

# Cardiovascular Prevention and Rehabilitation

## Basic and Translational Research

Mechanisms of  
Improved Function

Exercise in  
Medicine

**Endothelium**

**Heart  
Muscle  
Cells**

**Skeletal  
Muscle**

**Nitric  
Oxide  
Synthase**

**Progenitor  
Cells**

**Contractility &  
Ca<sup>2+</sup> handling**

**Protein  
Degradation**

**Molecular  
Signaling  
Pathways**

**Hypertrophy &  
Remodeling**

**Energy  
Metabolism**

# Basic and Translational Research



**Exercise Models**  
- cellular / molecular mechanisms



**Evidence-Based Training Programs For Defined Groups**

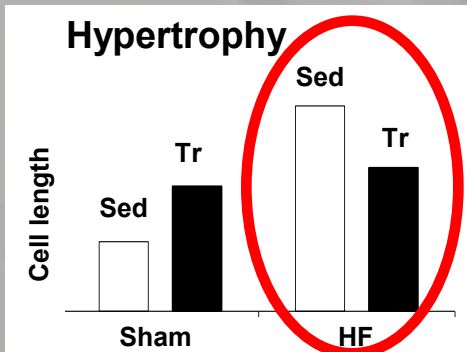
- Heart failure
- Coronary disease
- Metabolic syndrome
- Hypertension



# Working Hypothesis

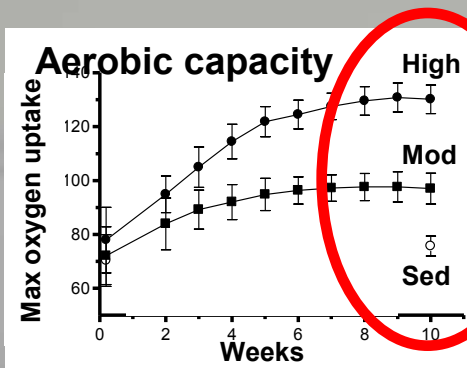
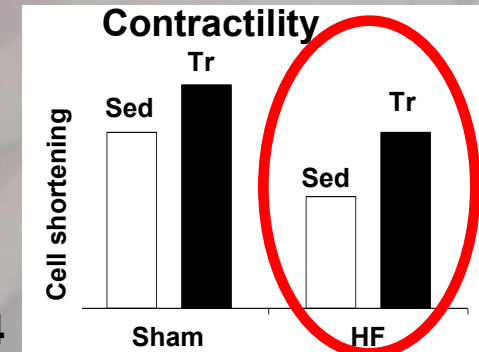
## Training Effect in Heart Failure

### Depends on Exercise Intensity



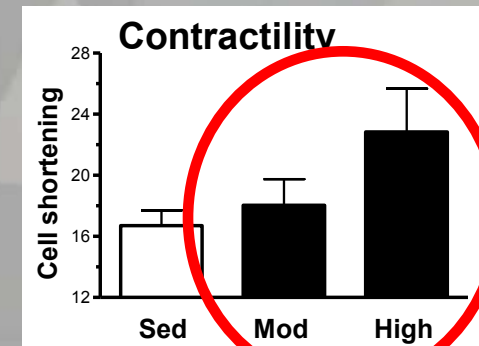
**Reduced Cardiac Hypertrophy and Increased Myocyte Contractility In Heart Failure**

