

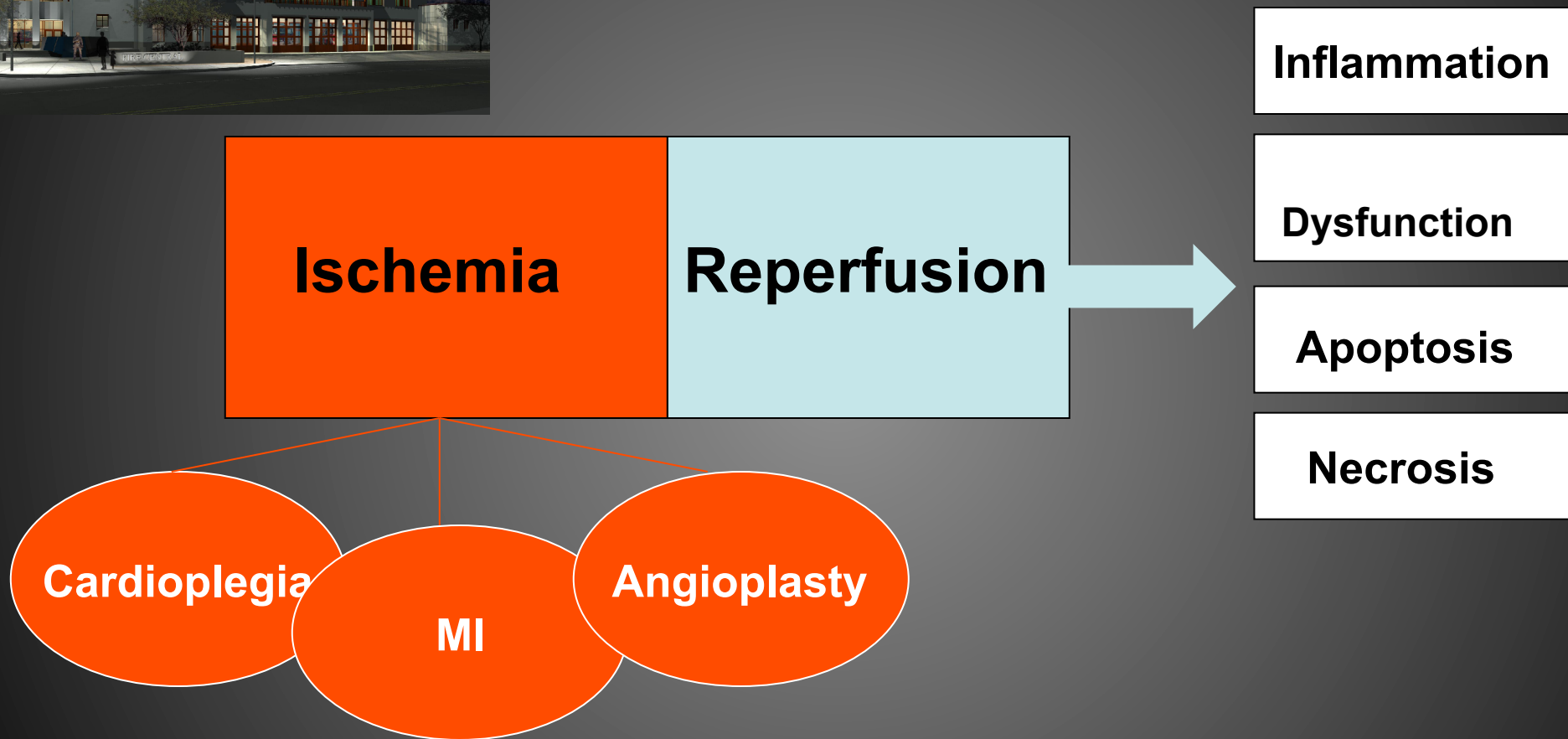
# Ischemic Remote Conditioning: An interesting concept or a clinical reality

