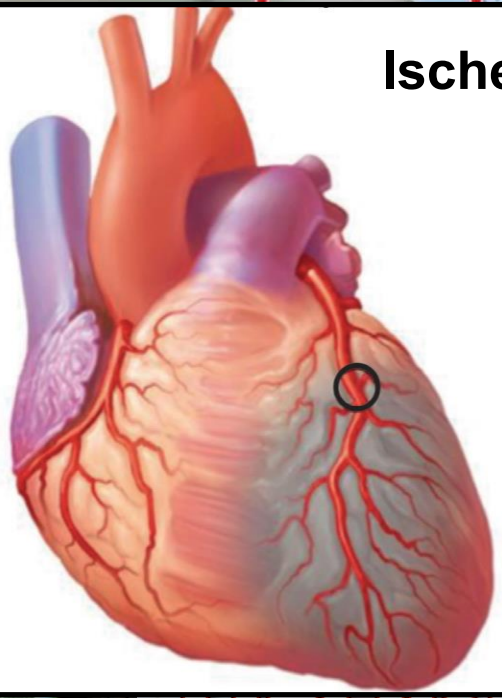
Ischemic heart disease



Plaque rupture/erosion with occlusive thrombus

Plaque rupture/erosion with non-occlusive thrombus

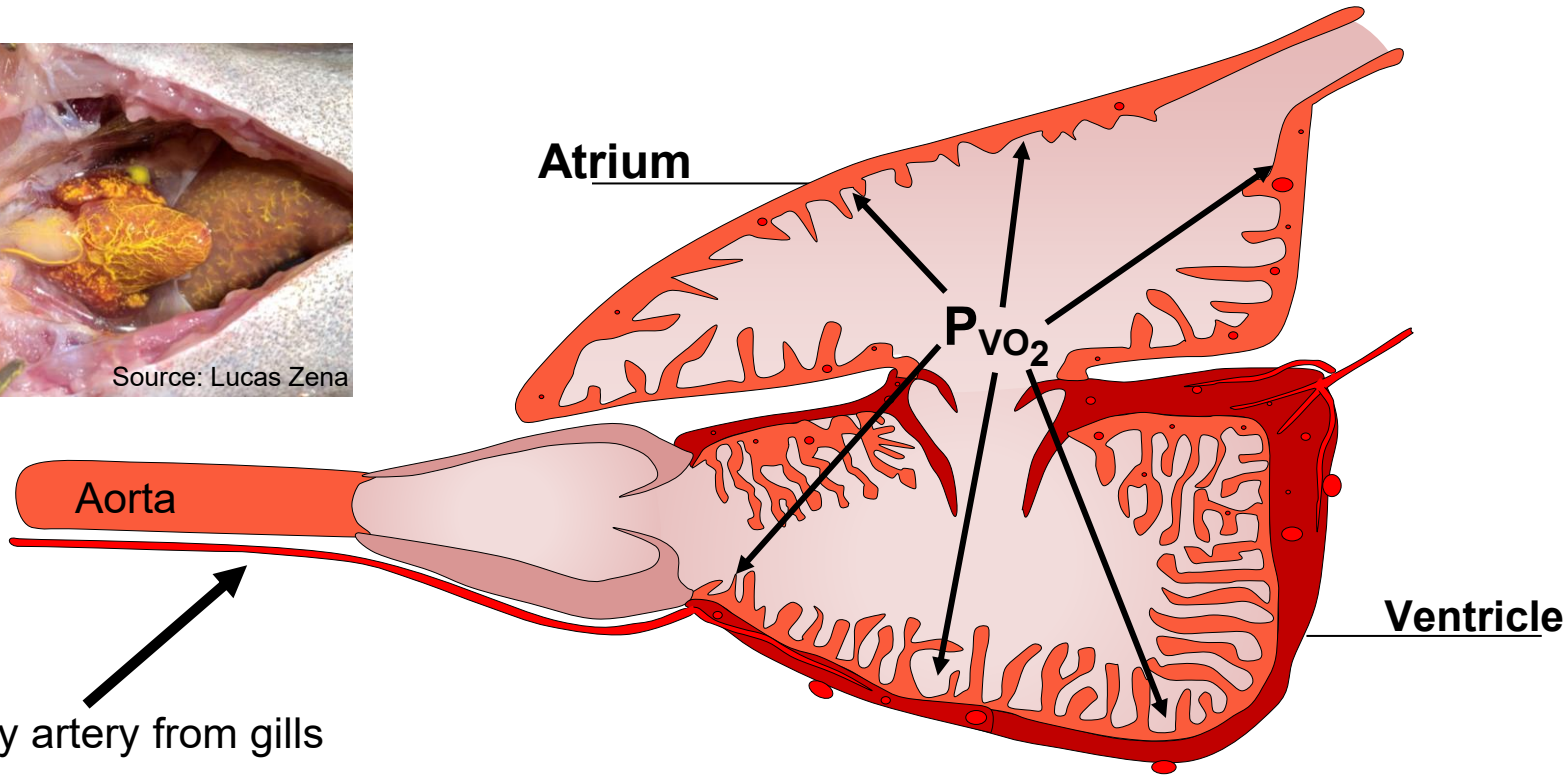
Oxygen supply to the salmonid heart
-two ways:

1) Luminal venous

Venous O_2 tension drives diffusion to spongy myocardium

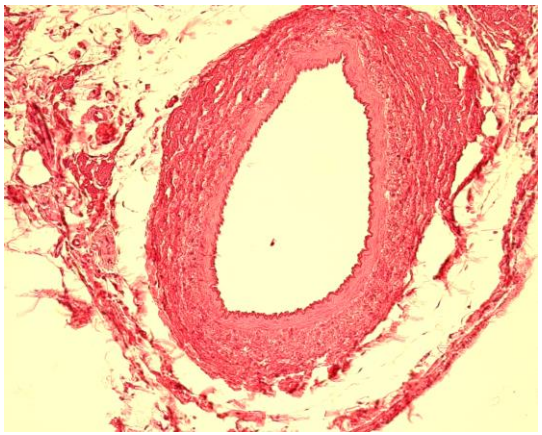
2) Coronary arterial (in some teleosts, e.g., salmonids)

Arterial O_2 supply to compact (and spongy) myocardium



Farrell, Eliason, Sandblom and Clark (2009) Fish cardiorespiratory physiology in an era of climate change. *Canadian Journal of Zoology*

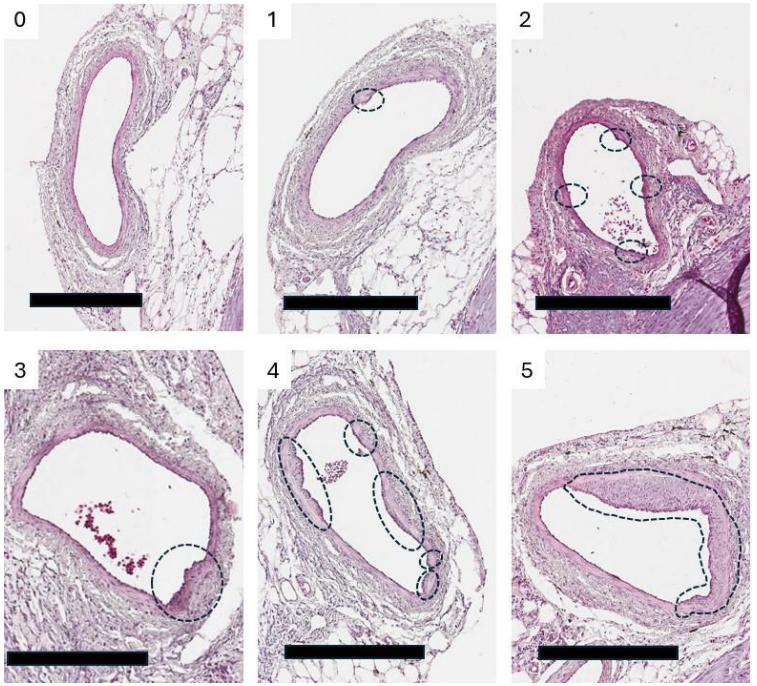
Coronary arteriosclerosis -an increasing welfare problem?



Rainbow trout, healthy

Rainbow trout, pathologic obstruction (*arteriosclerotic plaque*)

- ✓ Thickening of intima (SM proliferation)
- ✓ Both wild and farmed fish (’fact of life’)
- ✓ Intensive rearing conditions
  Fast growth, high temp etc.
- ✓ Acute stress in farm environment?