Wisløff U. 2002. *Cardiovasc Res* 54: 162-174



**Larger Effects With High Versus Moderate Exercise Intensity on Aerobic Capacity and Contractility**

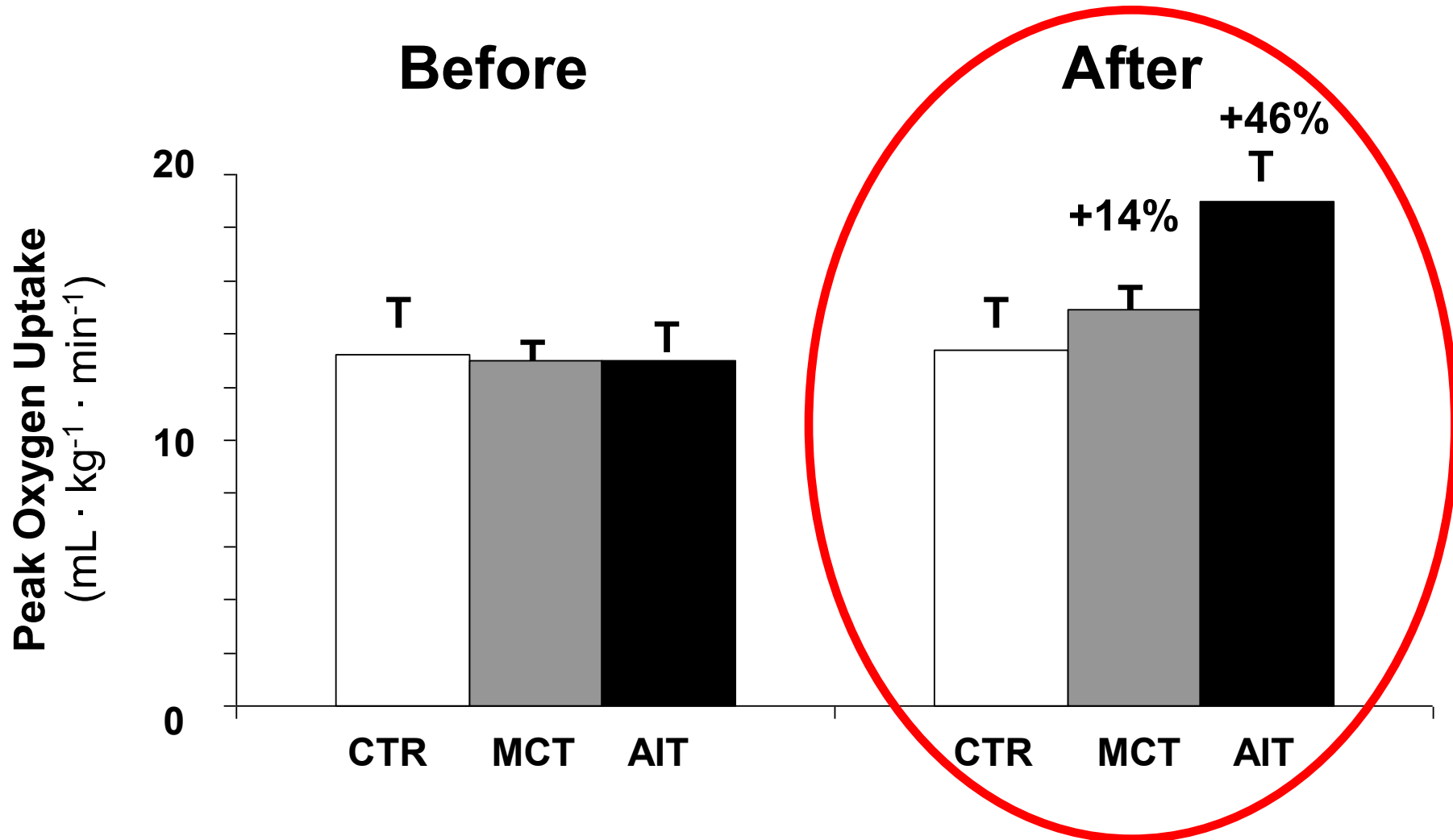
Kemi OJ. 2005. *Cardiovasc Res* 67: 161-72.



Works for me?