Terence Valenzuela MD MPH  
stolen from  
Christopher Caldarone, MD





# We cause/treat Ischemia-Reperfusion injury





# Reperfusion Injury

➤ Ischemia/reperfusion >> injury

➤ Major cause of morbidity

➤ Strategy:

- Avoid it
- Modify the body's response



# What is Ischemic Conditioning ?

▶ Brief and repeated cycles of Ischemia and Reperfusion can protect ischemic myocardium from injury by preserving mitochondria and ameliorating damage from oxygen radicals and other biochemical intracellular changes during ischemia and reperfusion.



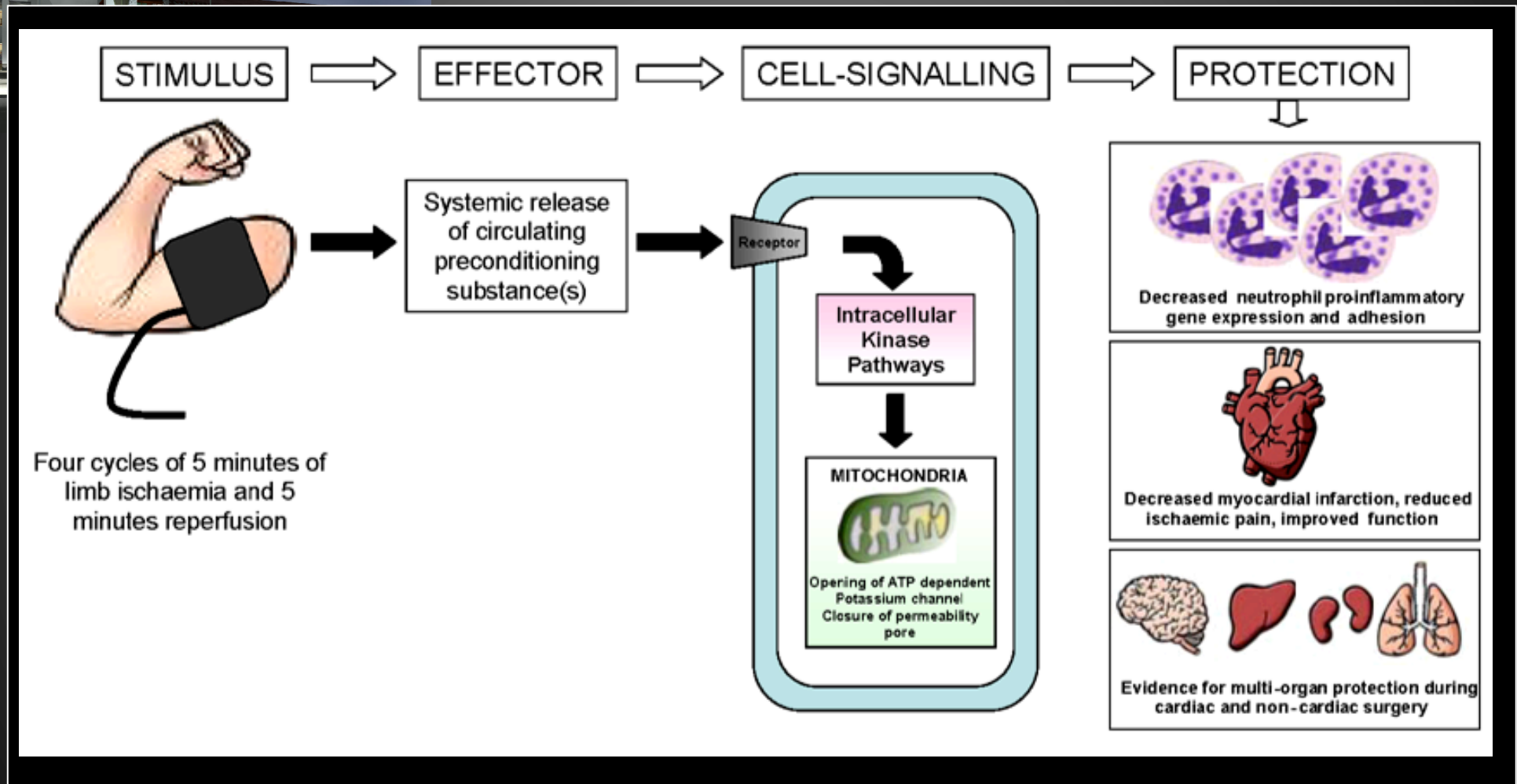
