

# What is an Academic Research Organization and How to Get Organized to Conduct RCTs

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# Surrogate Endpoints: Core Laboratory Experience

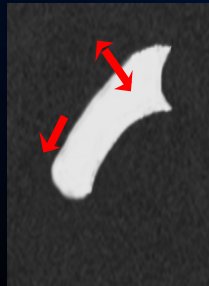
- **Angiographic Core Laboratory** for Phase 1 -4 angiographic trials for acute MI studies, unstable angina studies, interventional cardiology trials, peripheral interventional trials, venographic trials, angiogenesis trials (VEGF), imaging modality studies, managed care analyses for HCFA, and atherosclerosis regression trials such as the NIH-sponsored Harvard Atherosclerosis Reversibility Project (HARP). Developed methods used in many trials such as assessment of coronary blood flow
- **MRI Core Laboratory** for trials of reperfusion, amyloid, hypertrophic cardiomyopathy
- **CT, EKG, Holter** core lab services as well
- **Blood biomarkers**

# The TIMI Frame Count

*First Frame Definition*

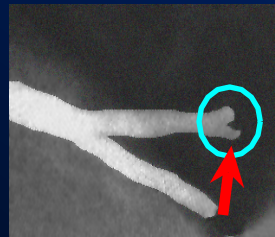


Frame 0: Dye Touches One or No Borders

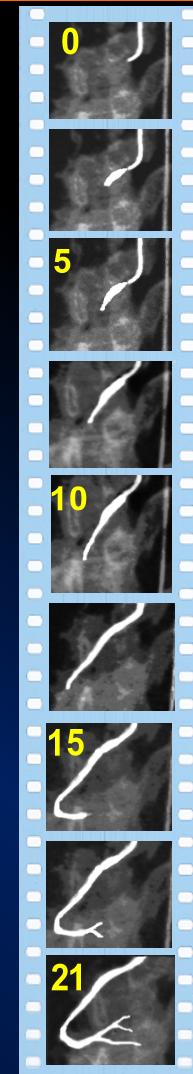
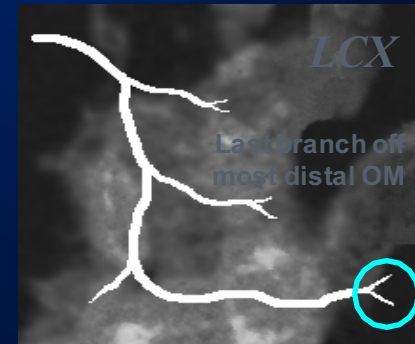
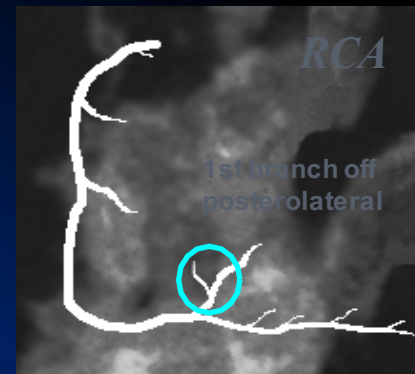