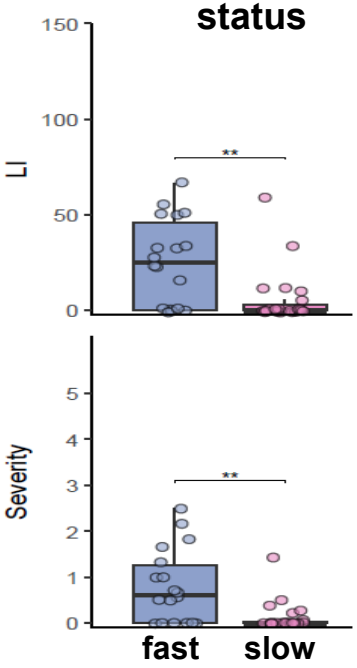


Atlantic salmon, Mortensen *et. al.* unpublished

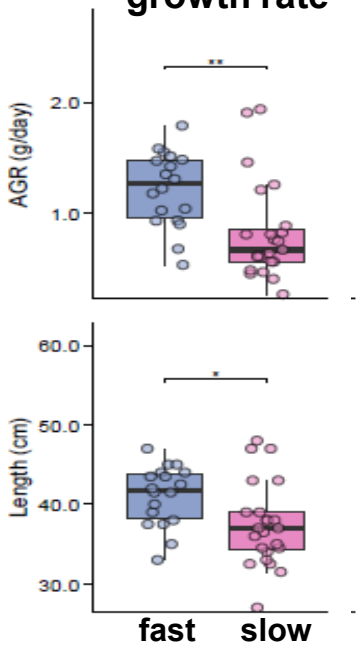
Brijs, Hjelmstedt, Berg, Johansen, Sundh, Roques, Ekström, Sandblom, Sundell, Olsson, Axelsson and Gräns (2020). Prevalence and severity of cardiac abnormalities and arteriosclerosis in farmed rainbow trout (*Oncorhynchus mykiss*). *Aquaculture*.

Coronary disease and farm mortality in intensive aquaculture?

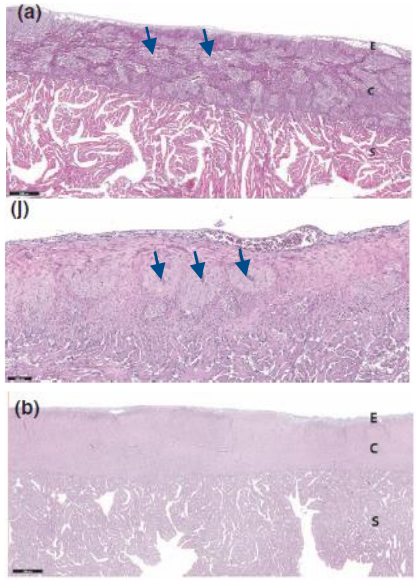
Coronary lesion status



Salmon smolt growth rate



Myocardial necrosis after fatal stress
(Poppe et al. J. Fish Disease 2021)



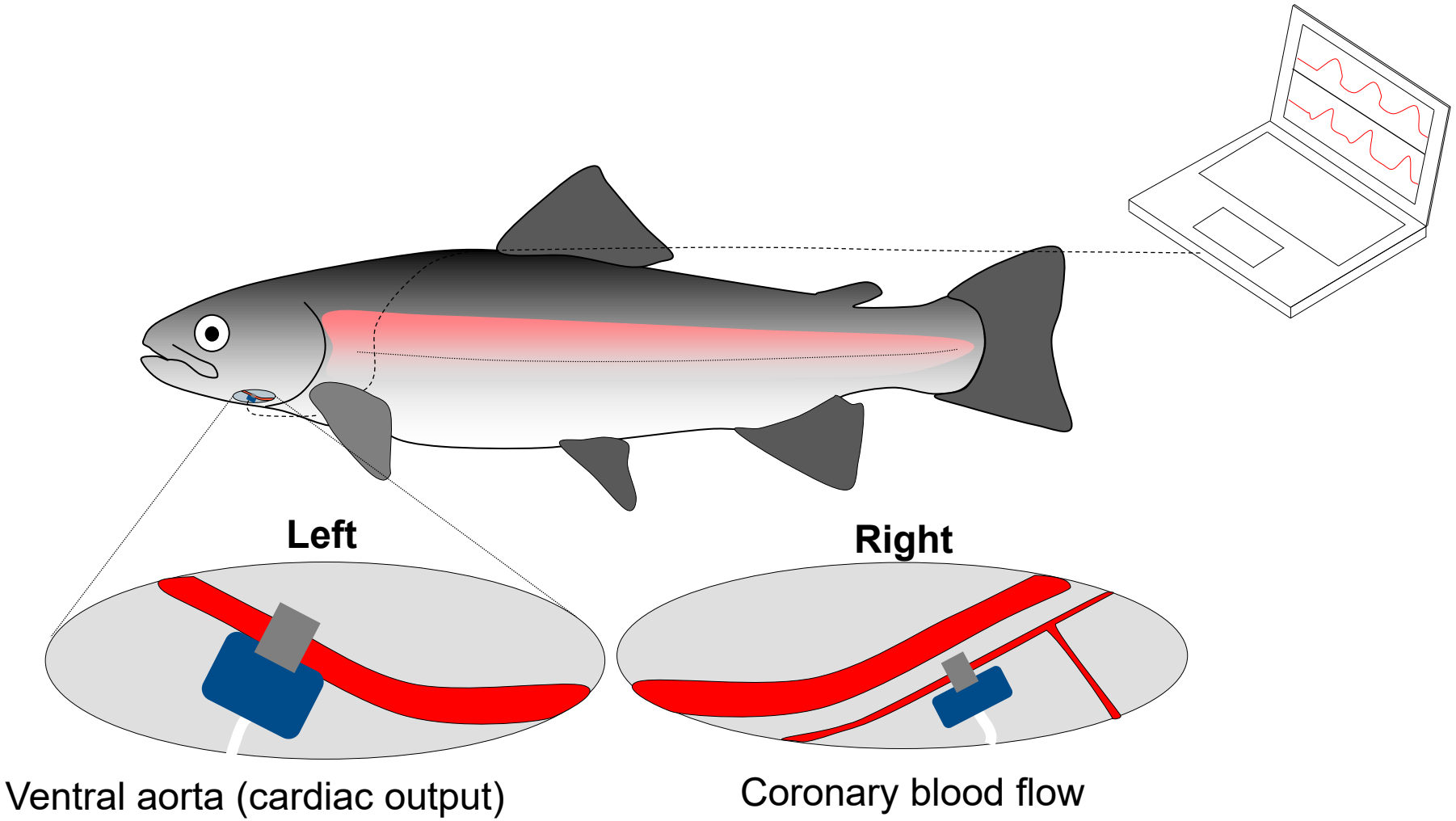
Farmed salmon

Farmed rainbow trout

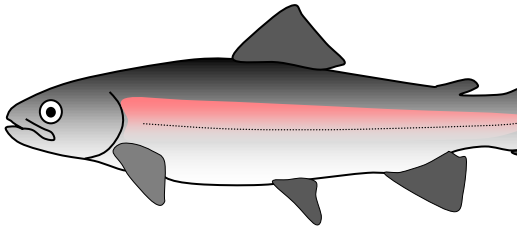
Wild salmon, *Healthy tissue*

Mortensen, Wisløff, Zena, Ekström, Gräns, Dam, Egholm, Vang, Johansen and Sandblom. Rapid growth trajectories are associated with increased coronary arteriosclerosis in farmed Atlantic salmon (*Salmo salar*) under commercial conditions (pending revision *Aquaculture*).

In vivo coronary blood flow during warming in mature rainbow trout

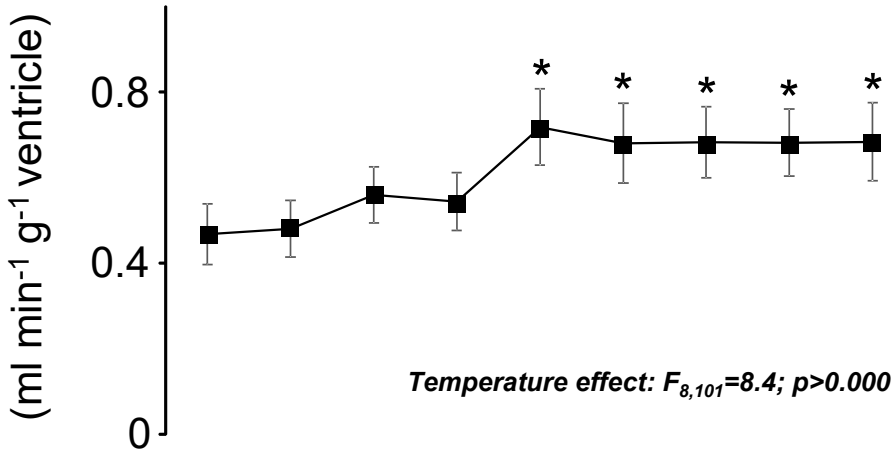


Ekström, Axelsson, Gräns, Brijs, and Sandblom (2017). Influence of the coronary circulation on thermal tolerance and cardiac performance during warming in rainbow trout. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology.*