# Stimulus location

## Remote IPC

- *Stimulus* organ (can be an arm) is preconditioned
- Confers protection on a distant *target* organ



# Remote ischemic preconditioning



*Kharbanda, Neilsen & Redington. Lancet 2009*



# ***Does Factor-x diminish post-op dysfunction (no infarct)***

***Remote Ischemic preconditioning (rIPC) elaborates  
A Transferable Blood Borne Effector***



***Preserves Mitochondrial structure and function***



***Preserves Cardiac performance***



Does It Pick Up Peanuts?







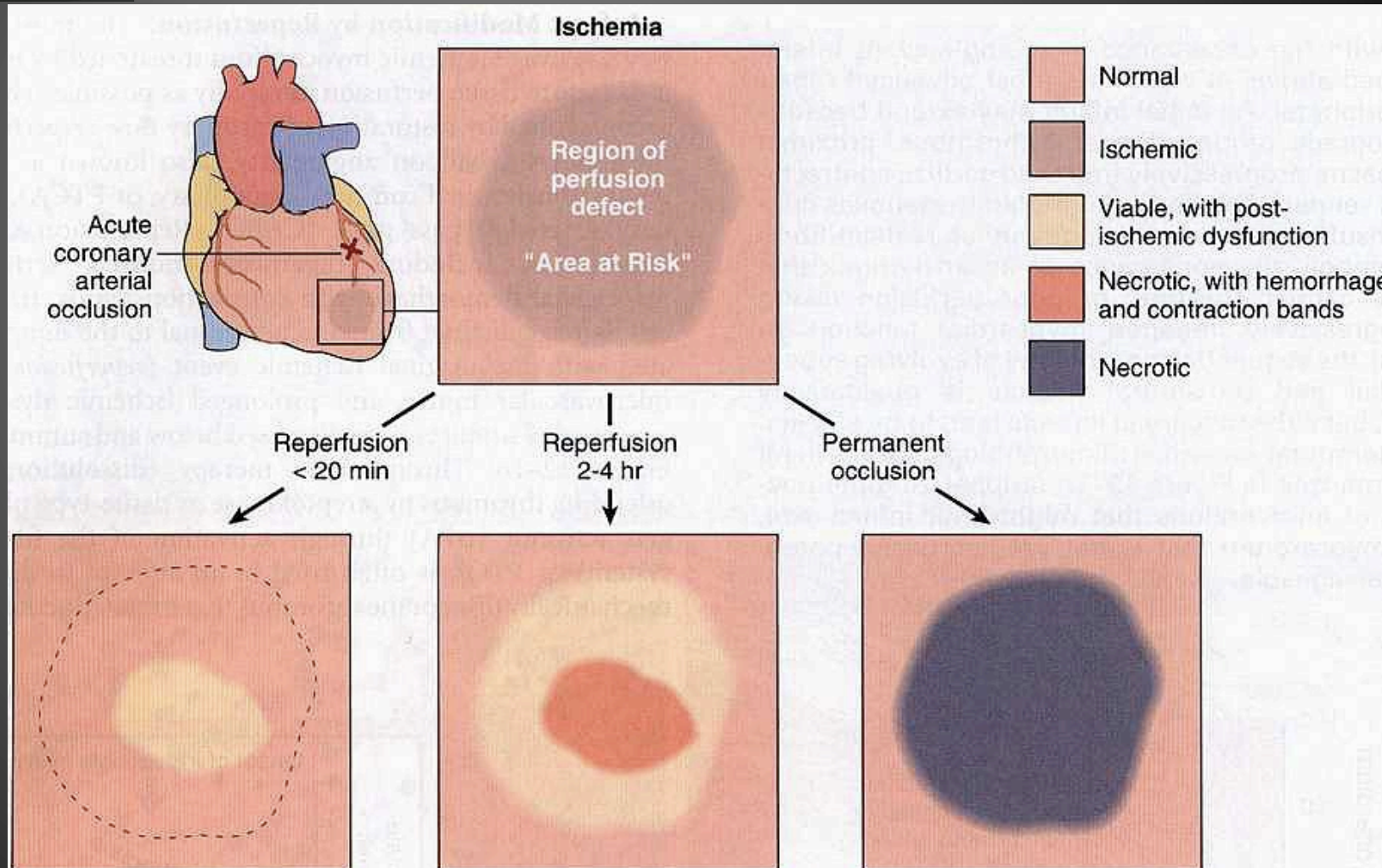
Botker HE et al Remote Ischemic  
Conditioning...*Lancet* 2010; 375: 727–34