Frame 1: Dye Touches Both Borders & Moves Forward

*Last Frame Definition*



Frame 21: Dye first enters landmark



Normal Flow in the Absence of MI :  
21.0 ± 3.1 frames



# Frame Count was used to Determine the Weight-Adjusted Dosing Of TNK

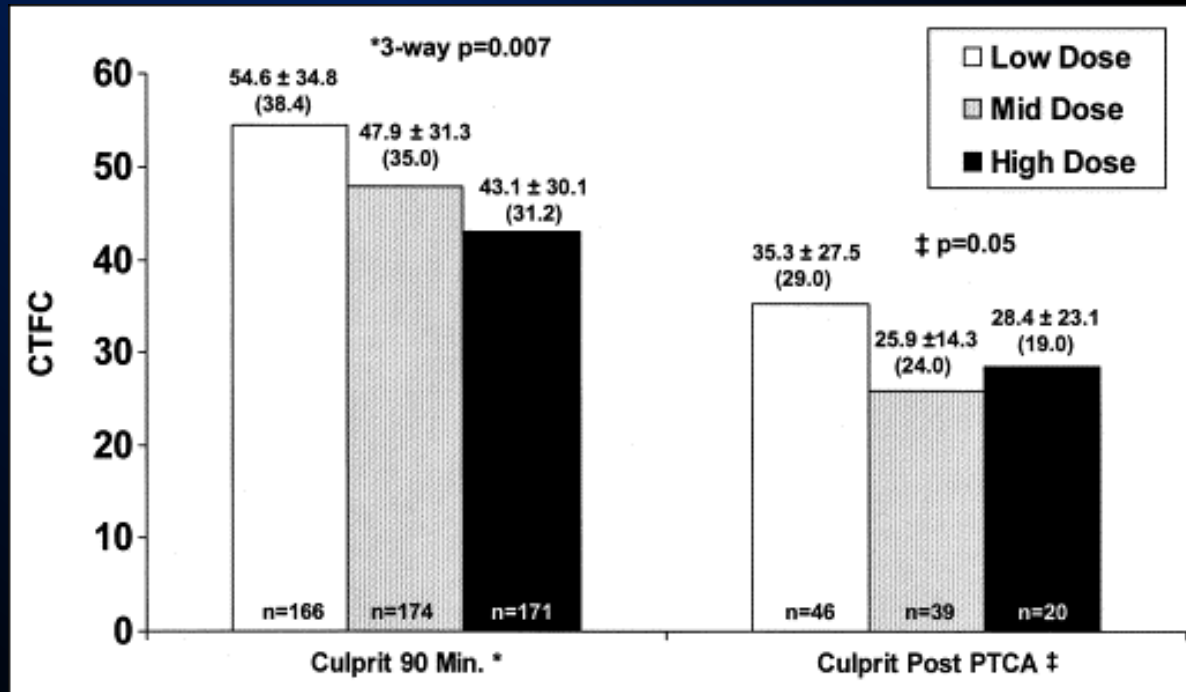


Figure 1. CTFCs divided into weight-adjusted tertiles (low, mid, and high doses) for culprit arteries at 90 minutes after thrombolytic administration and after PTCA. Faster flow (lower CTFCs) is seen in the culprit artery at 90 minutes after thrombolytic admin...