Coronary blood flow

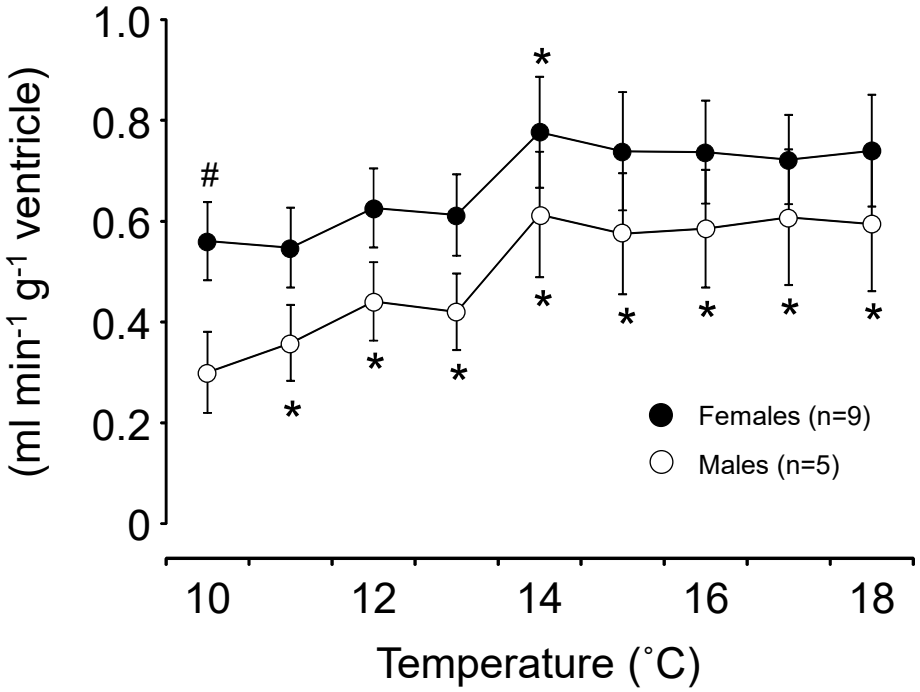
~4% of resting cardiac output



Proportion compacta

Females: 44%

Males: 36%



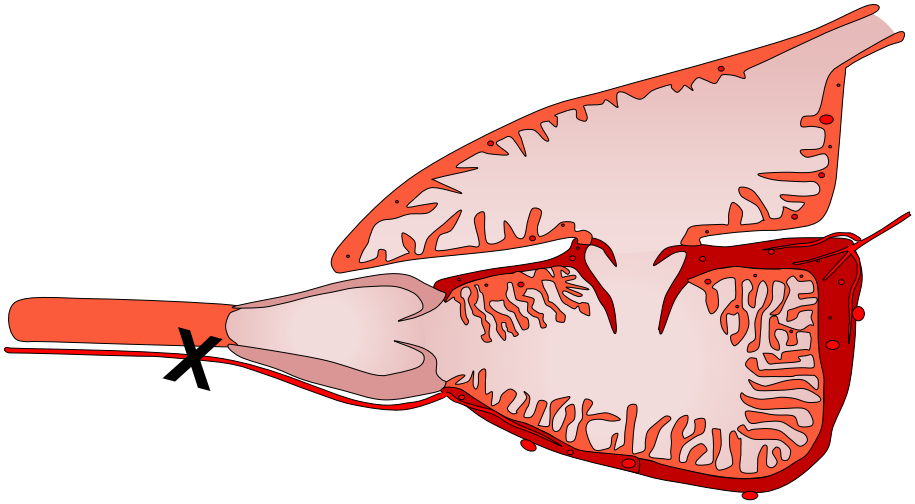
Scope for increase

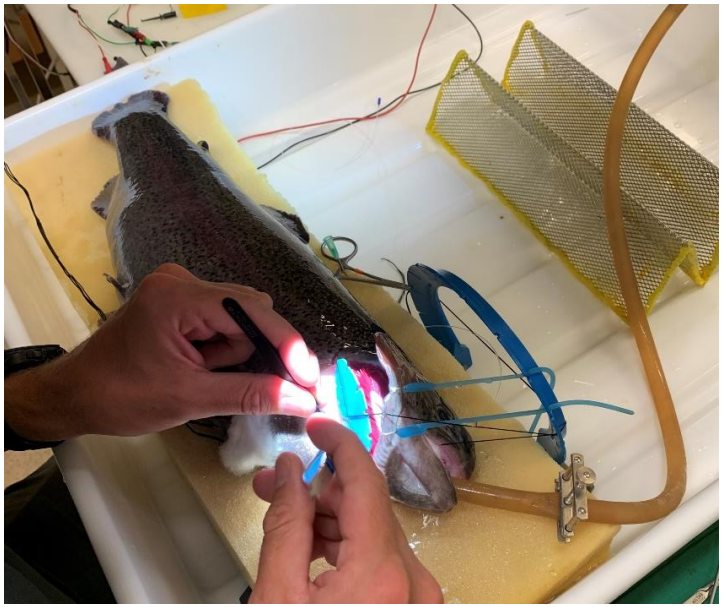
Females: 39%

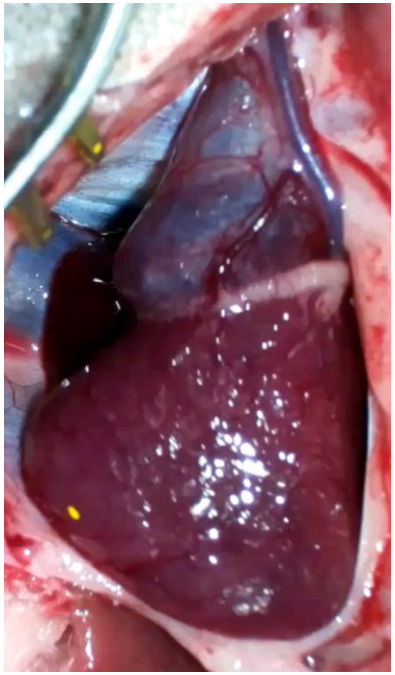
Males: 101%

Ekström, Axelsson, Gräns, Brijs, and Sandblom (2017). Influence of the coronary circulation on thermal tolerance and cardiac performance during warming in rainbow trout. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology.*

Surgical model of severe coronary arteriosclerosis



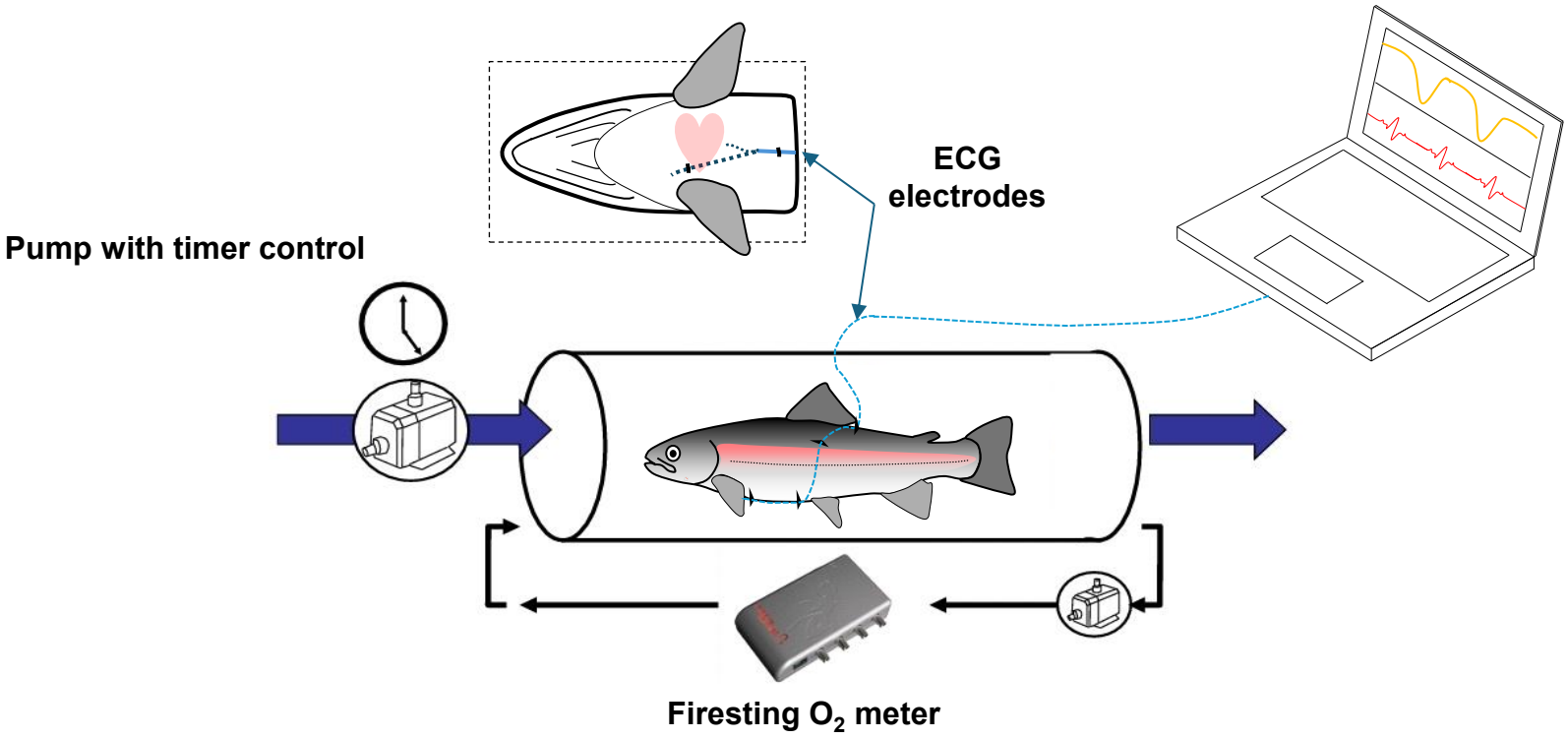




Sham operated **Coronary ligated**

Ekström, Axelsson, Gräns, Brijs, and Sandblom (2017). Influence of the coronary circulation on thermal tolerance and cardiac performance during warming in rainbow trout. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology.*