- ▶ 333 consecutive adult patients with a suspected first acute myocardial infarction were randomly assigned to receive primary percutaneous coronary intervention
- ▶ With (n=166 patients) versus Without (n=167) remote conditioning (intermittent arm ischemia through four cycles of 5-min inflation and 5-min deflation of a blood-pressure cuff ).



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Conditioning...*Lancet* 2010; 375: 727–34

- ▶ Patients received remote conditioning **during transport to hospital**, and primary percutaneous coronary intervention in hospital.
- ▶ The primary endpoint was myocardial salvage index at 30 days after primary percutaneous coronary intervention
- ▶ **Measured by myocardial perfusion imaging as the proportion of the area at risk salvaged by treatment**





## Botker HE et al Remote Ischemic Conditionining...*Lancet* 2010; 375: 727–34

### ➤ Remote conditioning group

➤ Median salvage index : 0.75 (IQR 0.50–0.93, n=73)

➤ Mean salvage index: 0.69 (SD 0.27)

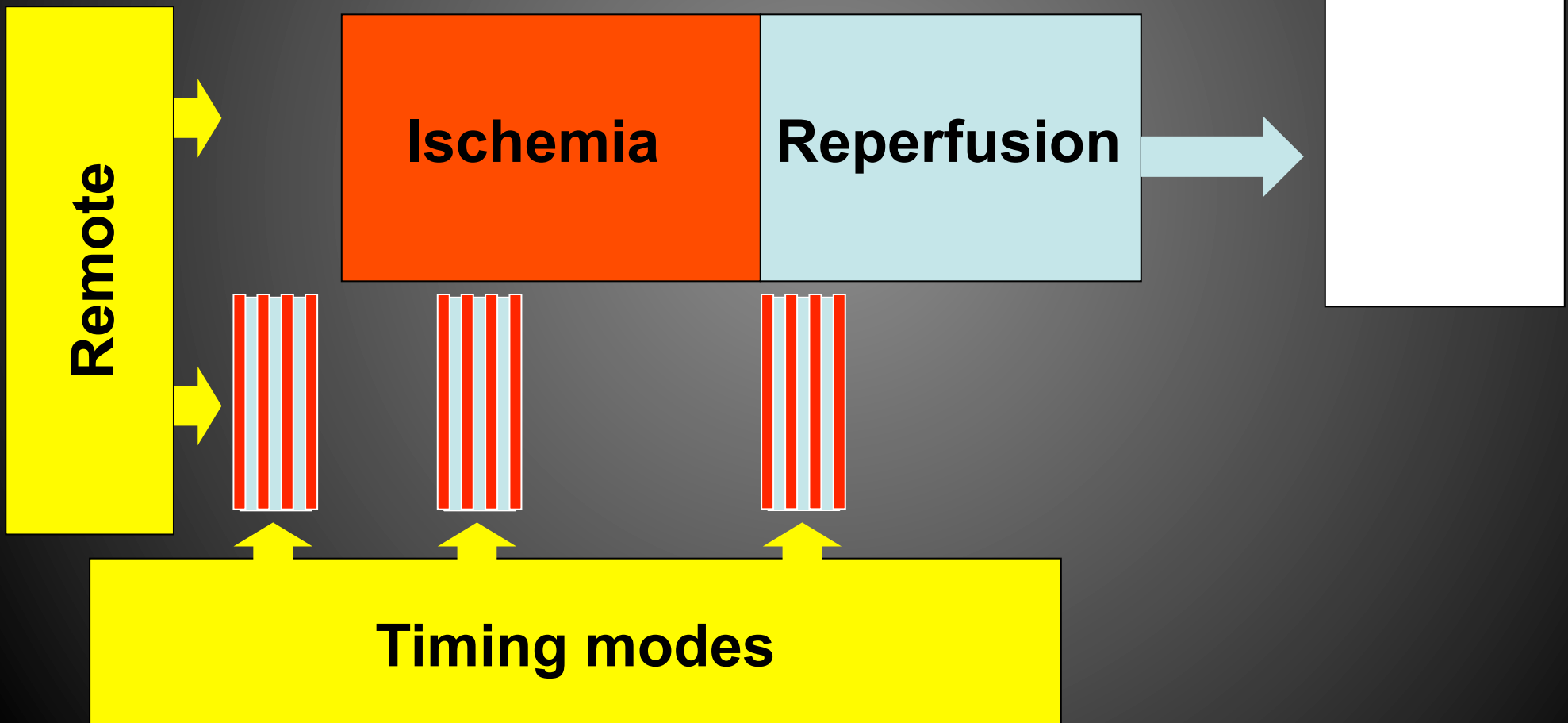
### ➤ Control group

➤ Median salvage index: 0.55 (IQR 0.35–0.88, n=69)

➤ Mean salvage index” 0.57 (SD 0.26)



# Windows of clinical opportunity





# Elective Coronary Angioplasty

## Cardiac Remote Ischemic Preconditioning in Coronary Stenting (CRISP Stent) Study A Prospective, Randomized Control Trial

Stephen P. Hoole, MA, MRCP; Patrick M. Heck, MA, MRCP; Linda Sharples, PhD;  
Sadia N. Khan, MA, MRCP; Rudolf Duehmke, MRCP; Cameron G. Densem, MD, MRCP;  
Sarah C. Clarke, MD, FRCP; Leonard M. Shapiro, MD, FRCP; Peter M. Schofield, MD, FRCP;  
Michael O'Sullivan, PhD, MRCP; David P. Dutka, MD, FRCP

### RIPC associated with:

<b><i>Diminished cTnI</i></b>	<b><i>p=0.04</i></b>
<b><i>Diminished chest pain</i></b>	<b><i>p=0.01</i></b>
<b><i>Diminished ST segment deviation</i></b>	<b><i>p=0.0006</i></b>
<b><i>**Diminished MACCE at 6 months</i></b>	<b><i>p=0.018</i></b>