# Acute MI Slows Blood Flow Globally Throughout the Heart in ACS

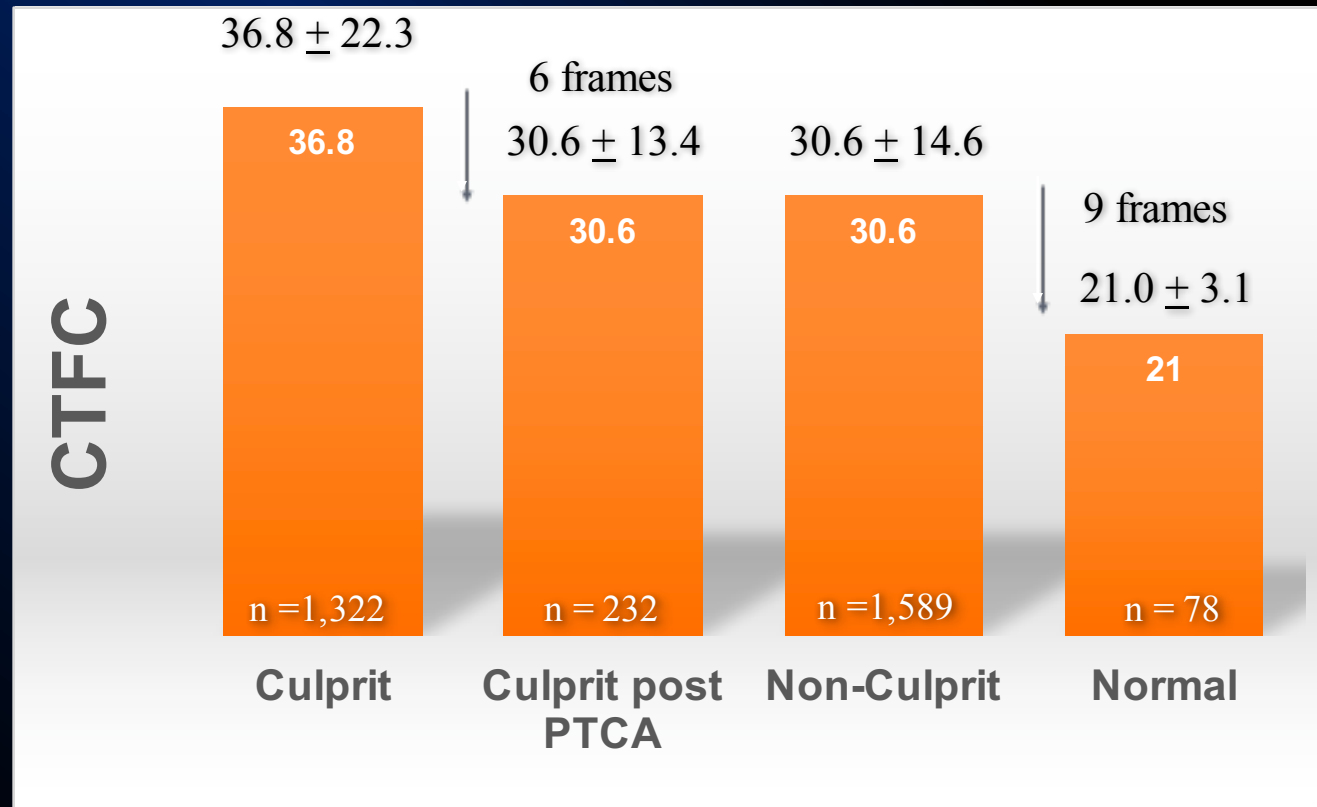


Reproducibility:

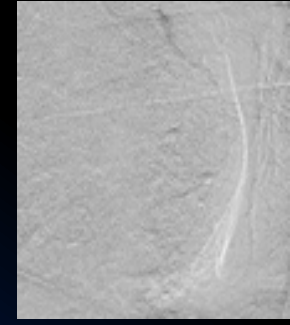
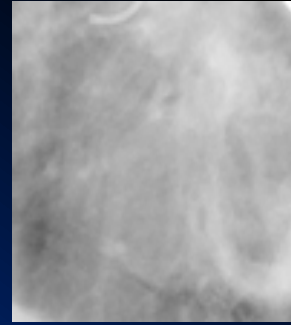
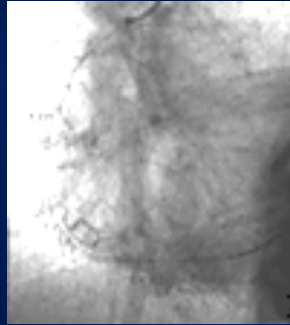
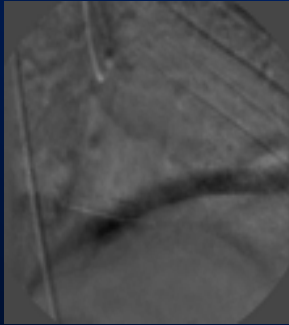
$r = 0.97$  between readers

Accuracy:

$r = 0.88$  vs Doppler velocity



# TIMI Myocardial Perfusion (TMP) Grades



## TMP Grade 3

Normal ground glass appearance of blush  
Dye mildly persistent at end of washout

**p = 0.05**

2.0%

n = 203

## TMP Grade 2

Dye strongly persistent at end of washout  
Gone by next injection

4.4%

n = 46

## TMP Grade 1

Stain present  
Blush persists on next injection

5.1%

n = 79

## TMP Grade 0

No or minimal blush

6.2%

n = 434

Mortality (%)



# The Goal is to Restore Both Normal Epicardial & Normal Myocardial Blood Flow