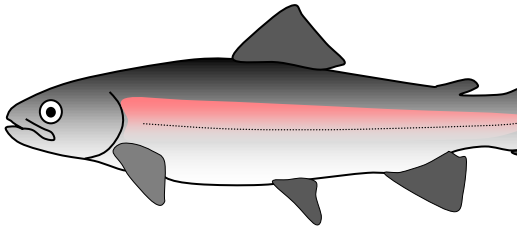
Recording of physiological variables *in vivo*

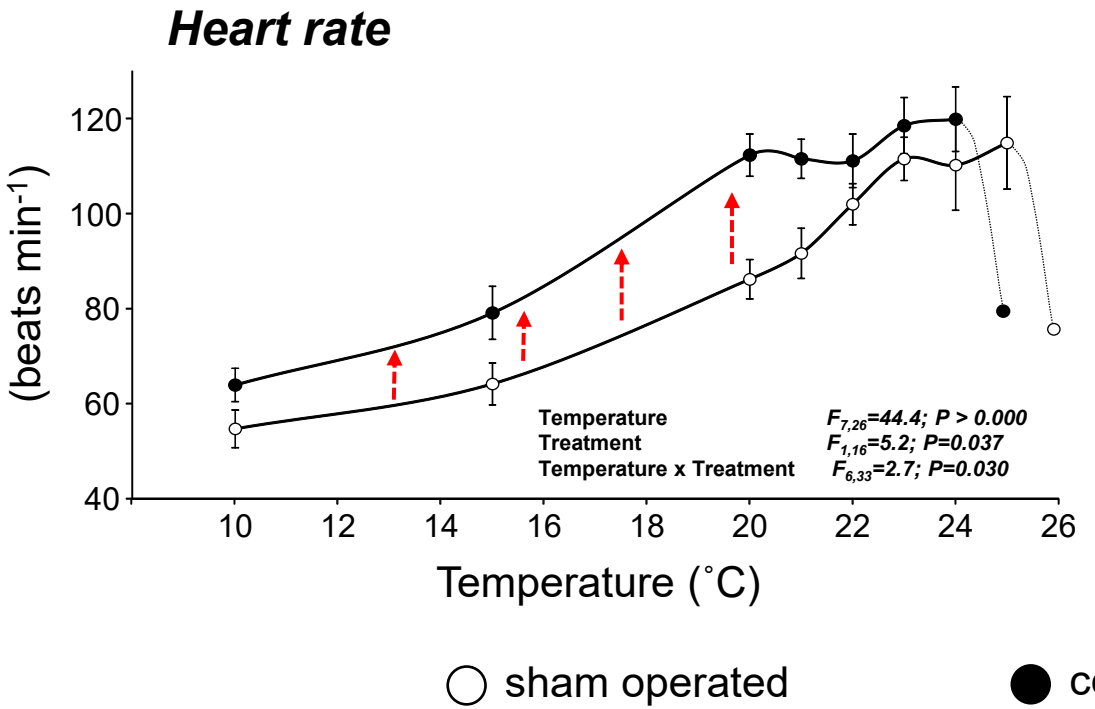


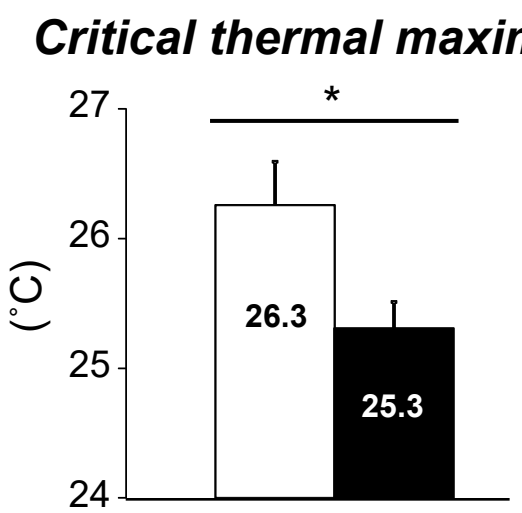
Examples of readouts:

- Respirometer for **Oxygen consumption rate** (aerobic metabolism)
- Sub-cutaneous electrodes for **ElectroCardioGram (ECG)** and **Heart rate**
- Perivascular flow probe for **Cardiac output, heart rate** and **stroke volume**

Reduced temperature tolerance



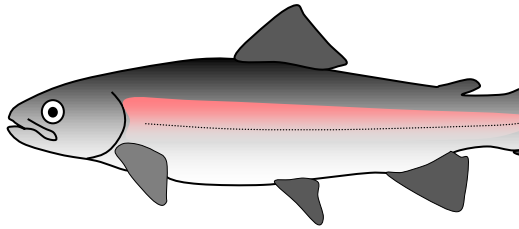




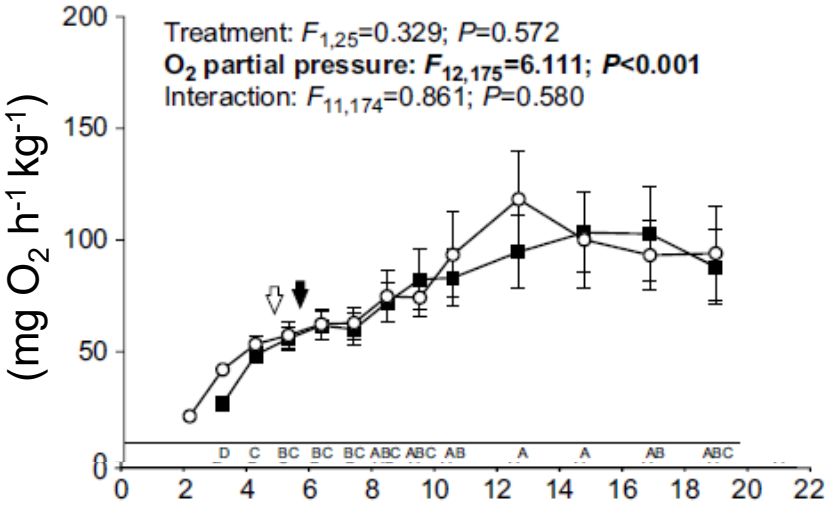
○ sham operated ● coronary ligated

Ekström, Axelsson, Gräns, Brijs, and Sandblom (2017). Influence of the coronary circulation on thermal tolerance and cardiac performance during warming in rainbow trout. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology.*

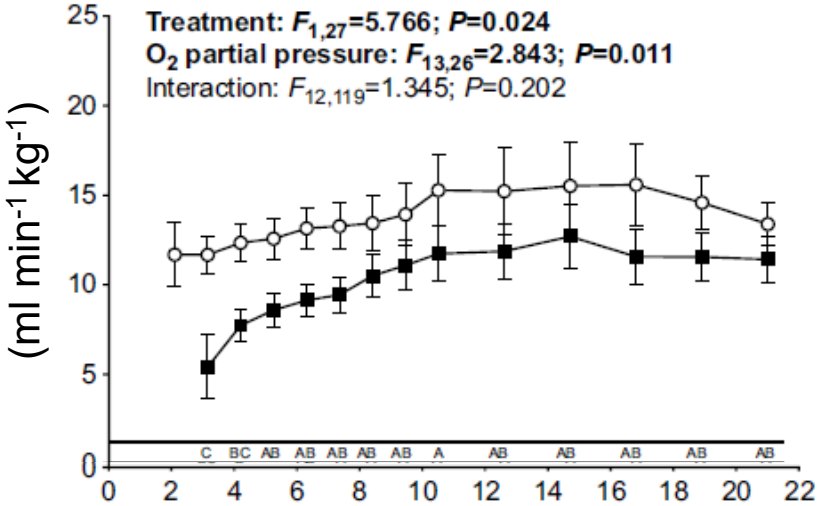
Reduced hypoxia tolerance



Oxygen consumption rate



Cardiac output

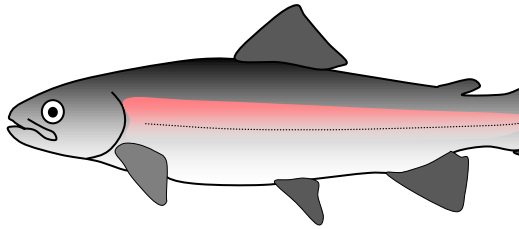


Water O_2 tension (kPa)