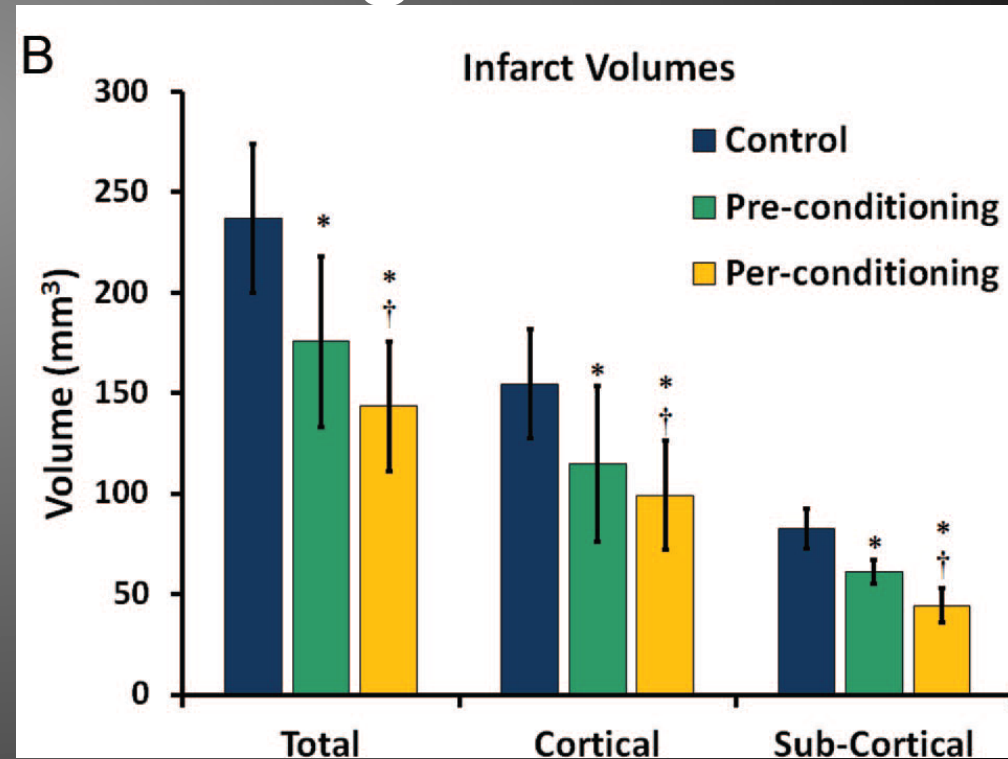
versus 0.10 ng/mL,  $P=0.010$ ). After remote IPC, cTnI was 0.04 ng/mL in 44 patients (42%) compared with 24 in the control group (24%;  $P=0.01$ ). Subjects who received remote IPC experienced less chest discomfort ( $P=0.0006$ ) and ECG ST-segment deviation ( $P=0.005$ ) than control subjects. At 6 months, the major adverse cardiac and cerebral event rate was lower in the remote IPC group (4 versus 13 events;  $P=0.018$ ).

**Conclusion**—Remote IPC reduces ischemic chest discomfort during PCI, attenuates procedure-related cTnI release, and appears to reduce subsequent cardiovascular events. (*Circulation*. 2009;119:820-827.)

# Neuroprotection:

## RIPC: Pre- and Per-Conditioning

- >> Diminished stroke
- >> Clinically feasible
- >> Per- is superior



*Hahn et al. Stroke 2011*



# *Remote ischemic conditioning Summary*

- Diminishes myocardial infarction (Pre-/Per-/Post-)
- Diminishes stroke (Pre-/Per-)
- Transferrable protection (Factor –X)
- Modifies post-op dysfunction and multi-organ injury
- Chronic RIPC can favorably modify post-infarct remodeling



# Attractive Features

- ▶ More RCT's in progress
- ▶ Grounded in thousands of lab studies
- ▶ "Grass roots' movement
  - No big pharma or device manufacturers driving research
  - Broad effort to translate to the bedside
  - No reported adverse events
  - Inexpensive



# Reading

Kharbanda RK *et al* Translation of remote ischaemic preconditioning into clinical practice ***Lancet 2009; 374: 1557–65***

Botker HE *et al* Remote Ischemic Conditioning as a complement to angioplasty, and effect on myocardial salvage in patients with acute myocardial infarction: a randomised trial ***Lancet 2010; 375: 727–34***