# Aerobic Capacity – $\text{VO}_{2\text{peak}}$

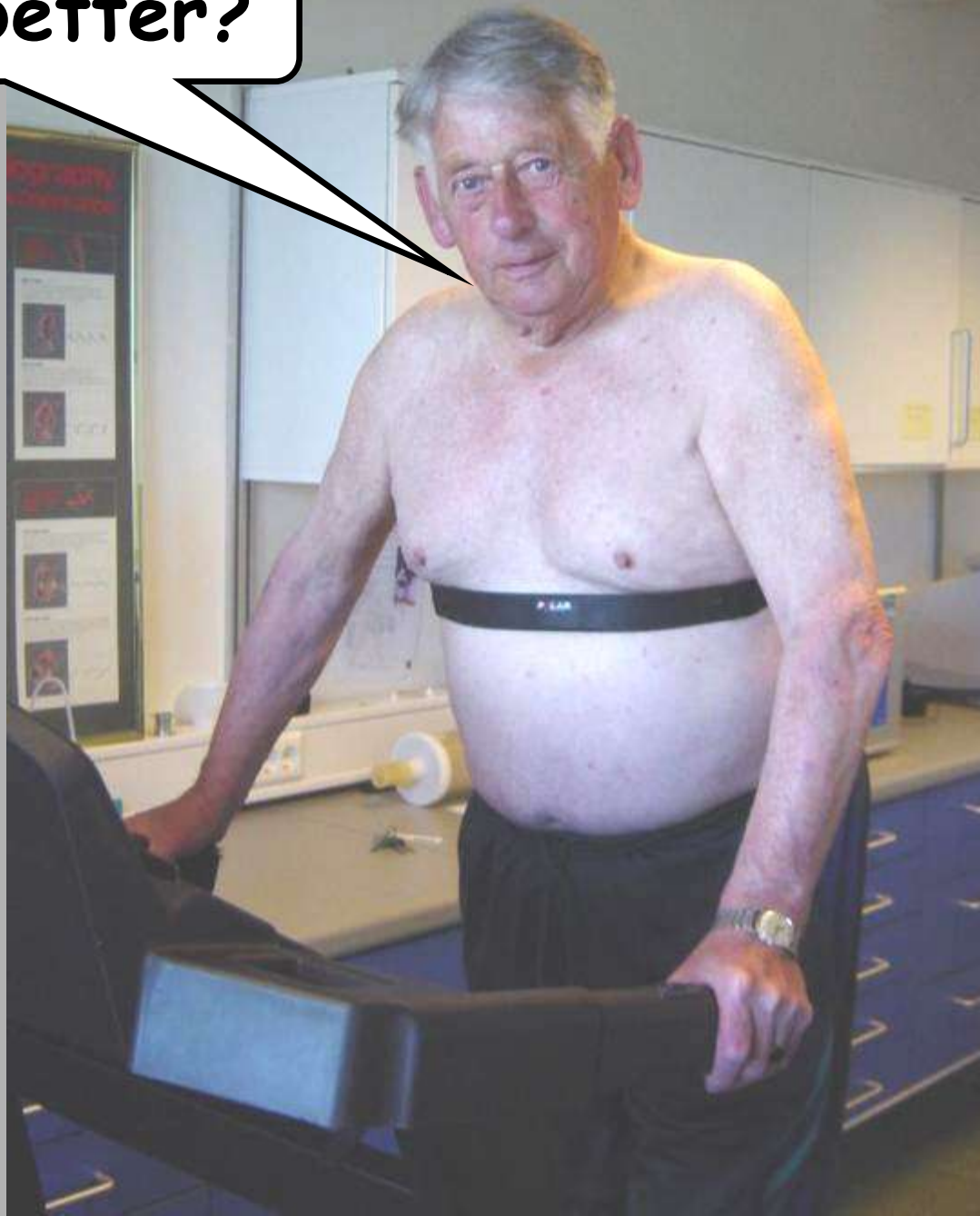


# **Myocardial Adaptation to Exercise**

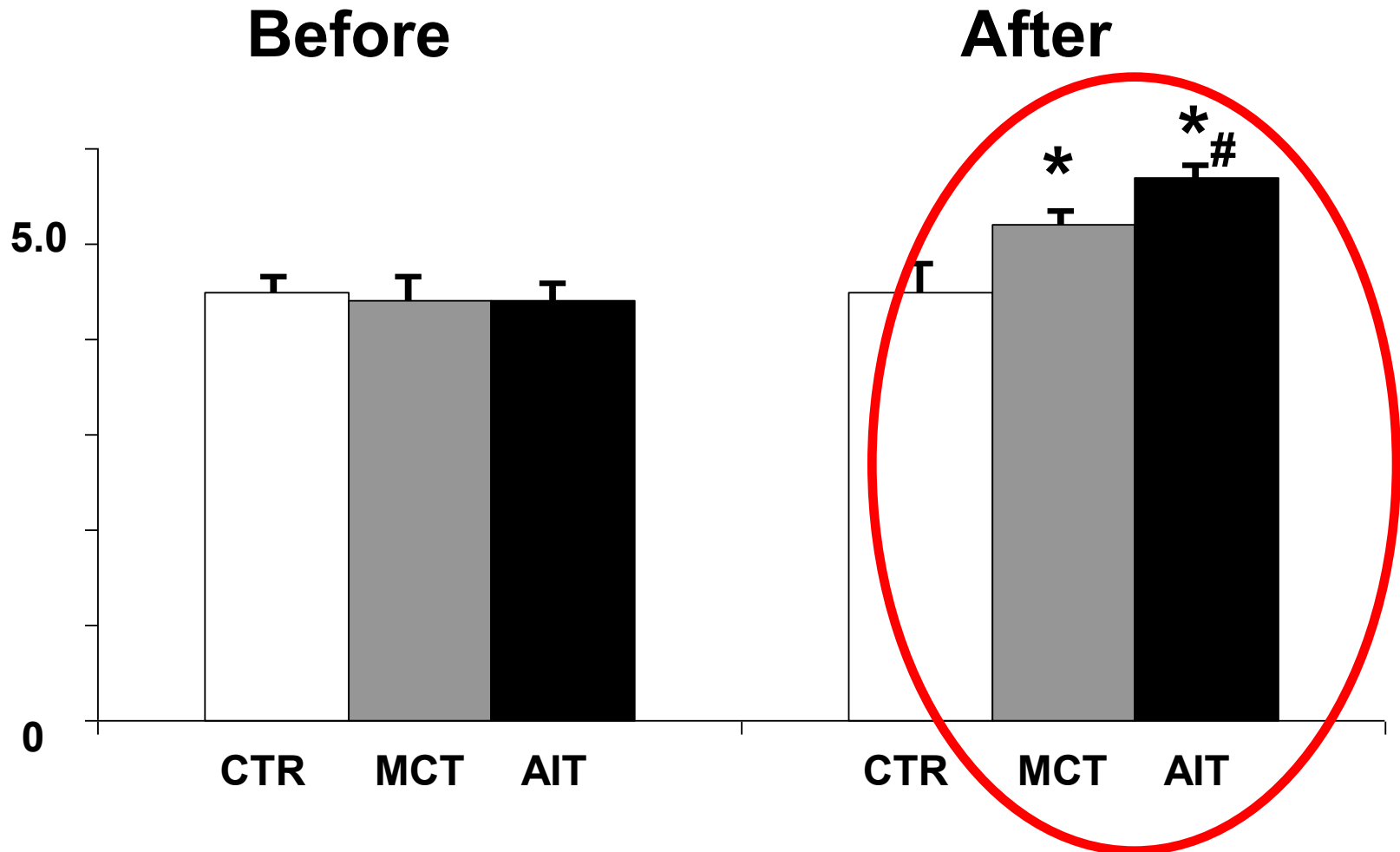
## **- *Aerobic Interval Training***

- 1. Higher aerobic capacity**
- 2. Increased contractility and Physiological Hypertrophy or Reverse remodeling**
- 3. Enhanced endothelial function**
- 4. Improved mitochondrial function and in skeletal muscle => glucose tolerance**
- 5. Works in patients: Coronary artery disease, Heart failure, Metabolic syndrome, Hypertension**

Feeling better?



# Quality of Life – MacNew Global Score





# Multicenter Study: SMARTEX-HF

## Study of **Myocardial Recovery** after **Exercise training** in **Heart Failure**

### **Randomized clinical trial with 3 arms**

- 1. Aerobic Interval Training (program) versus usual care**
- 2. Moderate Continuous Training (program)**
- 3. Regular Exercise (recommendation)**

### **Phase II type study – Establish clinical effects**

- European multicenter (EACPR - Basic Science)
- 200 patients, NYHA 2-3, EF < 35

### ***Assess reverse remodeling***

- LVEDD ( $VO_{2peak}$ , LVEF, BNP, QoL)

### ***Assess safety and estimate clinical endpoints***

- Mortality, CV hospitalization, worsening of HF

# **TranslatE Network Objectives**

- 1. Identify Cellular and Molecular Mechanisms of Beneficial Outcomes of Exercise Training**
- 2. Identify Optimal Exercise Intensity  
Establish Dose-Response relationship:  
Interval Training versus Moderate Intensity**
- 3. Develop Evidence-Based Standards for Exercise Training in Heart Failure**
- 4. Establish Sub-Studies of SMARTEX-HF and Experimental Studies**

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