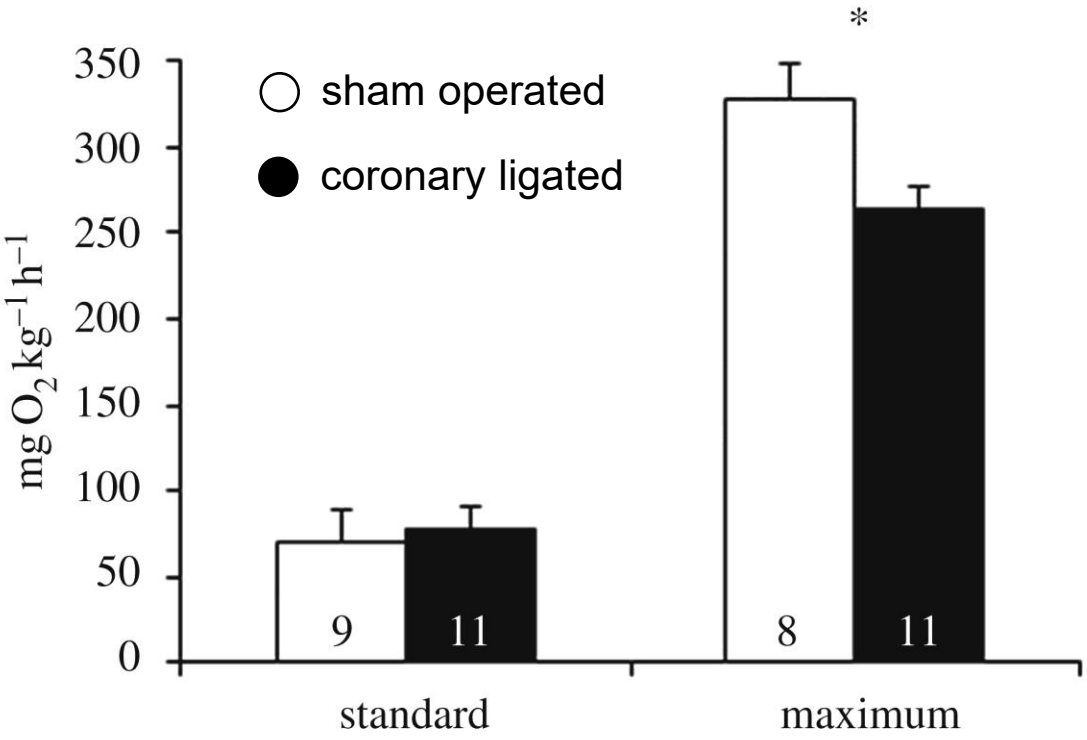
◯ sham operated ■ coronary ligated

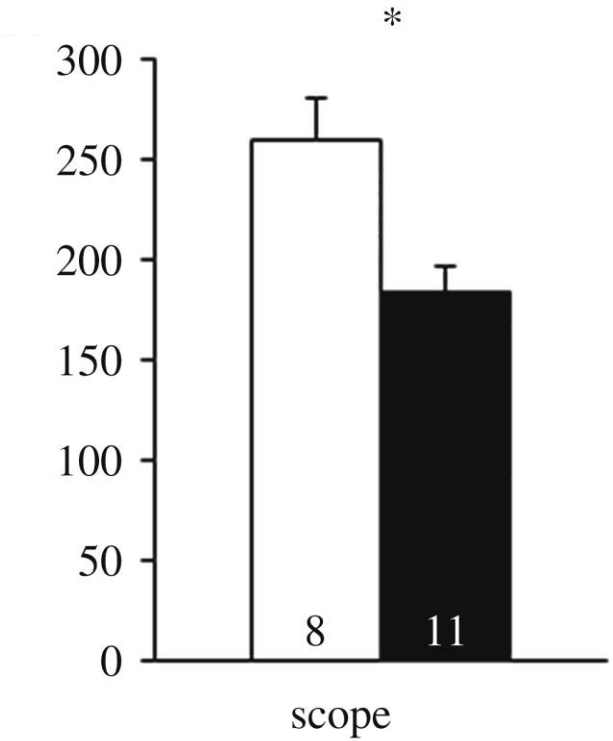
Morgenroth, McArley, Gräns, Axelsson, Sandblom and Ekström (2021). Coronary blood flow influences tolerance to environmental extremes in fish. *Journal of Experimental Biology*

Reduced aerobic performance under stress



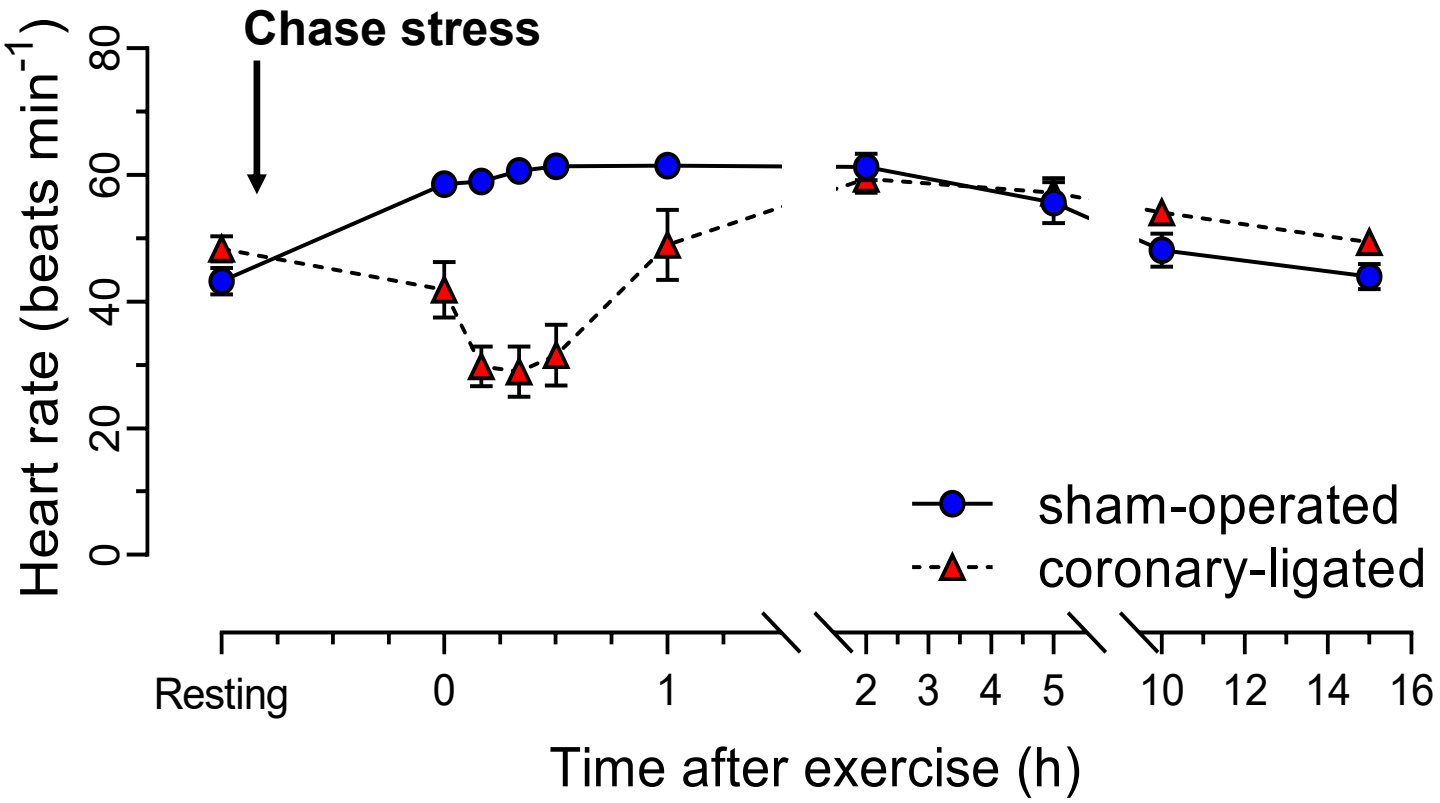
Oxygen consumption rate





Ekström, Axelsson, Gräns, Brijs, and Sandblom (2018). Importance of the coronary circulation for cardiac and metabolic performance in rainbow trout (*Oncorhynchus mykiss*). *Biology letters*

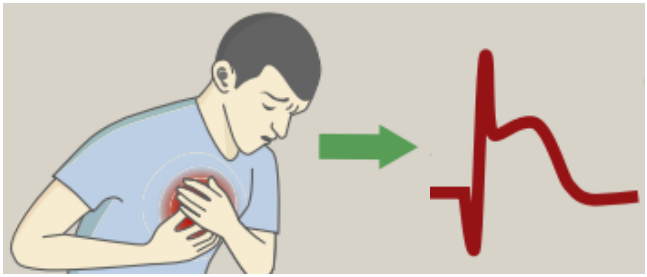
Post-exercise bradycardia in coronary ligated trout

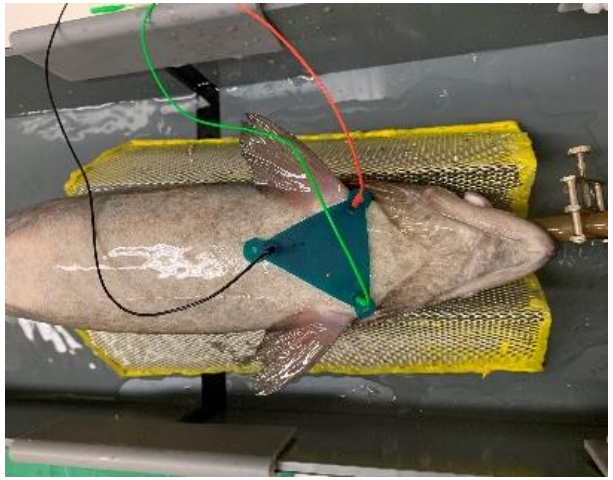


Wallbom, Zena, McArley, Ekström, Axelsson, Gräns, Sandblom and Morgenroth. (2023) Increased reliance on coronary perfusion for cardiorespiratory performance in seawater-acclimated rainbow trout. *Journal of Experimental Biology*

Electrocardiography as diagnostic tool for fish heart disease

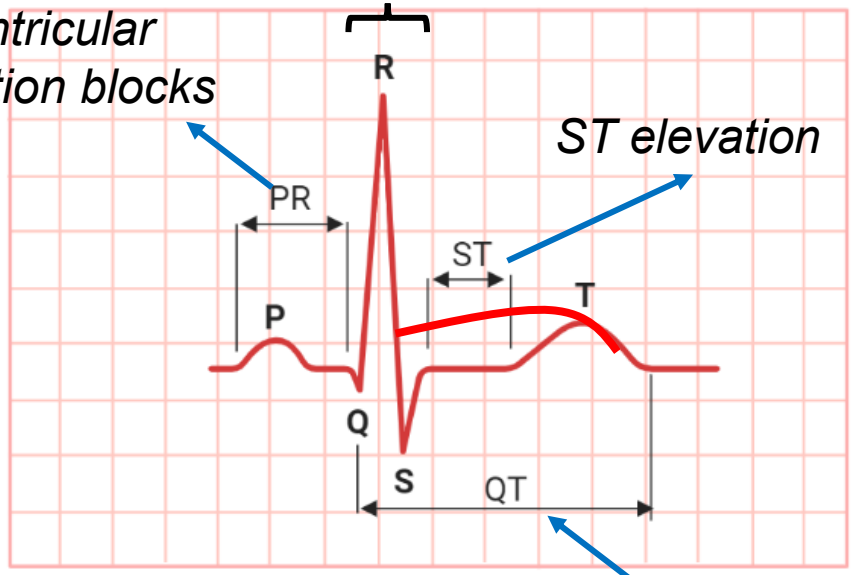
Diagnosis of acute myocardial infarction:
chest pain + ECG characteristics





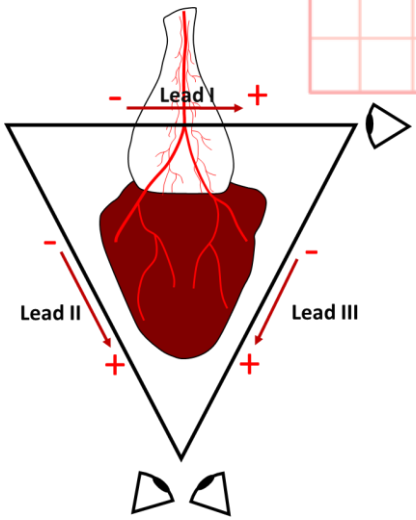
QRS widening and loss of voltage

Atrioventricular conduction blocks



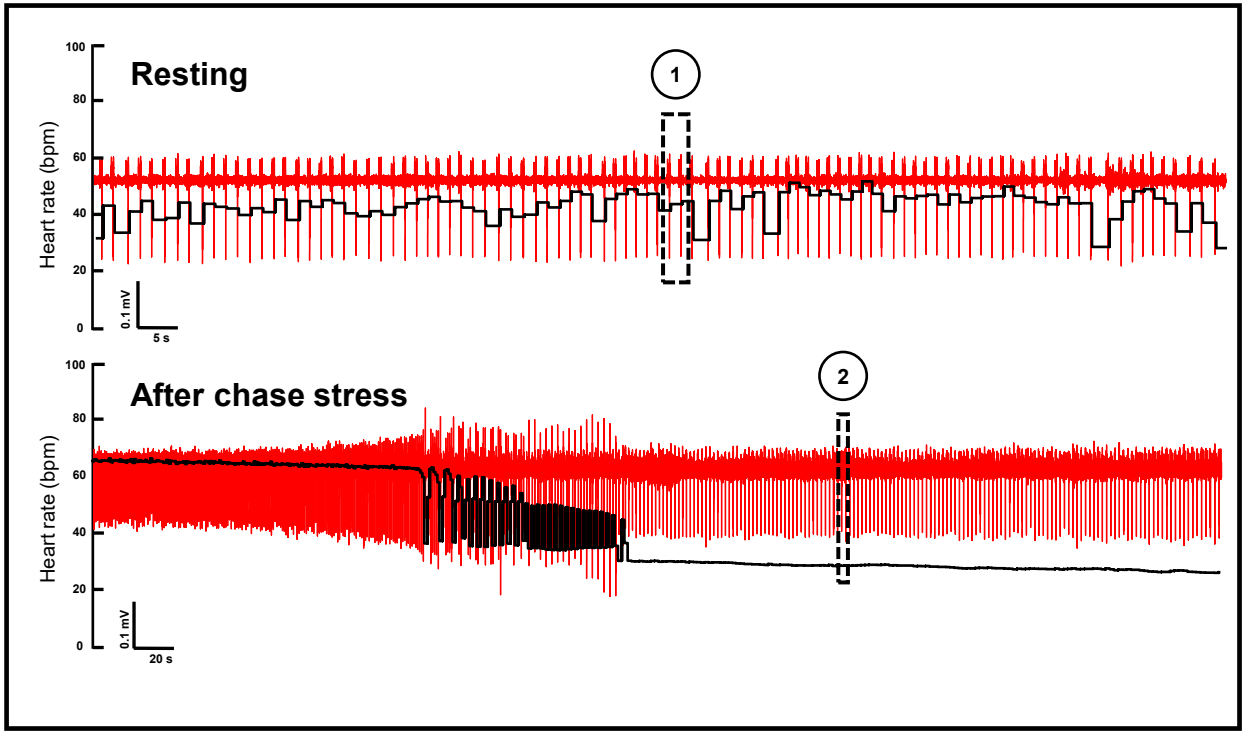
ST elevation

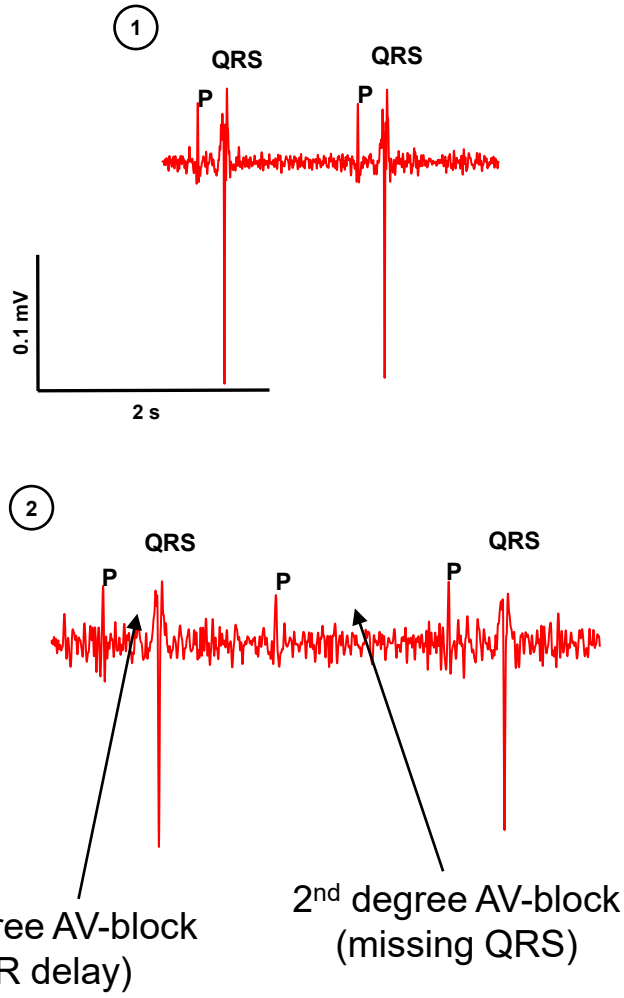
Delayed repolarization



Zena, Ekström, Morgenroth, McArley, Gräns, Axelsson, Johansen and Sandblom. (2024) Ischemia-induced alterations in the electrocardiogram of salmonid fish. *Aquaculture*

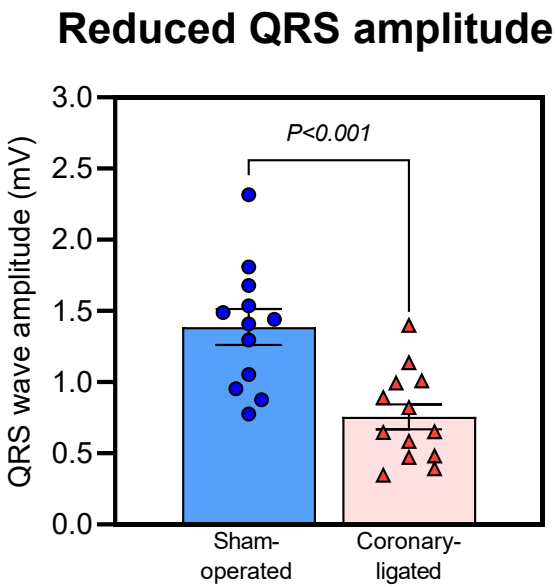
Exercise intolerance and AV block after coronary ligation

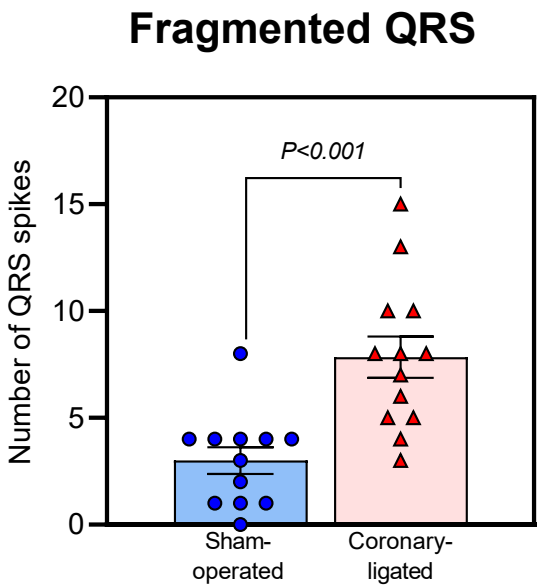


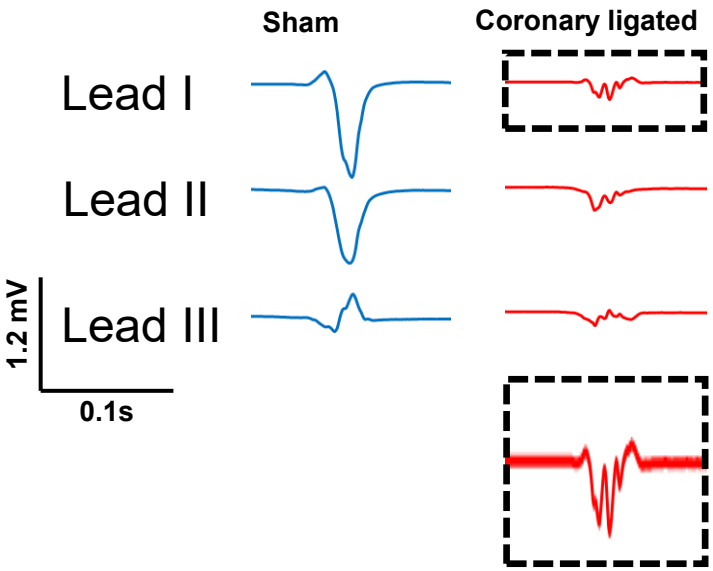


Wallbom, Zena, McArley, Ekström, Axelsson, Gräns, Sandblom and Morgenroth. (2023) Increased reliance on coronary perfusion for cardiorespiratory performance in seawater-acclimated rainbow trout. *J. Exp. Biol.*

QRS characteristics after acute coronary ligation



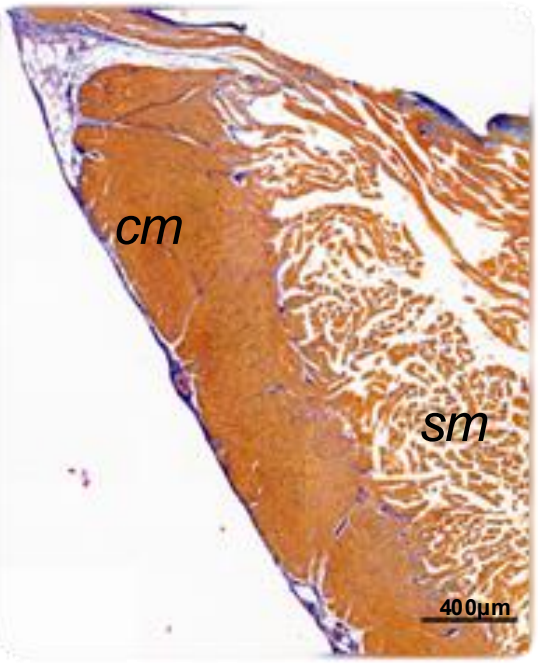




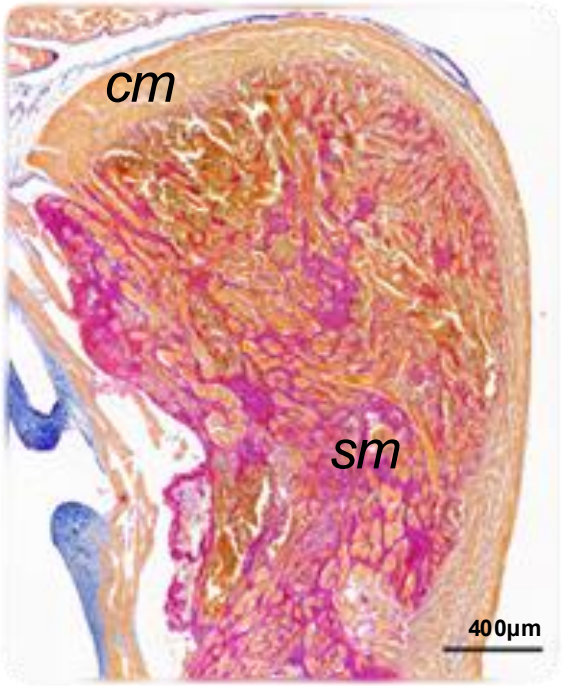
Zena, Ekström, Morgenroth, McArley, Axelsson, Sundh, Palmquist, Johansen, Gräns and Sandblom. (2024) Beating the heart failure odds: long-term survival after myocardial ischemia in juvenile rainbow trout. *American Journal of Physiology - Regulatory, Integrative and Comparative Physiology*

Acute histopathological changes in ventricle myocardium (3 days)

Sham



Coronary ligated

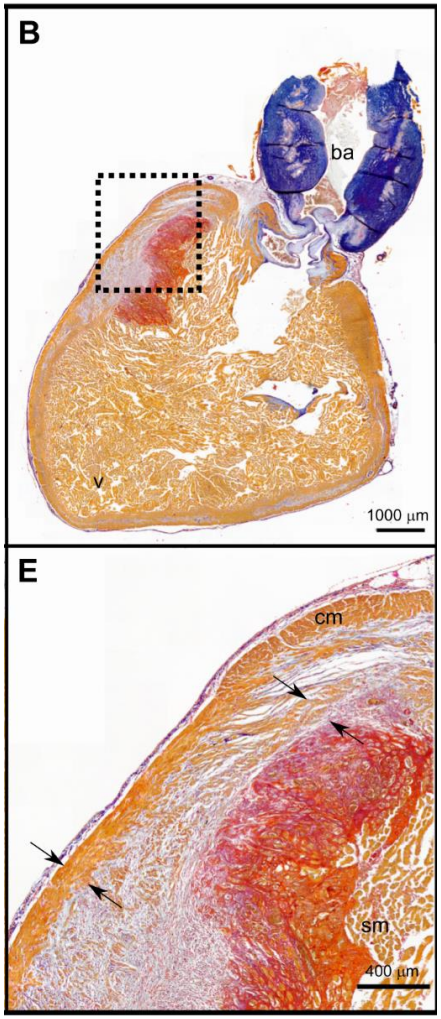


Clinical symptoms:

- ✓ ~4-fold greater interstitial spacing -edema
- ✓ Inflammatory response -fibrin and immune cell infiltration
- ✓ Reduced collagen and compact myocardium
- ✓ ”Wavy myofibres”

Zena, Ekström, Gräns, Olsson, Axelsson, Sundh and Sandblom. (2021) It takes time to heal a broken heart: Ventricular plasticity improves heart performance after myocardial infarction in rainbow trout, *Oncorhynchus mykiss*. *Journal of Experimental Biology*

Chronic histopathological changes in ventricle myocardium (40 days)



% Collagen content

Sham
8.1±0.5%

vs.

Coronary ligated
20.6±1.2%

% Compact myocardium

Sham
31.5±1.1%

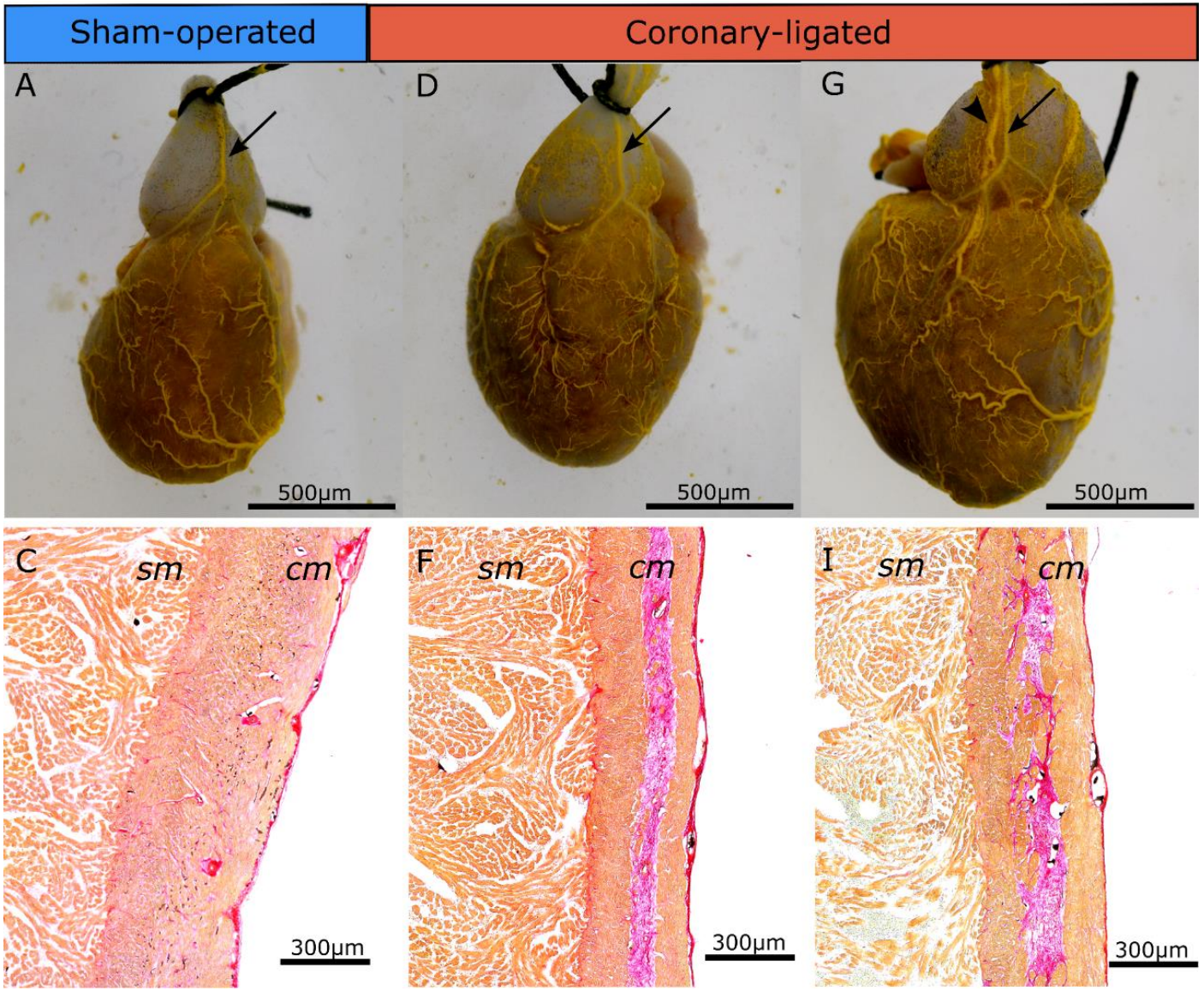
vs.

Coronary ligated
24.0±1.0%

Adaptive or pathological?
maintained ventricular integrity after loss of compact myocardium?

Zena, Ekström, Gräns, Olsson, Axelsson, Sundh and Sandblom. (2021) It takes time to heal a broken heart: Ventricular plasticity improves heart performance after myocardial infarction in rainbow trout, *Oncorhynchus mykiss*. *Journal of Experimental Biology*

Coronary revascularization but remaining mid-compact fibrosis (up to 173 days)



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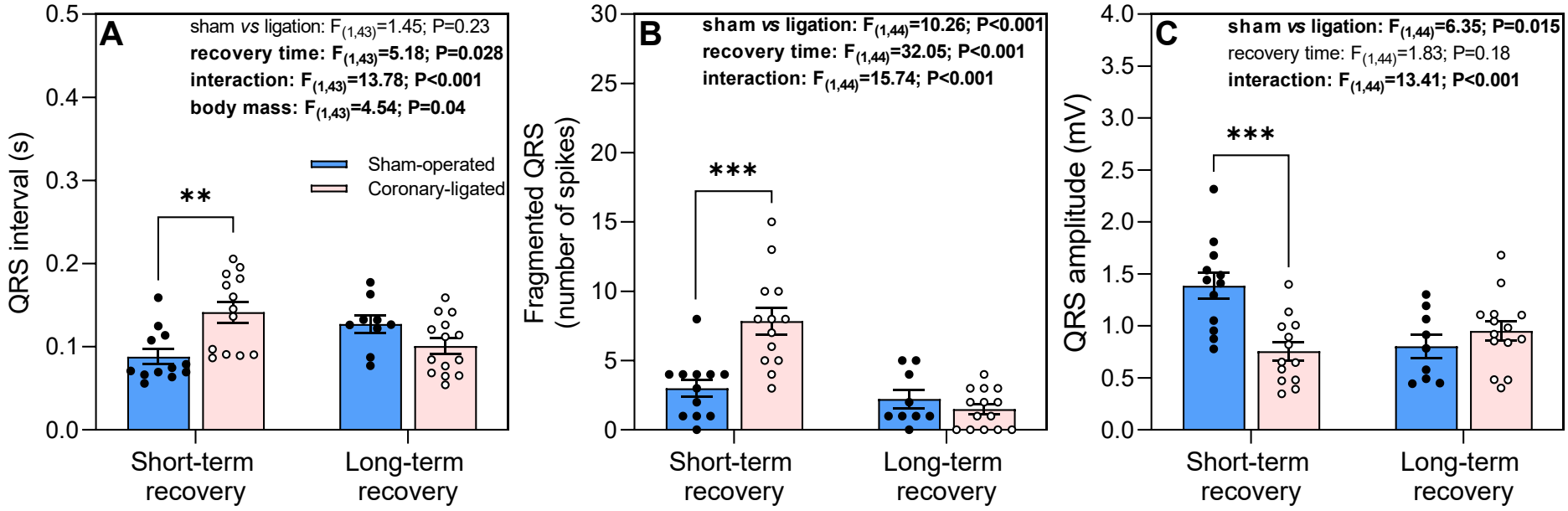
Normalized resting ECG characteristics (up to 173 days)



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TACK!

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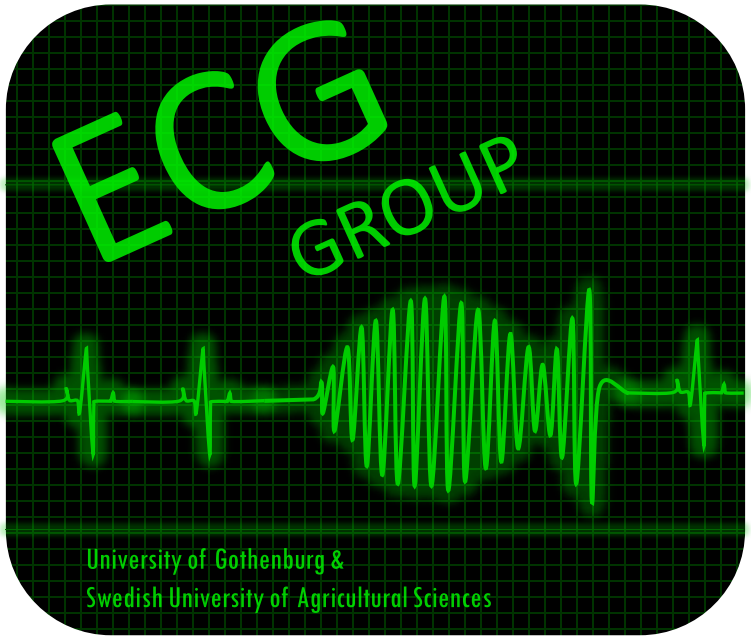
Nicklas Wallbom
Xhoni Dalipi
Michael Frisk
Ida Beitnes Johansen
Daniel Morgenroth
Elin Egholm
Helene Wisløff



UNIVERSITY OF GOTHENBURG

SLU Swedish University of Agricultural Sciences

NMBU Norwegian University of Life Sciences

PHARMAQ Analytiq

FIRUM knowledge for sustainable aquaculture

FORMAS

Swedish Research Council

Innovation Fund Denmark

Jordbruksverket Swedish Board of Agriculture

Wenner-Gren Stiftelserna
Wenner-Gren Foundations

FAPESP SÃO PAULO RESEARCH FOUNDATION

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granskingarráðið RESEARCH COUNCIL FAROE ISLANDS